THE MITOCHONDRIAL DNA HAPLOGROUP ANALYSES IN 30 THAI FAMILIES WITH G11778A LEBER HEREDITARY OPTIC NEUROPATHY (LHON)

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ABSTRACT

Leber hereditary optic neuropathy (LHON) is the most common mtDNA disorder that characteristically presents with subacute bilateral visual failure in young adult males. Many point mutations of the mitochondrial DNA (mtDNA) are considered to have a role in the pathogenesis of this disease. The G11778A mutation is found in most Thai LHON patients and is one of the most common mutations in LHON worldwide. Although mtDNA haplogroup J, determined by polymorphisms in mtDNA, has been shown to be associated in Caucasians with LHON, the most common haplogroup in normal Caucasians is haplogroup H. It has been suggested that polymorphisms in haplogroup J may be associated with the disease expression. This study aimed to analyse the association of the mitochondrial DNA haplogroup with the expression of G11778A mutation in Thai LHON families. Two groups of Thai individuals were selected: a control group of 100 healthy individuals and an experimental group of 30 LHON individuals. Both groups were analysed using 18 high-resolution RFLP and HVS-1 sequence in the control region. Approximately 24% of the whole mitochondrial sequences were screened using both methods. A total of 242 nucleotide polymorphisms were detected. Most of the haplogroup determined by the RFLP and 9-bp deletion information was similar to the haplogroup determined by HVS-1 sequence in the same individual (81% in the normal controls and 83.3% in the LHON individuals). Haplogroup M (60%), B (10%) and B* (13.3%) were found in these LHON individuals, whereas haplogroup A (1%), B (10%), B*(8%), C (1%), D (1%), F (15%) and M (45%) were found in the control group. The results indicated that none of the mitochondrial DNA haplogroups is specific in Thai LHON patients except for haplogroup F which tends to be associated with none disease expression. There is no clinical features difference between haplogroups among LHON patients except for the frequency of affected persons which was significantly different between haplogroups. Most affected persons were found in haplogroup B (80%) whereas 59.1% and 42.9% of haplogroup M and B*, respectively were unaffected.

KEY WORDS: LEBER HEREDITARY OPTIC NEUROPATHY / MITOCHONDRIA / MITOCHONDRIAL DNA HAPLOGROUP / MITOCHONDRIAL POLYMORPHISM / HETEROPLASMY

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การศึกษา HAPLOGROUP ของยีนไมโทคอนเดรียในผู้ป่วยโรค LEBER HEREDITARY OPTIC NEUROPATHY ชาวไทย 30 ครอบครัวที่มีการกลายพันธุ์ของยีนไมโทคอนเดรียที่ตำแหน่ง G11778A
(THE MITOCHONDRIAL DNA HAPLOGROUP ANALYSES IN 30 THAI FAMILIES WITH G11778A LEBER HEREDITARY OPTIC NEUROPATHY (LHON))

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บทคัดย่อ

Leber hereditary optic neuropathy (LHON) เป็นโรคที่ผู้ป่วยมีอาการตาบอดเนื่องจากประสาทตาฝ่อลีบอย่างเฉียบพลัน และมักจะเกิดในผู้ชาย อายุในวัยก่อน 20 ปี โรค LHON นี้เกิดจากการกลายพันธุ์ของยีนไมโทคอนเดรีย โดยในผู้ป่วยชาวไทยพบการกลายพันธุ์ที่ตำแหน่ง G11778A มากที่สุด เมื่อทำการศึกษาดูแบบแผนของยีนไมโทคอนเดรีย (mitochondrial DNA haplogroup) ซึ่งพิจารณาจาก polymorphism ที่เกิดขึ้นบนตำแหน่งต่างๆ ในยีนไมโทคอนเดรียของประชากรในทวีปต่างๆของโลก พบว่าในแต่ละทวีปมีแบบแผนของยีนไมโทคอนเดรียที่แตกต่างกัน เมื่อนำผู้ป่วย LHON ชาวยุโรปมาศึกษาแบบแผนของยีนไมโทคอนเดรีย พบว่าผู้ป่วยมีแบบแผน J มากที่สุด ในขณะที่ประชากรปรกติมีแบบแผน H มากที่สุด ทำให้คาดว่า polymorphism ในแบบแผน J มีผลต่อการแสดงออกของโรค และเพื่อให้ทราบถึง polymorphisms ในยีนไมโทคอนเดรียที่มีผลต่อการแสดงออกของโรค LHON ในไทย การศึกษานี้ได้ทำการเพิ่มจำนวนยีนไมโทคอนเดรียให้ครอบคลุมทั้งยีนและทำการตรวจสอบ polymorphism และหาแบบแผนของยีนไมโทคอนเดรีย ด้วยวิธี Restriction Fragment Length Polymorphism (RFLP) และลำดับเบสใน hypervariable segment 1 (HVS-1) ในผู้ป่วยโรค LHON ชาวไทยจำนวน 30 ครอบครัว (30 คน) เทียบกับคนปรกติ 100 คน จากการตรวจสอบทั้งสองวิธีนี้ยีนไมโทคอนเดรียได้ถูกตรวจสอบ ประมาณ 24 % ของจำนวนยีนทั้งหมด และพบความแตกต่างของยีนจำนวน 242 ตำแหน่ง โดยแบบแผนที่ได้จากการพิจารณาโดย RFLP และลำดับเบสใน HVS-1 ค่อนข้างเหมือนกันในคนปรกติ (81%) และในผู้ป่วย (83.3%) และพบว่าแบบแผนของยีนไมโทคอนเดรียในผู้ป่วยชาวไทย มี 3 แบบคือ M (60%), B (10%) และ B* (13.3%) ในขณะที่แบบแผนในคนปรกติมี 7 แบบ คือ A (1%), B (10%), B*(8%), C (1%), D (1%), F (15%) และ M (45%) และไม่มีแบบแผนของยีนไมโทคอนเดรียใดที่มีความสัมพันธ์ทางสถิติอย่างมีนัยสำคัญกับผู้ป่วย LHON ชาวไทยกลุ่มนี้ ยกเว้นแบบแผน F ซึ่งมีแนวโน้มที่จะมีความสัมพันธ์ทางสถิติกับการไม่เกิดโรค จากการวิจัยครั้งนี้สรุปได้ว่าในผู้ป่วย LHON ชาวไทยกลุ่มนี้ไม่มีความเฉพาะเจาะจงกับแบบแผนของยีนไมโทคอนเดรียแบบใดแบบหนึ่ง แต่มีความเฉพาะเจาะจงกับการไม่เกิดโรคในแบบแผน F นอกจากนี้ผู้ป่วยในแต่ละแบบแผนไม่มีความแตกต่างทางคลินิกอื่น ยกเว้นความถี่ของคนเป็นโรคที่แตกต่างระหว่างแบบแผนของยีนไมโทคอนเดรีย โดยสมาชิกส่วนใหญ่ในแบบแผน B (80%) มีการแสดงออกของโรค ขณะที่ 59.1% และ 42.9% ของสมาชิกในแบบแผน M และ B* ตามลำดับ เป็นสมาชิกในครอบครัวที่ไม่เป็นโรค

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LIST OF ABBREVIATIONS

bp	Base pair
°C	Degree celcius
dATP	Deoxyadenosine triphosphate
dCTP	Deoxycytosine triphosphate
dGTP	Deoxyguanosine triphosphate
dTTP	Deoxythymidine triphosphate
dNTP	Deoxynucleotide triphosphate
D-loop	Displacement loop
DNA	Deoxyribonucleic acid
et al.	*et alii* (and other people)
EDTA	Ethylenediaminetetraacetic acid
FC	Finger count
g	Gram(s)
HM	Hand motion
i.e.	*id est* (that is)
e.g.	*exempli gratia* (for example)
KCl	Potassiumchloride
LHON	Leber Hereditary Optic Neuropathy
LE	Left eye
mg	Milligram(s)
ml	Milliliter(s)
mtDNA	Mitochondrial Deoxyribonucleic acid
mM	Millimolar
$MgCl_2$	Magnesium chloride
nDNA	Nuclear Deoxyribonucleic acid
µg	Microgram(s)
µl	Microliter(s)

LIST OF ABBREVIATIONS (continued)

ng	Nanogram
nm	Nanometer
np	Nucleotide position
NaCl	Sodium chloride
No	Number
pmol	Picomole
PCR	Polymerase chain reaction
rRNA	Ribosomal ribonucleic Acid
RCLB	Red cell lysis buffer
RE	Right eye
tRNA	Transfer ribonucleic Acid
Taq	*Thermus aquaticus*
Tris HCl	Tris-hydrochloride
TAE	Tris-acetate EDTA
TBE	Tris-boric acid EDTA
UV	Ultraviolet
V	Volt
VA	Visual acuity

CHAPTER I
INTRODUCTION

Leber hereditary optic neuropathy (LHON) is the disease that affects the central nervous system, including the optic nerves, causing bilateral loss of vision (1-3). The onset of visual loss typically occurs between the age of 15-35 years in most pedigree (4, 5). Men are more frequently affected with visual loss than women, comprising 80-90% of case series (5, 6). LHON is caused by point mutation in the mitochondrial genome that is associated with the respiratory chain complexes (5, 7). Point mutations in the mitochondrial genome involving various subunits of Complex I of the respiratory chain are necessary for the bilateral loss of central vision seen in LHON (8). The base changes are commonly classified as primary or secondary LHON mutation. Primary mutations are sufficient by themselves to cause the disease, are not detected in controls, usually change evolutionarily conserved amino acids, and are found in multiple LHON families(6, 9). The secondary mutation may influence LHON expression when associated with primary or other secondary mutations (10).

The common primary LHON mutations are at nucleotide positions 3460 (*ND1* gene; Complex I), 11778 (*ND4* gene; Complex I), and 14484 (*ND6* gene; Complex I) (3, 5). The common secondary mutations are nucleotide positions 4216 (*ND1* gene; Complex I), 4917 (*ND2*; Complex I), and 13708 (*ND5*; Complex I) (6, 9). The three common primary mutations in LHON are found in about 90% of total LHON cases worldwide and about 50% of European patients (2, 11). Sixty nine percent of northern Europeans with LHON carried the 11778 mutation while the frequencies of G11778A mutation in Japanese, Taiwan-Chinese, and Thai are 88%, 98% and 97%, respectively (7, 9, 14).

Mitochondria genome is a circular double-stranded DNA molecule. The human mitochondrial DNA contains 37 genes (16,569 base pairs), including 13 genes that encode subunits of proteins of the respiratory chain that are seven subunits of the NADH dehydrogenase (*ND1* to *ND6*) in Complex I, the cytochrome *b* of Complex III

(*Cyt b*), three subunits of cytochrome oxidase in Complex IV (*COI* to *COIII*), and two subunits of ATP synthase (*ATPase6*, *ATPase8*). The remaining genes code for 2 rRNAs and 22 tRNAs that are essential to the protein-synthesizing machinery of mitochondria. Many mitochondrial proteins are encoded by nuclear genes then imported posttranslationally and assemble within mitochondria.

Point mutations in the mitochondrial genome are necessary for the bilateral loss of central vision seen in LHON, but other factors play a role in disease expression and penetrance. Factors proposed to influence the risk of vision loss in mutation harboring pedigrees are both of genetic, mitochondrial or nuclear genetic background, such as, secondary mitochondrial mutations, heteroplasmy, and an X-linked factor, and environmental factor, such as, tobacco and alcohol consumption (3, 15, 16).

The study of mtDNA sequence variation from around the world has led to define population-specific mtDNA lineage haplogroups. The mtDNA haplotype grouping is defined by one or more variants in mitochondrial genome. The high frequency of these specific mutations within one major group and their specificity to either Europeans, Asians, or Native Americans make them powerful genetic markers for inferring the ethnic and geographic origin of modern and ancient humans (1). The African mtDNA formed one major mtDNA cluster that is haplogroup L (18). The haplogroups in Native Americans are A, B, C, D, and X (19-21). The nine European mtDNA haplogroups observed in European are H, T, U, V, W, X, I, J, and K (23-25). The most common haplogroups in Southeast Asia are M, A, B, and F (26-27).

The distribution patterns among the mtDNA haplotypes of the LHON disease groups differed considerably from the control population (18). The analyses of Caucasian LHON pedigrees from North America and Europe demonstrated that the G11778A and T14484C mutations tend to be associated with the European-specific haplogroup J (10, 28-30). This finding has been interpreted as to indicate that some of the mtDNA polymorphic variants that characterize haplogroup J are positive modifiers of the expression of these two primary LHON mutations, and thus presumably increase their penetrance.

This thesis is, therefore, aimed to examine the mitochondrial DNA haplogroups of our 30 Thai distinct LHON families compare to the normal population. All of LHON individuals have a G11778A mutation. The mtDNA haplogroup of the LHON

individuals and normal population in Thailand will be analysed in order to look for the mtDNA polymorphisms associated with the expression of LHON in Thai population.

Objective

To analyses the association of the mitochondrial DNA haplogroup and the expression of G11778A mutation in 30 Thai Leber hereditary optic neuropathy (LHON) families.

CHAPTER II
LITERATURE REVIEW

1. Leber Hereditary Optic Neuropathy

Leber hereditary optic neuropathy (LHON) is the most common mtDNA disorder that characteristically presents with subacute bilateral visual failure in young adult males (31). The clinical features of LHON, the first disease in which a pathogenic mtDNA point mutation was found, include subacute, painless bilateral visual loss with central scotomas and abnormal colour vision due to optic atrophy (1-3). The age of onset is usually between 15 and 35 years, but an individual can become affected at any age between early childhood and over 60 years (4, 5). Most of the affected are men; the male preponderance is about 80% (5, 6). The underlying causes of this disease are the combination of environmental and genetic factors (3, 15, 16, 32) as shown in Figure 1.

1.1 The mitochondrial point mutation associated with LHON

Thus far 20 mtDNA mutations have been associated with LHON (see Appendix A). They all are missense mutations, and most of them are located in Complex I genes of the respiratory chain complex.

Mitochondrial DNA mutations associated with LHON can be classified into primary and secondary mutations. Primary mutations are sufficient by themselves to cause the disease, are not detected in controls, usually change evolutionarily conserved amino acids, and are found in multiple LHON families (6, 9). The 11778 primary LHON mutation changes a highly conserved arginine residue to histidine at amino acid position 340 (designated ND4/R340H) of the ND4 subunit of complex I (NADH-ubiquinone oxidoreductase). There is now broad agreement that sequence changes at nucleotides 3460 (ND1/A52T) and 14484 (ND6/M64V) are also primary LHON mutations and that these three mutations account for the vast majority of LHON cases (7, 9, 15). The 11778 mutation is responsible for 31-89% of LHON pedigrees in

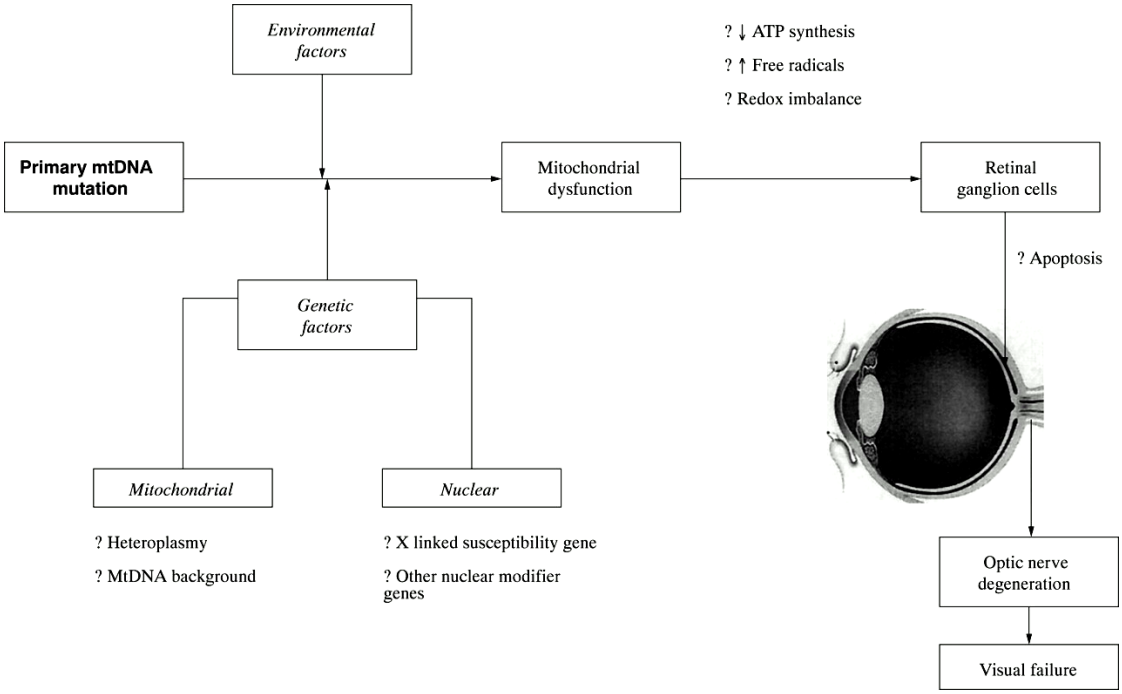


Figure 1. The pathways leading to optic nerve degeneration in LHON (32). The combination of genetic and environmental factors were the cause of the mitochondrial dysfunction which was leading to the visual failure in the LHON patients.

Europe, North America, and Australia, 88% of LHON pedigrees in Japan and 97% of Thai LHON pedigrees (14, 15). The 3460 and 14484 mutations each account for approximately 10-15% of cases (5, 15). In addition, a few other base substitutions such as ATPase6/9101, COXIII/9804, ND6/14459, ND4/11696 and ND/14596 have also been suggested to be primary mutations in LHON (10).

Several mtDNA mutations are considered to have a secondary role of so-called secondary mtDNA mutation in the pathogenesis of LHON: i.e., T4216C, A4917G, G9804A, G9438A, G13708A, G15257A, and G15812A. These nucleotide substitutions are found at a higher frequency in LHON patients relative to controls and some investigators argue that they act synergistically either with a primary mutation or with the other secondary mutations (9, 33, 34), increasing the risk of disease expression.

1.2 The other factors associated with LHON

The optic neuropathy in LHON families shows incomplete penetrance. About 50% of male and 10% of female who harbor one of the three primary mutations actually develop the optic neuropathy (33, 35). The male:female ratio of the individuals who develop the symptoms was vary from mutation to mutation. The male:female ratio in the primary G11778A mutation was about 3.7:1 (35) whereas the male:female ratio in the T14484C and G3460A mutation were about 7.7:1 and 4.3:1, respectively (37, 38). This incomplete penetrance indicated that additional genetic and environmental factors interact with the primary mtDNA defect and determine whether an individual harboring the LHON mtDNA mutation develops the disease (1, 32). The genetic factors proposed to influence disease penetrance include the nuclear factors and the mitochondrial genetic factors. The nuclear factors, including the X chromosome was suggested to play role in the disease expression both the incomplete penetrance and gender bias (1, 6). For mitochondrial factors, the heteroplasmy and the secondary mutations were reported to be associated with the expression of the LHON. Heteroplasmy is a term used to describe the coexistance of mutant and normal mtDNA within the same cell. In most LHON pedigrees, the primary mutation is homoplasmic (every mtDNA molecule harbors the mutant allele). By contrast, 10-15% of LHON carriers are thought to be heteroplasmic (32, 39). The degree of heteroplasmy may

differ among tissues and also vary between the individuals (40). It has been suggested that heteroplasmy might influence the expression and inheritance pattern of LHON (41, 42). The other mitochondrial genetic factor is the mitochondrial DNA background since the mitochondrial haplogroup J was the most common in the Caucasian LHON patients (see detail in 2.3.2 below). The predominance of men may reflect interaction with an X-linked nuclear genetic factor (6), which has not yet been clarified (6, 32). That LHON patients must exceed a tissue-specific energy utilization threshold to manifest disease has led some to conclusion that malnutrition and environmental toxins may play a role in the development of vision loss in susceptive patients (1). In clinical series, the prevalence of alcohol consumption ranges from 14% to 67% and for tobacco consumption from 46% to 75% (15). A series of patients diagnosed with tobacco-alcohol ambly-opia was subsequently determined to have LHON by molecular genetic testing. It suggested that heavy alcohol and/or tobacco use also increases the risk of the optic neuropathy in LHON family members (3, 6, 7).

2. Mitochondria

The mitochondrion is an essential cytoplasmic organelle that provides most of the energy necessary for a cell. Mitochondria are bounded by two membranes, outer and inner membrane. The inner membrane is conspicuously folded, forming tubular or lamellar structures called cristae. The energy-generating apparatus is composed of five multipolypeptide enzyme complexes and is located in the inner membrane, which surrounds the matrix space of the mitochondrion.

2.1 Mitochondrial Function

The mitochondrion converts energy derived from chemical fuels by an oxidative phosphorylation process. In mitochondrion, the metabolism of one molecule of glucose produces about 30 molecules of ATP (adenosine triphosphate), while only two molecules of ATP are produced by glycolysis alone. This means that organs with a high energy demand are vulnerable to the depletion of mitochondrial energy production. The oxidative phosphorylation pathway (OXPHOS), i.e., ATP synthesis by the oxygen-consuming respiratory chain (RC), is composed of ETC (Electron transport chain) and ATPase and the whole OXPHOS system embedded in the lipid

bilayer of the mitochondrial inner membrane. It is composed of five multiprotein enzyme complexes (I-V) and two electron carriers, coenzyme Q and cytochrome *c* (Figure 2). The main function of the system is the coordinated transport of electrons and protons and the production of ATP. Complex I (NADH:ubiquinone reductase), the first site of the respiratory chain, transfers electrons from nicotinamide adenine dinucleotide (NADH) to CoQ (coenzyme Q), thereby generating ubiquinone. This complex consists of 43 polypeptides, seven of which are encoded by mtDNA; it is the most represented respiratory enzyme in the mtDNA. Ubiquinol is also produced by Complex II (succinate:ubiquinone reductase), which, in a pathway parallel to that of complex I, transfers electrons from flavin adenine dinucleotide ($FADH_2$) to CoQ. Thus, complex III also receives electrons from this parallel path, which bypasses complex I. Complex II is the only RC complex that does not contain any mtDNA-encoded protein because this complex is the respiratory enzyme completely encoded by nuclear DNA (four subunits). Complex III (ubiquinol;cytochrome *c* reductase) carries two electrons from $CoQH_2$ to cytochrome *c*, which in turn shuttles the electrons to complex IV. Complex III contains 11 subunits, one of which (cytochrome *b*) is encoded by mtDNA. Complex IV (cytochrome *c* oxidase, COX) is the terminal component of the respiratory chain which transfers electron from cytochrome *c* to oxygen, producing water. It contains 13 subunits, three of which are encoded by mtDNA.

All the respiratory complexes containing mtDNA-encoded subunits (complex I, III, and IV) couple the electron transfer with the proton translocation across the inner mitochondrial membrane from the matrix side to the intermembrane space. The resulting electrochemical gradient drives the reverse flow of protons back to the matrix through the membrane portion of complex V (ATP synthase, F_1F_0-ATPase), which then catalyzes the ATP synthesis, phosphorylating ADP to ATP. Three ATP molecules are made for each NADH oxidized. Complex V has two subunits encoded by mtDNA (ATPase6 and ATPase8) and about 13 other subunits encoded by nDNA.

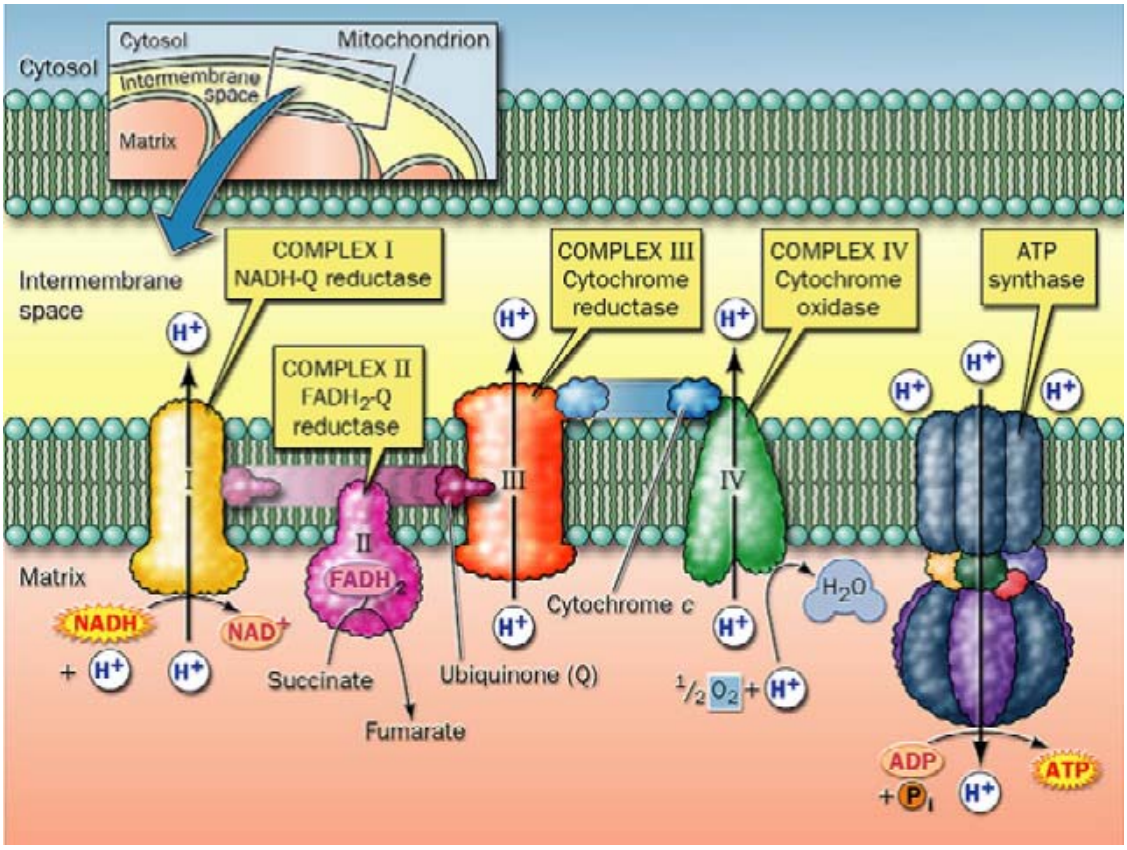


Figure 2. The OXPHOS system in the inner membrane of mammalian mitochondria (43). Electrons (e^-) are transferred via NADH into OXPHOS complex I (I) and transported to coenzyme Q (Q). Some electrons from organic acid oxidation are transferred via various nuclear-encoded electron transfer flavoproteins, such as complex II (II), directly to CoQ. There they are transferred via complex III (III) and cytochrome *c* (cyt *c*) to complex IV (IV), where the oxygen is reduced to water. The movements of H^+ from the matrix to the intermembrane space are coupled with energy release from the electrons. The protons create a proton gradient which is used for the production of ATP by complex V (ATP synthetase).

2.2 Mitochondrial genome

The human mitochondria have their own genome that is circular and 16,569-bps in length (Figure 3). MtDNA has two strands; a guanine-rich heavy (H) strand and a cytosine-rich light (L) strand, and encodes 13 proteins, 22 transfer RNAs (tRNA) and 2 ribosomal RNAs (rRNA). The proteins encoded by mtDNA are subunits of OXPHOS complexes. MtDNA has genes coding for seven subunits of complex I (ND1, 2, 3, 4, 4L, 5 and 6), one subunit of complex III (cytochrome *b*), three subunits of complex IV (COX I, II and III) and two subunits of complex V. The majority of the proteins in the OXPHOS complexes are nuclear-encoded and imported from the cytosol. There are at least 70 OXPHOS polypeptides encoded by the nuclear genome, compared with the 13 polypeptides encoded by mtDNA.

MtDNA replication is not dependent on the phase of cell division, and no recombination has been shown. MtDNA is maternally inherited and has a high mutation rate causing a number of polymorphisms which accumulate along radiating maternal lineages. The mtDNA also exists in the cell in multiple copies.

Moreover, the control region of mtDNA, the displacement loop (D-loop), is the only segment which does not encode genes, and otherwise there are no non-coding segments between the genes. There is a 1121 bp non-coding region, the D-loop, spanning nts 16024-575, as it contains elements for the initiation of leading strand replication, origins for the transcription of both mtDNA strands and regulatory regions for replication and transcription. This region has a three-to-four-fold greater sequence diversity than the coding region of mitochondrial genome. In addition, the control region has the two hypervariable regions, Hypervariable segment 1 (HVS-1, nts 16024-16383) and Hypervariable segment 2 (HVS-2, nts 57-372), that have the high number of nucleotide polymorphisms or sequence variants which are useful for the forensic examinations and anthropology.

The translation of mitochondria occurs inside mitochondria and is separated from cytoplasmic translation. The ribosomal RNAs (rRNAs) and transfer RNAs (tRNAs) needed for translation are encoded by the mitochondrial genome. Mitochondria have a unique genetic code in several aspects. In human mitochondria, AUA codes for methionine instead of isoleucine, UGA codes for trypthophan instead

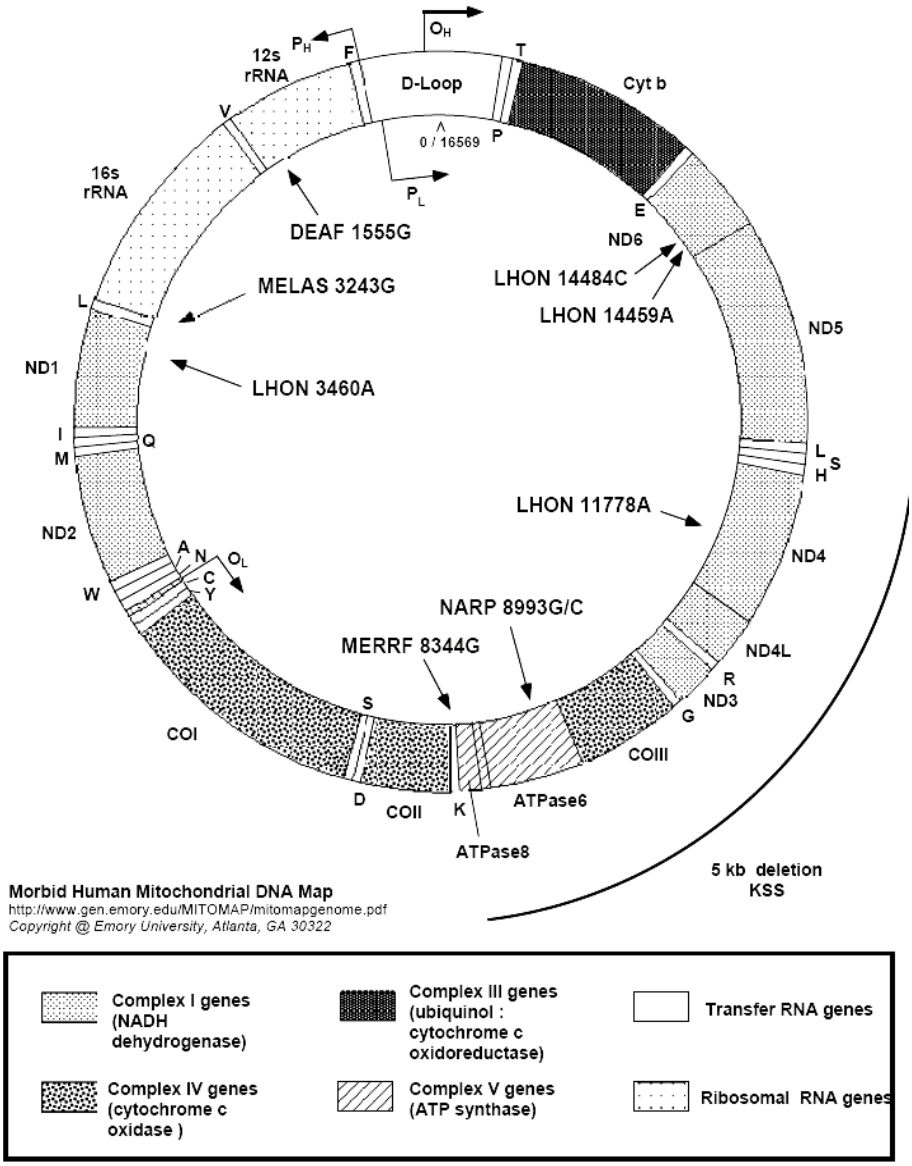


Figure 3. The human mitochondrial genome, encompassing 16,569 bps with the numbering starting at O_H and proceeding counterclockwise around the circle (44). The mtDNA encodes 13 subunits for OXPHOS complexes: seven for complex I (ND1-6, ND4L), one for complex III (Cyt *b*), three for complex IV (COX I-III) and two for complex V (ATPase6, ATP6 and ATPase8, ATP8). In addition, the mtDNA encodes two rRNAs (12S and 16S) and 22 tRNAs, abbreviated to indicate the corresponding amino acid tRNA genes. The mtDNA is replicated from two origins, O_H is of H-chain origin and O_L of L-chain origin. P_H and P_L indicate the promoters of transcription.

of being a stop codon, and AGA and AGG are stop codons instead of coding for arginine.

2.3 Mitochondrial DNA sequence variation

The first complete sequence of human mtDNA, the Cambridge reference sequence (CRS), was published in 1981 (45) and has recently been revised (the revised CRS is here in termed the "rCRS") (46). Variations in the mtDNA sequence have been analyzed in human populations, both in terms of evolution and population dispersals and in terms of the role in human disease (25, 28).

Because the mtDNA is strictly maternally inherited, the mtDNA sequence has evolved by the sequential accumulation of base substitutions along radiation maternal lineages. Thus, as women migrated out of Africa into the different continents about 150000 YBP (Years before the present), they accumulated mtDNA mutations that today are seen as high frequency, continent-specific mtDNA sequence polymorphisms. These polymorphisms are associated with specific mtDNA haplotypes, and groups of related haplotypes (haplogroups) (28). However, the generation of comprehensive and unambiguous phylogenetic data, especially for the mtDNA coding regions, is limited by the availability of a relatively small number of polymorphisms that have been identified on the basis of the presence or absence of restriction enzyme recognition sites (47). Alternatively, sequences from the first hypervariable segment of the rapidly evolving noncoding control region, or D-loop, have been used to establish phylogenetic networks of European mtDNA sequences, and a combination of both methods was recently used for a comparative analysis (48, 49). Reliance on hypervariable control-region sequences, however, is not without controversy, particularly because of the effects that homoplasmy and saturation have at sites with high mutation rates (23). In the initial analysis of these mtDNA sequences, the haplogroup-specific and haplogroup-associated polymorphisms were focus on because of their fundamental importance in studies of human evolution, phylogeography, and population genetics (22, 48). An mtDNA haplogroup is a particular group of mitochondrial genomes defined by a unique set of variants acquired from the same ancient common female ancestor. Haplogroups are coded with capital letters and subclusters with a running number. The classification of mtDNA haplogroups is based on information gained from RFLP analysis of the coding

region and from the nucleotide (nt) sequences of the hypervariable segments (HVS) in the control region (25, 26, 48). Analysis of human mtDNA variation has identified specific combinations of polymorphisms that have been used to systematically classify mtDNAs into haplogroups, and to study origin, dispersal and evolution of human populations (50).

A more detailed analysis of mtDNA variation has been necessary for clinical studies and for addressing additional anthropological question on the age and origin of Africans, Europeans, Asians, and Native Americans. MtDNA has been used for a couple of decades as a molecular marker in population genetics (28). To increase the sensitivity of the analyses, the high-resolution RFLP analysis was developed in which the mtDNAs from a variety of human samples could be amplified by using PCR in 9 overlapping fragments. Each fragment was then digested with 14 restriction endonucleases enabled a much more detailed mtDNA phylogeny to be obtained (25, 29). This procedure screen 15-20 % of the mtDNA sequence for variation, and the aggregate of the restriction-site polymorphisms for each mtDNA is used to define the mtDNA haplotypes (18). A further improvement in resolution was obtained when information on the control region sequence was included with the RFLP data (49). The best resolution that can be obtained is gained by analysing complete mtDNA sequences which have just begun to emerge (51). These phylogentic trees reveal the relateness of the mtDNAs, with the more similar mtDNAs clustering together.

MtDNA haplogroups determined by polymorphisms that occurred tens of thousands of years ago are today high-prevalence population-specific substitutions. Haplotypes are subclusters of haplogroups, and the polymorphisms that determine them are less prevalent and have occurred more recently. Most of the polymorphisms determining haplogroups are continent-specific (52).

Moreover, several homopolymeric tracts in the mtDNA exhibit length polymorphisms, i.e., the presence in cells of multiple mtDNA species with various lengths of the homonucleotide run. The D-loop region contains homopolymeric tracts that exhibit length polymorphisms. One of the homopolymeric tracts, which is associated with a mtDNA T16189C variant located within and interrupting a homopolymeric tract of cytosines between nt 16184 and nt 16193 of the first hypervariable segment of the human mtDNA control region (53-56). The 16189C

mutation occurs in some individuals resulting in an unstable homopolymeric tract of cytosines, and length variation of the poly[C] is observed in a heteroplasmic manner. Tracts are predominantly 10, 11, or 12 nt long, but cloning has revealed the length variation of between 8 and 14 cytosines found in one individual (53, 55). The frequency of these variations is about 15% of Europeans (53). Of interest is the observation that the relative proportion of various lengths polycytosines (i.e., the pattern of the length heteroplasmy) associated with the 16189C variant is maintained in an individual. This variant has also been suggested to be associated with several common human diseases such as diabetes mellitus, low birth weight, and dilated cardiomyopathy, and thus is also of medical significance (55, 57). Furthermore, the other length heteroplasmy in an interrupted homopolymeric cytosine tract found in the control region that is between nt 303 and nt 315 (56).

2.3.1 Mitochondrial DNA haplogroups on different continents

The evolution of human mtDNA is characterized by the emergence of ethnically distinct lineages. Most of the polymorphisms determining haplogroups are continent-specific (28, 58) (see detail in Table 1). The mitochondrial haplogroups found in each continent area were showed in Figure 4.

African-specific haplogroup designated ‘L’ which is defined by the African-specific *Hpa*I site at np 3592 together with the *Dde*I site at np 10394 (18, 28, 44, 47). About 76% of all African mtDNAs fall into haplogroup L (28, 44). Haplogroup L has the highest sequence diversity of any continent-specific haplogroup and that Africa encompasses the greatest diversity of any continent (19, 58).

For European, nine distinct European mtDNA haplogroups; H, T, U, V, W, X, I, J, and K, have also been observed (22, 24, 25, 28, 44, 47, 49). Those lacking the *Dde*I site at np 10394 are haplogroups H, T, U, V, W, and X; those retaining the *Dde*I site at np 10394 are I, J, and K. Haplogroup H lacks an *Alu*I site at np 7025 (C to T at np 7028). This haplogroup encompasses 40.5% of European mtDNAs (24, 28, 44). Haplogroup T is defined by the presence of a *Bam*HI site at np 13366 and an *Alu*I site at np 15606 and accounts for 15.2% of European mtDNAs (25, 28). Haplogroup U is defined by the presence of a *Hin*fI site at np 12308 and accounts for 14.7% of European mtDNAs (25, 28). Haplogroup V is delineated by the loss of an *Nla*III site at np 4577 and is found in 4.8% of Europeans (28, 59), whereas haplogroup W is

Table 1. Shown are the continent-specific haplogroups and their criteria in both of RFLP and HVS-1 sequence and the percentage of their populations.

Haplogroup	Polymorphic restriction sites	HVS-1 nucleotide variants	% in population
Africa (18, 28, 44, 47)			
L	+3592*Hpa*I, +10394*Dde*I		70% of Africans
L1	+3592*Hpa*I, +10806*Hin*fI, +10394*Dde*I		52% of haplogroup L samples
L2	+3592*Hpa*I, +16389*Hin*fI, -16390*Ava*II, +10394*Dde*I		48% of haplogroup L samples
L3	-3592*Hpa*I, -10394*Dde*I		A few percent of Africans
Europe (22, 24, 25, 28, 44, 47, 49, 59)			
H	-7025*Alu*I, -14766*Mse*I, -10394*Dde*I		40.5% of Caucasians
T	+13366*Bam*HI, +15606*Alu*I, -10394*Dde*I		15.2% of Caucasians
U	+12308*Hin*fI, -10394*Dde*I		14.7% of Caucasians
V	-4577*Nla*III, -10394*Dde*I		4.8% of Caucasians
W	+8249*Ava*II, -8250*Hae*III, -8994*Hae*III, -10394*Dde*I		2.3% of Finns and Swedes
X	+14465*Ava*II, -10394*Dde*I, -1715*Dde*I	T16189C, C16223T, C16278T	6.9% of Caucasians
I	-1715*Dde*I, -4529*Hae*II, +8249*Ava*II, -8250*Hae*III, +10028*Alu*I, +10394*Dde*I, +16389*Bam*HI, -16390*Ava*II		6.7% of Caucasians
J	-13708*Bst*NI, +10394*Dde*I, -16065*Hin*fI		11.3% of Caucasians
K	+12308*Hin*fI, -9052*Hae*II, -9053*Hha*I, +10394*Dde*I		9.1% of Caucasians

Table 1 (continued). Shown are the continent-specific haplogroups and their criteria in both of RFLP and HVS-1 sequence and the percentage of their populations.

Haplogroup	Polymorphic restriction sites	HVS-1 nucleotide variants	% in population
Native America (19, 23, 27, 28)			
A		T16362C, G16319A, C16290T, C16223T	44% of Native Americans
A1	+663*Hae*III, -10394*Dde*I, -10397*Alu*I		
A9	+663*Hae*III, +16517*Hae*III, -10394*Dde*I, -10397*Alu*I		
B	9-bp deletion, +16517*Hae*III, -10394*Dde*I, -10397*Alu*I	T16189C, T16217C, T16519C	22% of Native Americans
C	-13259*Hin*cII, +13262*Alu*I, +10394*Dde*I, +10397*Alu*I	C16327T, T16298C, C16223T	18% of Native Americans
D	-5176*Alu*I, +10394*Dde*I, +10397*Alu*I	T16362C, C16223T	16% of Native Americans
Asia (25-28, 44, 60, 61, 63)			
M	+10394*Dde*I, +10397*Alu*I	C16223T	57% of Asians
C	-13259*Hin*cII, +13262*Alu*I, +10394*Dde*I, +10397*Alu*I	C16327T, T16298C, C16223T	21% of Asians
D	-5176*Alu*I, +10394*Dde*I, +10397*Alu*I	T16362C, C16223T	14% of Asians
E	-7598*Hha*I, +16389*Hin*fI, -16390*Ava*II, +10394*Dde*I, +10397*Alu*I		23% of Koreans
G	+4830*Hae*II, +483*Hha*I, +10394*Dde*I, +10397*Alu*I		28.1% of Sabah Aborigins, 21.4% of Malay, 7.7% of Koreans
Z	+10394*Dde*I, +10397*Alu*I, +11074*Dde*I, +16517*Hae*III		5.8% of Koryaks, 6.4% of Itel'men

Table 1 (continued). Shown are the continent-specific haplogroups and their criteria in both of RFLP and HVS-1 sequence and the percentage of their populations.

Haplogroup	Polymorphic restriction sites	HVS-1 nucleotide variants	% in population
Asia (25-28, 44, 60, 61, 63)			
A		T16362C, G16319A, C16290T, C16223T	12% of Asians
A1	+663*Hae*III, -10394*Dde*I, -10397*Alu*I		
A9	+663*Hae*III, +16517*Hae*III, -10394*Dde*I, -10397*Alu*I		
B	9-bp deletion, +16517*Hae*III, -10394*Dde*I, -10397*Alu*I	T16189C, T16217C, T16519C	4% of Asians
B*	9-bp deletion, +16517*Hae*III, +10394*Dde* I, -3534*Dde*I , -3537*Alu*I, -15234*Hin*fI, +15235*Mbo*I	T16140C, T16189C, T16519C	7.7% of Koreans, 3.1% of Sabah Aborigins, 7.1% of Vietnameses
F	-12406*Hin*cII, -12406*Hpa*I, -10394*Dde*I, -10397*Alu*I	T16304C	4% of Asians, 32% of Vietnameses, 14.3% of Malays, 15.4% of Koreans
Y	+10394*Dde*I, -10397*Alu*I, +7933*Mbo*I, -8391*Hae*III, +16517*Hae*III		64.9% of Nivkh, 9.7% of Koryaks, 4.3% of Itel'men
Papua New Guinea (27, 64-66)			
B	9-bp deletion, +16517*Hae*III, -10394*Dde*I, -10397*Alu*I	T16189C, T16217C, T16519C	11% of Papua New Guinea
P	+207*Hin*cII, +207*Hpa*I, +15606*Alu*I, -10394*Dde*I, -10397*Alu*I	T16357C	About 30% of highland Papua New Guinea
Q	+10394*Dde*I, +10397*Alu*I, +16178*Taq*I	G16129A, T16144C, C16148T, C16223T, A16241G, A16265G, T16311C, A16343G	About 30% of highland Papua New Guinea

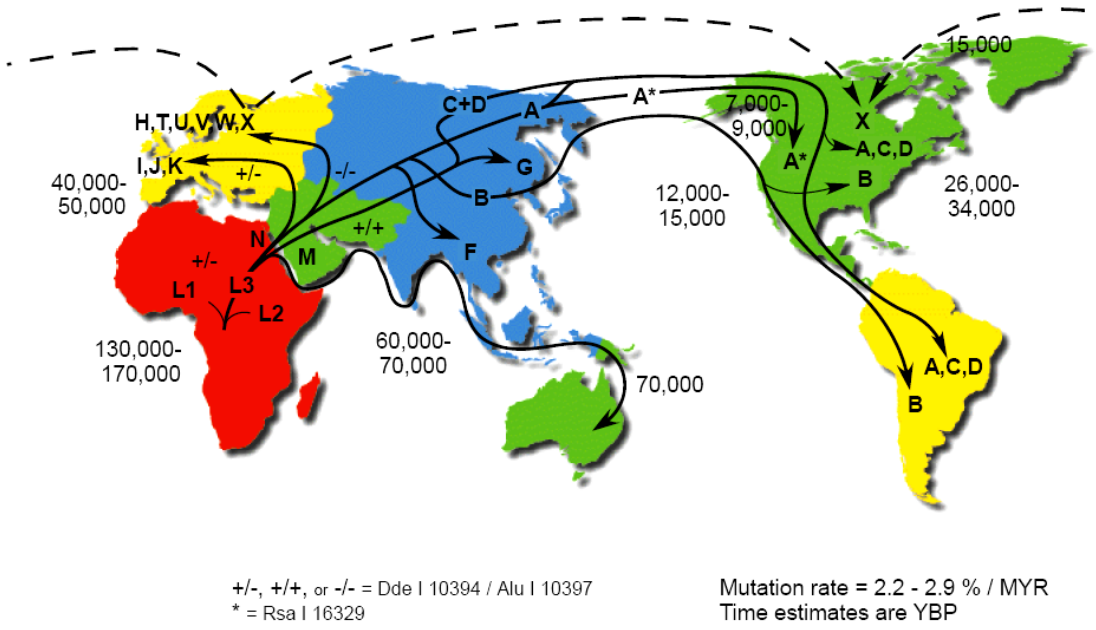


Figure 4. Shown are the world map and the migration route of mitochondrial DNA from Africa into Europe, Asia, Australia and America (44). The continent-specific haplogroups in each continent are also shown.

defined by the gain of the *Ava*II site at np 8249, the loss of *Hae*III site at np 8250 and np 8994 and is found 2.3% of Finns and Swedes (25). Haplogroup X is, in part, defined by the loss of a *Dde*I site at np 1715 and the gain of an *Ava*II site at np 14465 and is also found in about 6.9% of European mtDNAs (25, 28). In addition, haplogroup I is defined by the loss of the *Dde*I np 1715 site, and the gain of an *Ava*II site at np 8249, the loss of *Hae*III site at np 8250 and an *Alu*I site at np 10028 and represents 6.7% of European mtDNAs (24, 28). Haplogroup J is identified by the loss of a *Bst*NI site at np 13708 and is found in about 11.3% of European mtDNAs (28, 44). Haplogroup K is delineated by the loss of a *Hae*II site at np 9052 and the gain of a *Hin*fI site at np 12308 and is found in 9.1% of Europeans (24, 28).

For the Asian haplogroup, the macro-haplogroup defined by the presence of the *Dde*I np 10394 and the *Alu*I np 10397 sites has been designated macro-haplogroup M (28, 44). The constant association of the *Dde*I np 10394 and *Alu*I np 10394 in Asians, but not in Africans or Europeans, implies that the *Alu*I np 10397 mutation must have arisen on an mtDNA carrying the *Dde*I np 10394 mutation as women migrated out of Africa and into Asia (28). The co-occurrence of the *Alu*I site at np 10397 and the *Dde*I site at np 10394 in macro-haplogroup M mtDNAs throughout Asia indicates that the *Alu*I site gain occurred at the beginning of Asian habitation (25, 27).

In addition to this major bifurcation of Asian mtDNAs, there are a number of distinctive sublineages of relevance to Asian and Native American prehistory. Haplogroups A, B, C, and D have proved to be the progenitors of virtually all Native American mtDNAs (19, 23, 28). Haplogroups A and B lack both the *Dde*I site at np 10394 and the *Alu*I site at np 10397, whereas haplogroups C and D have these sites, with haplogroup C and D also belonging to macro-haplogroup M (28) . In addition, haplogroup A is defined by an *Hae*III site at np 663 (A to G at np 663) (19), haplogroup B by an independent occurrence of the 9-bp deletion between the COII and $tRNA^{Lys}$ genes and the *Hae*III site gain at np 16517 (19, 28), haplogroup C by the simultaneous *Hin*cII site loss at np 13259 and an *Alu*I site gain at np 13262 (A to G at np 13262) (19, 27), and haplogroup D by the loss of an *Alu*I site at np 5176 (C to A at np 5178) (19, 27). These haplogroups are further delineated in most Asians and Native Americans by specific control-region variants. The other haplogroup, B*, was

the haplogroup which also defined by the 9-bp deletion and the *Hae*III site gain at np 16517 as same as the polymorphisms defined haplogroup B. In addition to these polymorphisms, haplogroup B* also has the loss of the *Dde*I site at np 3534 , the *Alu*I site at np 3537 and the *Hin*fI site at np 15234 and also has the gain of the *Mbo*I site at np 15235 and the *Dde*I site at np 10394 (27). For haplogroup A, the HVS-1 variants at nps 16362 (T to C), 16319 (G to A), 16290 (C to T), and 16223 (C to T) were included. The haplogroup B variants in the HVS-1 were at nps 16217 (T to C) and 16189 (T to C) whereas the HVS-1 variants of haplogroup B* at nps 16189 (T to C) and 16140 (T to C). For haplogroup C, these include variants at nps 16327 (C to T), 16298 (T to C), and 16223 (C to T); and, haplogroup D variants in the HVS-1 were at nps 16362 (T to C) and 16223 (C to T) (27, 28).

Three other prominent Asia haplogroups are E, F, and G. Haplogroups E and G have the combined *Dde*I and *Alu*I sites at nps 10394 and 10397, whereas haplogroup F lacks these sites (28, 44). Haplogroup E is further defined by the *Hha*I site loss at np 7598, haplogroup G by the presence of an *Hae*III site at np 4830 and an *Hha*I site at np 4831 (28, 60). Haplogroup F is delineated by the combined *Hpa*I/*Hin*cII site loss at np 12406, the first Asian-specific polymorphism observed (28, 44). All of these haplogroups show marked frequency variation throughout Asia. Haplogroup F is prominent in southern Asian populations, being found in 32% of Vietnamese mtDNAs and 21% of Malay mtDNAs (26). It is present in about 15% of Koreans and Tibetans, but is virtually absent in Siberia (28). By contrast, haplogroups A, C, D, E, and G are absent in southern Asian populations, including Vietnamese, Malays, Sabah, Malay aboriginals, and New Guineans, but these groups are found at significant frequencies in Tibetans, Koreans, and Han Chinese (28). Furthermore, haplogroups A, C, and D extend into the Siberia populations analysed, reaching maximum frequencies of 68%, 84% and 28%, respectively (28, 61).

Moreover, haplogroup Y and Z were also found in the Asia continent. The gain of the *Dde*I site at np 10394, the *Mbo*I site at np 7933, the *Hae*III at np 16517 and also the loss of the *Hae*III site at np 8391 and the *Alu*I site at np 10397 were the polymorphisms of restriction site which defined haplogroup Y (61). This haplogroup was found in the Siberians which were the highest frequency in the Nivkhs (64.9%) and also found in the Koryaks (9.7%) and Itel'men (4.3%) (61). In addition to the

Siberians, haplogroup Y was also observed in the Koreans (7.7%) (61). For haplogroup Z, the gain of the *Dde*I site at np 10394 and the *Hae*III at np 16517 and also the loss of the *Alu*I site at np 10397 were the polymorphisms which determined haplogroup Z. As of haplogroup Y, haplogroup Z was also detected in the Siberians which were 5.8% of the Koryaks and 6.4% of the Itel'men (61).

The mitochondrial genome also harbors variation in the presence or absence of several length mutations. The 9-bp deletion between the second subunit of cytochrome oxidase (COII) and lysine transfer RNA ($tRNA^{Lys}$) genes is the most frequently studied of which is due to the lack of a 9-bp sequence (5' CCCCCTCTA 3') between nt 8272 and 8289 in the mitochondrial DNA (62, 63). This intergenic COII/$tRNA^{Lys}$ mtDNA 9-bp deletion has been a useful marker in the Asian populations to define a major Asian lineage, haplogroup B (28, 63). This mutation is very common in Asians and populations of Asian ancestry. It is found in moderate frequencies throughout Southeast Asia and seems to be fixed or nearly fixed in Polynesia (26, 27, 64, 65). This 9-bp deletion is largely absent in Melanesian populations, for example, aboriginal groups of Australia and highland Papua New Guinea (PNG), while it is present in coastal populations of PNG that are thought to be more recent arrivals to the island (66). Furthermore, haplogroup P and Q were also found in Papua New Guinea (27, 64). Haplogroup P was defined by the all of the gain of the *Hin*cII site at np 207, the *Hpa*I site at np 207, the *Alu*I site at np 15606 and the loss of both of the *Dde*I site at np 10394 and the *Alu*I site at np 10397 and also possessed the HVS-1 mutation which was the T to C at nt 16357 (27, 65). The polymorphic restriction sites determined haplogroup Q were both of the gain of the *Dde*I site at np 10394 and the *Alu*I site at np 10397 and also the gain of the *Taq*I site at np 16178. The G16129A, T16144C, C16148T, C16223T mutations in the HVS-1 were the unique combination mutations to defined the haplogroup Q (27, 65).

2.3.2 Mitochondrial variation associated with LHON

Differences in the genetic background and population structure may influence the prevalence of specific mutations. The mtDNA population polymorphisms may interact with environmental factors and/or mtDNA pathogenic mutations. Possibly regional variations in mtDNA haplogroup frequency may influence the penetrance or expression of mtDNA mutations (28, 47).

In patients of European descent, the LHON 11778 mutation accounts for about 50% of cases, whereas the LHON 3460 and LHON 14484 mutations encompass roughly 15% each (5, 28). In Asia, the LHON 11778A mutation accounts for 95% of patients (14, 28). Extensive analysis of the mtDNAs of LHON patients has revealed that certain mtDNA haplotypes are prone to expression of LHON more than others. This indicates that different population-specific mtDNA may be functionally different and hence might have been influenced by selection (28).

Phylogenetic analyses of LHON families have recently provided new insight into the population history of LHON as well as into the etiological significance of the various mutations associated with the disease (10, 29, 67, 68). Most of the mtDNA variation is ethnic-specific. And for example, virtually all European mtDNAs are subsumed within nine mtDNA haplogroups (denoted as H, I, J, K, T, U, V, W and X) (22, 24, 25, 28, 44, 47, 49). Haplogroup J is present in only about 11.3% of the general European population, but it was found in 37% of LHON patients harboring the LHON G11778A mutation and 80% of LHON patients harboring the LHON T14484C mutation (28, 30). It seems to be more frequent among LHON families than in controls, and the pathogenic mutations ND4/11778 and ND6/14484 show significantly preferential association with haplogroup J (32). Based on phylogenetic anslysis, it has been shown that the secondary mutations in the LHON patients; T4216C, G13708A, G15257A, and G15812A are also cluster on a specific mtDNA background, haplogroup J (32, 50, 67). The most accepted explanation is that this particular mtDNA haplogroup, including some specific polymorphisms altering amino acid positions in *ND* subunit genes of complex I, can increase the penetrance of LHON, justifying the most frequent recognition of the 11778/ND4 and 14484/ND6 mutations in association with haplogroup J (30, 32, 69).

The prevalence of LHON and the continent-specific haplogroups were varying in the difference ethnic groups. Haplogroup J was the most common in the Caucasian with LHON. The investigation of the mitochondrial haplogroup in Thai LHON patients was needed to understand the haplogroup associated with Thai LHON patients and whether these haplogroups modulated the disease expression.

CHAPTER III
MATERIALS AND METHODS

1. Materials

1.1 Subjects

Thirty unrelated LHON patients in this study were from Department of Ophthalmology, Faculty of Medicine Siriraj Hospital and from Department of Ophthalmology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand. All of them were positive for the G11778A mutation. These 30 patients were from various parts of Thailand; 14 from Central part, 6 from North-Eastern, 2 from Northern, 1 from Eastern and 3 of unknown habitat. The 100 normal control individuals were from Central part (N=49), North-Eastern (N=10), Northern (N=4) and unknown (N=34).

The maternal relatives of these 30 LHON patients were also included in this study. Age of unaffected samples was 16 years or older. All samples used in this study were obtained with informed consent.

1.2 Oligonucleotide primers

The oligonucleotide primers used in this study were synthesized by Bio Synthesis, USA. The sequences of these primers were shown in Table 2 and 3.

1.3 Restriction enzymes

Twenty two restriction endonuclease enzymes used in the PCR-RFLP analysis were *Alu*I, *Ava*II, *Bam*HI, *Bcl*I, *Bfa*I, *Bst*NI, *Dde*I, *Hae*II, *Hae*III, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Hpa*II, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Tru*9I, *Xba*I and *Xho*II. Most of the restriction enzymes were purchased from New England Biolabs, USA. except for enzymes *Hae*III, *Hin*cII, *Pvu*II and *Xba*I which were purchased from Amersham Biosciences, England and enzymes *Hha*I, *Rsa*I and *Tru*9I were purchased from Promega, USA.

Table 2. The list of forward primers used in this study.

Primers (nucleotide position[a])	Code	Sequencing of primer (5'→ 3')	Length (bp)
1562-1571	L1562	GTAACATGGTAAGTGTACTG	20
3007-3023	L3007	CCCGATGGTGCAGCCGC	17
3115-3134	L3115	TCCTCCCTGTACGAAAGGAC	20
3231-3254	L3231	TTAAGATGGCAGAGCCCGGTAATC	24
4049-4071	L4049	ACGCACTCTCCCCTGAACTCTAC	23
4476-4499	L4476	CCCCTGGCCCAACCCGTCATCTAC	24
5317-5333	L5317	CCACCATCACCCTCCTT	17
7240-7260	L7240	CATACACCACATGAAACATCC	21
7392-7410	L7392	GGATGCCCCCCACCCTACC	19
8211-8231	L8211	TCGTCCTAGAATTAATTCCCC	21
8278-8297	L8278	CTACCCCCTCTAGAGCCCAC	20
8907-8924	L8907	CTTCTTACCACAAGGCAC	18
9501-9520	L9501	TGAGCCTTTTACCACTCCAG	20
9911-9932	L9911	CGAAGCCGCCGCCTGATACTGG	22
11673-11691	L11673	CCCCCTGAAGCTTCACCGG	19
11728-11777	L11728	CTCATTACTATTCTGCCTAGCAAACT CAAACTACGAACGCACTCATGATC	50
13466-13486	L13466	GCCTAGCATTAGCAGGAATAC	21
13914-13930	L13914	CGGATTCTACCCTAGCA	17
14191-14211	L14191	AAACAATGGTCAACCAGGAAC	21
15234-15256	L15234	GAATCTGAGGAGGCTACTCATTA	23
15481-15504	L15481	CTCACCAGACCTCCTAGGCGACCC	24
15790-15812	L15790	CATCATTGGACAAGTAGCATCCG	23
16453-16472	L16453	CCGGGCCCATAACACTTGGG	20

[a] numbers shown is the nucleotide position according to the revised Cambridge Reference Sequence (rCRS) (46).

Table 3. The list of reverse primers used in this study.

Primers (nucleotide position[a])	Code	Sequencing of primer (5'→3')	Length (bp)
731-708	H731	TTAGAGGGTGAACTCACTGGAACG	24
1696-1677	H1696	GGAGTGGGTTTGGGGCTAGG	20
3728-3709	H3728	GATTTGAGGGGGAATGCTGG	20
4260-4241	H4260	GGTTTGAGGGGGAATGCTGG	20
5482-5459	H5482	GGTAGGAGTAGCGTGGTAAGGGCG	24
5917-5898	H5917	CGGTCGGCGAACATCAGTGG	20
7608-7588	H7608	CCTACTTGCGCTGCATGTGCC	21
8311-8297	H8311	AAGTTCGCTTTACAG	15
8921-8902	H8921	CCTTGTGGTAAGAAGTGGGC	20
10107-10088	H10107	GTAGTAAGGCTAGGAGGGTG	20
11942-11919	H11942	GTAGGAGAGTGATATTTGATCAGG	24
13928-13905	H13928	CTAGGGTAGAATCCGAGTATGTTG	24
14873-14850	H14873	GGATCAGGCAGGCGCCAAGGAGTG	24
15360-15343	H15360	GATCCCGTTTCGTGCAAG	18
16115-16095	H16115	GGTGGCTGGCAGTAATGTACG	21
16417-16398	H16417	TTTCACGGAGGATGGTGGTC	20
16540-16514	H16540	GTGGGCTATTTAGGCTTTATGACCCTG	27

[a] numbers shown is the nucleotide position according to the revised Cambridge Reference Sequence (rCRS) (46).

1.4 Equipments

- Eppendorf centrifuge 5417C, Eppendorf, Germany
- Agarose Gel Electrophoresis set, Hoefer, USA.
- Polyacrylamide Gel Electrophoresis set, Mini-PROTEAN® II and III, Bio-Rad, USA.
- Waterbath, Memmert, German
- UV-transluminator, Vilber Lourmat, France
- Polaroid camera, Fotodye, USA.
- Vortex, Scientific Industries, USA.
- Pipetteman, Gilson, France
- Refrigerator -20ºC, Sanyo, Thailand
- PTC-150 MiniCycler™ PCR machine, MJ Research, USA.

1.5 Softwares

The software of computer programs used in the analysis of this study were the Microsoft Excel 2000, Microsoft Notepad, ClustalW software in the Bioedit version 5.0.9 (downloaded from: http://www.mbio.ncsu.edu/Bioedit/biodit.html), Restriction mapper software (online software: http://www.restrictionmapper.org), PAUP* version 4.0b10 program (purchased from Sinauer Associates, USA), TreeView version 1.6.6 program (downloaded from: http://taxonomy.zoology.gla.ac.uk/rod/treeview.html) and SPSS program version 13.0 for Windows (SPSS, Inc., Chicago, IL).

2. Methods

2.1 DNA extraction from venous blood by the modified phenol-chloroform method

Five milliliter of whole blood obtained from each individual using EDTA (Ethylenediaminetetraacetic acid) as an anticoagulant was centrifuged at 3,000 rpm for 5 minutes in order to separate plasma from packed cells. The leukocytes were separated from packed cells by the addition of 10 ml Red Cell Lysis Buffer (RCLB: 10 mM Tris-HCl pH 7.6, 5 mM $MgCl_2$, 10 mM NaCl) and centrifuged at 5,000 rpm for 3 minutes and the supernatant was discarded. RCLB was added again and the pellet was centrifuged as above until the supernatant was clear. The lysed red cell pellet was

mixed in 250 µl of sterile distilled water using the vortex. Then, 250 µl lysis buffer (50 mM Tris pH 9.0, 100 mM EDTA, 2% SDS) and 25 µl (20 mg/ml) Proteinase K (Sigma, USA) were added and the mixture was incubated at 37°C overnight. After the addition of 500 µl saturated phenol, the mixture was centrifuged at 10,000 rpm for 1 minute and the upper layer was transferred into the new tube. Then, 250 µl of phenol and isoamyl:chloroform was added and the tube was centrifuged at 10,000 rpm for 1 minute. The supernatant was transferred into the new tube. Then, 500 µl of isoamyl:chloroform was added and the tube was centrifuged as above and the pellet was discarded. The supernatant was transferred into the new tube and gently mixed by absolute ethanol 1,000 µl then kept in -20°C overnight before centrifugation at 10,000 rpm for 20 minutes. The pellet was washed with 1,000 µl of the 70% ethanol and centrifuged as above. The supernatant was discarded and the DNA pellet was dried and resuspended in 200 µl of the sterile distilled water. The DNA solution was kept in -20°C until used in the further study.

2.2 Detection of LHON mutations

LHON mutations were detected in 30 unrelated LHON patients as the following

2.2.1 Detection of G11778A mutation

2.2.1.1 Amplification of DNA by Polymerase Chain Reaction (PCR)

The amplification of 215 bp of the mitochondrial DNA from position 11728 to 11942 was performed in MiniCycler^{TM} PCR machine. The reaction mixture consisted of 10x amplification buffer (500 mM KCl, 100 mM Tris-HCl, 0.1% w/v gelatin, 1% Triton X-100), 25 mM $MgCl_2$, 10 mM dNTP, 10 pmol of each primer (L11728 and H11942), 2.5 units of *Taq* DNA polymerase (QIAGEN, Germany) and 10 ng DNA template, in the final volume of 50 µl. The PCR reaction was carried out at 95°C for 4 minutes followed by 30 cycles of the denaturation (at 95°C for 1 minute), annealing (at 55°C for 1.5 minutes), elongation (at 72°C for 2.5 minutes). The last cycle was extended at 72°C for 7.5 minutes. The PCR product was then stored at 4°C if not processed further.

2.2.1.2 Precipitation of DNA from PCR product

In this process, 50 µl of the PCR product was precipitated by the addition of 5 µl NaOAc (3M, pH 5.2) and 200 µl absolute ethanol. After the incubation at -20°C overnight, the mixture was centrifuged at 10,000 rpm for 20 minutes. The pellet was washed with 200 µl of 70% ethanol and centrifuged as above. The supernatant was discarded and the DNA pellet was dried and resuspended in 20 µl of the sterile distilled water. The DNA solution was kept in -20°C until used in the restriction enzyme digestion study.

2.2.1.3 Restriction enzyme digestion

For restriction enzyme digestion, 2-5 µl of precipitated DNA was incubated with 4 units of enzyme *Bcl*I and enzyme buffer (NEB buffer 3: buffer for enzyme *Bcl*I). The digestion was performed as indicated by the manufacturer instruction at 50°C for 12-16 hours.

2.2.1.4 Agarose Gel Electrophoresis

The Agarose (UltraPure™, GibcoBRL, USA) used for the detection of the digestion fragments was dissolved in 1xTAE (Tris-Acetate-EDTA: 40 mM Tris buffer pH 7.8, 1 mM EDTA pH 8, Glacial acetic acid) into 4% gel. The digested products were mixed with the loading buffer (30% glycerol and 0.25% bromophenol blue) and electrophoresed on 4% agarose gel for 120 minutes at 60 volt. The gel was stained with 1 µl/ml ethidium bromide solution and destained with the distilled water. The bands of the digested fragments were visualized by the UV-light transluminator (Vilber Lourmat, France) and photographed by Polaroid camera (Fotodye, USA). The 148, 46 and 21 bp fragments were detected in the sample positive for G11778A, whereas the 194 and 21 bp fragments were detected in the sample negative for G11778A.

2.2.2 Detection of the other LHON mutations

In order to detect the other primary and secondary mutations of LHON, the PCR-RFLP and direct sequencing were used. The primary mutations, G15257A was detected by PCR-RFLP and G3460A, T14484C and G14459A were detected by DNA sequencing. In addition, the secondary mutations, A4917G, G5244A, G7444A and G15812A, were detected by PCR-RFLP but another 19 secondary mutations

described below were detected by sequencing.

2.2.2.1 Detection of the other LHON mutations by PCR-RFLP

The mitochondrial DNA covering the region containing the mutation was amplified from each patient. The PCR product was precipitated and digested with the restriction enzyme according to each mutation and electrophoresed on agarose gel as mentioned in 2.2.1.2-2.2.1.4. The oligonucleotide primers, restriction enzymes and their incubated temperature and the percentage of agarose gel are shown in Table 4. The RFLP pattern of both positive and negative fragments of each mutation was also shown in Table 4.

2.2.2.2 Detection of the other LHON mutations by direct sequencing

The primary LHON mutation G3460A, T14484C and G14459A and 19 another secondary mutations shown in Table 3 were detected by direct sequencing.

2.2.2.2.1 Amplification of DNA by Polymerase Chain Reaction (PCR)

The mitochondrial DNA covering the region containing the mutations were amplified from each patient. The PCR reaction and condition were carried out as mentioned in 2.2.1.1 using the different pairs of oligonucleotide primers for different mutations as also shown in Table 3.

2.2.2.2.2 Purification of the PCR product

The PCR product from 2.2.2.2.1 was purified using the Wizard^{TM} PCR Prips DNA Purification Kit (Promega, USA). The PCR product was vortexed briefly with the direct purification buffer. The mixture was left in the room temperature for 1 minute and 1 ml of resin was added and briefly mixed by vortex 3 times over a one minute period. The mixture was passed through the minicolumn and the lower phase was discarded. Two milliliter of 80% Isopropanol was push into the column and the mixture was centrifuged at 10,000 rpm for 2 minutes. The column was transferred into a new tube and 50 μl of sterile distilled water was added into the column and left at the room temperature for 1 minute. The column was centrifuged at 10,000 rpm for 20 seconds. The purified DNA was then collected and kept in -20°C until used in the sequencing reaction.

Table 4. The conditions used in the detection of all LHON point mutations.

Mutation	PCR Primers	PCR products (bp)	Detected method	Sequencing primer	Restriction Enzyme	Incubating temperature (°C)	Gel electrophoresis	Digested fragments (bp)	
								normal	positive mutation
Primary mutations									
G11778A	L11728-H11942	215	RFLP		*Bcl*I	50	4% agarose gel (60V 120 min)	194, 21	148, 46, 21
G15257A	L15234-H15360	127	RFLP		*Tru*9I	65	4% Nusieve® 3:1 agarose gel (60V 120 min)	127	106, 21
G3460A	L3115-H4260	1146	sequencing	L3231					
T14484C	L14191-H14873	683	sequencing	L14191					
G14459A	L14191-H14873	683	sequencing	L14191					
Secondary mutations									
A4917G	L4476-H5482	1007	RFLP		*Bfa*I	37	4% Nusieve® 3:1 agarose gel (60V 120 min)	345, 262, 204, 91, 90, 15	306, 262, 204, 91, 90, 39, 15
G5244A	L4476-H5482	1007	RFLP		*Hpa*II	37	3% agarose gel (60V 100 min)	396, 240, 236, 135	636, 236, 135
G7444A	L7240-H7608	369	RFLP		*Xba*I	37	3% agarose gel (60V 100 min)	201, 168	369
G15812A	L15481-H16115	635	RFLP		*Rsa*I	37	3% agarose gel (60V 100 min)	333, 237, 47, 18	570, 47, 18

Table 4 (continued). The conditions used in the detection of all LHON point mutations.

Mutation	PCR Primers	PCR products (bp)	Detected method	Sequencing primer	Restriction Enzyme	Incubating temperature (°C)	Gel electrophoresis	Digested fragments (bp)	
								normal	positive mutation
Secondary mutations									
G3316A	L3115-H4260	1146	sequencing	L3231					
T3394C	L3115-H4260	1146	sequencing	L3231					
G3496T	L3115-H4260	1146	sequencing	L3231					
C3497T	L3115-H4260	1146	sequencing	L3231					
G3635A	L3115-H4260	1146	sequencing	L3231					
A4136G	L3115-H4260	1146	sequencing	L4049					
T4160C	L3115-H4260	1146	sequencing	L4049					
C4171A	L3115-H4260	1146	sequencing	L4049					
T4216C	L3115-H4260	1146	sequencing	L4049					
G9738T	L8907-H10107	1201	sequencing	L9501					
G9804A	L8907-H10107	1201	sequencing	L9501					
G13708A	L13466-H14873	1407	sequencing	L13466					
G13730A	L13466-H14873	1407	sequencing	L13466					
C14482G	L14191-H14873	683	sequencing	L14191					
C14482A	L14191-H14873	683	sequencing	L14191					
A14495G	L14191-H14873	683	sequencing	L14191					
T14498C	L14191-H14873	683	sequencing	L14191					
C14568T	L14191-H14873	683	sequencing	L14191					
A14596T	L14191-H14873	683	sequencing	L14191					

2.2.2.2.3 Direct sequencing

The sequencing reaction used was ABI PRISM BigDye Terminator Cycle Sequencing Ready Reaction Kit (Applied Biosystems, USA). The sequencing reaction was performed in Minicycler^{TM} PCR machine. The sequencing mixture consisted of 1 μl (3 pmol/μl) of primer, 4 μl of the BigDye reagent, 10 μl of the sterile distilled water and 5 μl of the purified DNA template, in the final volume of 20 μl. The sequencing primers used to detect each mutation were also shown in Table 3. The sequencing reaction was carried out at 94°C for 1 second, at 50°C for 1 second and at 60°C for 55 seconds for 24 cycles. After completion, the reaction was stored at 4°C. Prior to the loading, the reaction was vortexed briefly with 16 μl of the sterile distilled water and 64 μl of absolute ethanol. The mixture was left at the room temperature for 15 minutes in the dark place and was centrifuged at 12,000 rpm for 20 minutes. Then, 250 μl of 70% ethanol was added into the pellet and the tube was centrifuged at 12,000 rpm for 10 minutes. The supernatant was discarded and the pellet was dried at the room temperature for 1 hour in the dark place and resuspended gently in 25 μl of TSR (Template Suppression Reagent). The mixture was incubated at 95°C for 2 minutes and then at 0°C for 3 minutes. Then, 0.5-1.5 μl of sequencing reaction was loaded in the ABI PRISM 377 DNA Sequencer (Applied Biosystems, USA) and run for 10 hours. The nucleotide sequences were detected by fluorescent detector.

2.3 Determination of mtDNA haplotypes by Restriction Fragment Length Polymorphism (RFLP)

The mitochondrial DNA haplotypes determined by Restriction Fragment Length Polymorphism (RFLP) were carried out in 30 LHON patients and 100 normal controls. The mtDNA was amplified using the oligonucleotide primers into 9 overlapping regions covering the whole mitochondrial genome. The 9 primer pairs were shown in Table 5. The PCR product from each primer pair was precipitated and then digested with 18 restriction endonucleases, *Alu*I, *Ava*II, *Bam*HI, *Dde*I, *Hae*II, *Hae*III, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Hpa*II, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Xba*I and *Xho*II and another one restriction endonuclease, *Bst*NI, in the PCR product of primer L11673 and H13928 for determination of haplogroup J. The pattern of the digested

Table 5. The 9 overlapping covering the mitochondrial genome oligonucleotide primers used in the RFLP analysis of haplotype determination.

Primer pair no.	Forward primer	Reverse primer	PCR products (bp)	Optimal annealing Temperature
1	L1562	H3728	2167	57°C
2	L3007	H5917	2911	68°C
3	L5317	H7608	2292	61°C
4	L7392	H8921	1530	59°C
5	L8278	H10107	1829	62°C
6	L9911	H11942	2032	65°C
7	L11673	H13928	2256	65°C
8	L13914	H16540	2627	57°C
9	L16453	H1696	1812	65°C

fragments were resolved either by the agarose gel or polyacrylamide gel electrophoresis as shown in Table 6. The 2% agarose gel was run for 120 minutes at 80 volt and 4% agarose gel was run for 180 minutes at 80 volt whereas 12% polyacrylamide gel was run for 100 minutes at 80 volt. The 12% polyacrylamide gel consisted of 6 ml of 30% Acrylamide solution at the 32:1 ratio of acrylamide and bis-acrylamide (Sigma, USA), 3 ml of 5xTBE (Tris-Boric acid-EDTA), 105 µl of 10% Ammoniumpersulfate, 22.5 µl TEMED and 6 ml distilled water, in the final volume of 15 ml. The digestion products were mixed with loading buffer (15% Ficoll solution, 2.5xTBE, 0.25% (w/v) Xylene cyanol and 0.025% (w/v) Bromophenol blue) prior to the electrophoresis. The detail of digested pattern resulting from each polymorphism in the mtDNA detected from these PCR products and restriction enzymes were in Appendix B. The number shown is the first nucleotide of recognition site of each restriction enzyme relative to the revised Cambridge Reference Sequence (rCRS) (46).

2.4 Detection of the 9-bp COII/tRNA^{Lys} deletion

The 9-bp COII/tRNA^{Lys} deletion was also determined in 30 LHON patients and 100 normal controls. The amplification of 101 bp of mtDNA from position 8211 to 8311 using primer L8211 and H8311 was carried out as mentioned in 2.2.1.1 except for the annealing step which was 48°C for 1.5 minutes. The PCR product was electrophoresed on 4% Nusieve® 3:1 agarose gel for 120 minutes at 60 volt. The 9-bp COII/tRNA^{Lys} deletion yields the PCR product of 92 bp in size whereas the 101 bp in size was detected in non deleted samples.

2.5 Determination of the mitochondrial control region (D-loop)

The mitochondrial DNA covering the hypervariable segment 1 (HVS-1) from nucleotide position 16024 to 16383 in the mitochondrial control region was determined in 30 LHON patients and 100 normal controls. The HVS-1 was amplified using either L15904 and H16417 or L15790 and H731 primers. The PCR reaction of L15904 and H16417 primers was carried out as mentioned in 2.2.1.1 whereas the PCR reaction of L15790 and H731 primers was carried out different in the annealing step which was 57°C for 1.5 minutes. The PCR product was purified and sequencing as mentioned in 2.2.2.2.2-2.2.2.2.3 using H16417 as the primer for the DNA sequencing and either L15904 or L15790 as the primer for the sequencing reaction when the sequence had the length heteroplasmy.

Table 6. The percentage and type of the gel used to separate the digested fragments of each PCR product and restriction enzyme.

PCR products of primer pair no.	% gel electrophoresis used in determined the digested fragments		
	2% Agarose	4% Agarose	12% Polyacrylamide
1	*Ava*II, *Bam*HI, *Hae*II, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Hpa*II, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Xba*I, *Xho*II	*Hae*III	*Alu*I, *Dde*I, *Mbo*I
2	*Ava*II, *Bam*HI, *Dde*I, *Hae*II, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Xba*I, *Xho*II	*Hpa*II	*Alu*I, *Dde*I, *Hae*III
3	*Ava*II, *Bam*HI, *Hae*II, *Hha*I, *Hin*cII, *Hpa*I, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Xba*I, *Xho*II	*Hae*III, *Hpa*II, *Taq*I	*Alu*I, *Dde*I, *Hin*fI
4	*Alu*I, *Ava*II, *Bam*HI, *Hae*II, *Hae*III, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Xba*I, *Xho*II	*Dde*I, *Hpa*II	
5	*Alu*I, *Ava*II, *Bam*HI, *Hae*II, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Hpa*II, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Xba*I, *Xho*II		*Dde*I, *Hae*III
6	*Ava*II, *Bam*HI, *Dde*I, *Hae*II, *Hae*III, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Hpa*II, *Mbo*I, *Pst*I, *Pvu*II, *Taq*I, *Xba*I, *Xho*II	*Alu*I, *Rsa*I	
7	*Ava*II, *Bam*HI, *Bst*NI, *Hae*II, *Hae*III, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Hpa*II, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Xba*I, *Xho*II		*Alu*I, *Dde*I
8	*Alu*I, *Ava*II, *Bam*HI, *Hae*II, *Hha*I, *Hin*cII, *Hpa*I, *Hpa*II, *Mbo*I, *Pst*I, *Pvu*II, *Taq*I, *Xba*I, *Xho*II	*Hae*III	*Dde*I, *Hin*fI, *Rsa*I
9	*Ava*II, *Bam*HI, *Hae*II, *Hae*III, *Hha*I, *Hin*cII, *Hin*fI, *Hpa*I, *Hpa*II, *Mbo*I, *Pst*I, *Pvu*II, *Rsa*I, *Taq*I, *Xba*I, *Xho*II		*Alu*I, *Dde*I

2.6 Phylogenetic analysis

The phylogenetic relationships between haplotypes were inferred from the restriction site and 9-bp deletion data and the nucleotide sequences of HVS-1 in the control region of all the subjects using the computer program PAUP* (Phylogenetic Analysis Using Parsimony and Other Methods) 4.0 beta version.

2.6.1 Data preparation

Since PAUP* uses the NEXUS format for input data files, so both of RFLP data and HVS-1 sequence data were converted to the NEXUS format prior the analysis. The phylogenetic trees constructed from both RFLP and 9-bp deletion and the HVS-1 sequence data used "Khwe" (the haplogroup L of the Africa) as an outgroup. This Africa outgroup was downloaded from the website http://www.genpat.uu.se/mtDB/Sequneces.php/.

2.6.1.1 RFLP data

For PAUP* program, the restriction site and 9-bp deletion data were changed into number 1 or 0 depending on the presence or absence of each particular position in the Microsoft Excel software. A "1" indicated the presence of a site and a "0" indicated the absence of a site except for the 9-bp deletion data which a "1" indicated the presence of 9-bp deletion and a "0" indicated the non 9-bp deletion. All the data were saved into the text file (*.txt) and transferred to the Microsoft Notepad to replaced the gap or space within the data except for the gap between the name of sample and the restriction site data (0, 1) in order to separate the name of the samples and the analysed data. The text file of the data was converted to the NEXUS format with "tonexus format=text fromfile=*.txt tofile=*.nex datatype=standard" command-line interface in the display window of PAUP* program. For the RFLP data of Khwe outgroup, the whole genome sequence was digested with 18 restriction endonuclease by the Restriction mapper online software in order to get the information of RFLP.

2.6.1.2 Sequence Data

The nucleotide sequences from nucleotide position 16024-16383 in the HVS-1 region of all samples and Khwe outgroup were aligned by ClustalW software in the Bioedit program and then exported the sequence alignment by saved into the nexus file (*.nex).

2.6.2 Phylogenetic tree based on Distance Method computed by PAUP* program

The phylogenetic tree of both RFLP data and HVS-1 sequence data were constructed using the distance method. After opened and executed the data file either RFLP data or HVS-1 sequence data, the command "set criterion=parsimony" was used in the command-line interface of the display window in PAUP* program in order to search for a optimal tree under this criteria. After the type of distance analysis of the phylogenetic tree was set with the command either "dset distance=neili" for RFLP data or "dset distance=hky85" for the HVS-1 sequence data, the tree was computed using the Neighbor-Joining method according to the current distance transformation used the command "nj". For displaying the phylogenetic tree estimated with PAUP* program, the TreeView program was used for this application. In the TreeView, the tree can be changed either root or unroot and also the outgroup of the data can be defined. Furthermore, the phylogenetic tree was saved as graphic in the picture file for using further by TreeView.

2.7 Mitochondrial DNA haplogroup determination

The mitochondrial haplogroup of all 130 samples was determined by at least 3 of 4 criteria which were the group of the polymorphisms of nucleotide sequence within the recognition site of the restriction endonuclease or within the HVS-1 sequence in the control region or the relationship between samples in the same branch or cluster within phylogenetic tree constructed from RFLP and 9-bp deletion information or from HVS-1 sequence. The detail of haplogroup determination from RFLP and 9-bp deletion information or from HVS-1 sequence was shown as in Table 1.

2.8 Statistical analysis

All statistical analysis in this study were performed using the statistical program SPSS version 13.0 for Windows. The p-value less than 0.05 was considered statistical significant and accepting the hypothesis.

2.8.1 Subjects and Variable definition

In addition to 100 normal controls and 30 LHON individuals from unrelated families, the maternal relatives of these 30 LHON individuals were also included in the statistical analysis. For statistical analysis of LHON patients and their

maternal relatives, the variables used to analyses were gender, level of mutant mtDNA (homoplasmy or heteroplasmy), age of onset and final visual acuity (final VA). The homoplasmic case was defined as the person who has equal or higher than 95% of G11778A mutant mtDNA. In order to analyse the final visual acuity, only affected eyes were included and the visual acuity value was expressed as the logarithm of the minimal angle of resolution (logMAR) values (logMAR=log[1/Snellen visual acuity]). The unmeasured visual acuity, finger count (FC) and hand motion (HM), were corresponded Snellen visual acuity with 6/600 and 6/6000, respectively. These visual acuity values were 2.0 and 3.0 of logMAR, respectively. The unaffected cases were the asymptomatic samples whose age were 16 years and older.

2.8.2 Statistical Method

Most of the comparison between 2 and 3 groups of data were analysed using Chi-Square test and their degree of freedom were 1 and 2, respectively. While the comparison of age of onset and final visual acuity (logMAR) between 2 and 3 groups were analysed using Mann-Whitney test and Kruskal-Wallis test, respectively.

2.8.2.1 Hypothesis of statistical analysis

2.8.2.1.1 The clinical manifestation of G11778A with secondary mutation patients and their maternal relatives were different from those of the G11778A without secondary mutation.

2.8.2.1.2 The frequency of each of RFLP and HVS-1 polymorphisms were different between 100 normal controls and 30 LHON individuals.

2.8.2.1.3 Length heteroplasmy was associated with T16189C mutation in the HVS-1 sequence.

2.8.2.1.4 The 9-bp deletion in COII/$tRNA^{Lys}$ was associated with T16189C mutation and length heteroplasmy.

2.8.2.1.5 The frequency of mitochondrial haplogroup was different among the normal controls and LHON patients.

2.8.2.1.6 The gender and mutation load found in the affected persons of the G11778A LHON families were different from those in the unaffected persons.

2.8.2.1.7 The clinical manifestation and mutation load of G11778A affected persons were different among haplogroup M, B and B*.

2.8.2.1.8 The gender and frequency of G11778A heteroplasmy in the unaffected persons were different among haplogroup M, B and B*.

2.8.2.1.9 The affected male in the G11778A LHON families were different in the clinical manifestation and G11778A heteroplasmy from the affected female in those LHON families.

2.8.2.1.10 The clinical manifestation and mutation load of affected male in the G11778A LHON families were different among haplogroup M, B and B*.

2.8.2.1.11 The clinical manifestation and mutation load of affected female in the G11778A LHON families were different among haplogroup M, B and B*.

2.8.2.1.12 The homoplasmic affected persons were different in the clinical manifestation from the heteroplasmic affected persons.

2.8.2.1.13 The clinical manifestation of affected homoplasmic persons in the G11778A LHON families were different among haplogroup M, B and B*.

2.8.2.1.14 The clinical manifestation of affected heteroplasmic persons in the G11778A LHON families were different among haplogroup M, B and B*.

CHAPTER IV
RESULTS

1. Detection of LHON mutations

1.1 Detection of G11778A primary mutation

All of the 30 unrelated LHON subjects used in this study were positive for the G11778A mutation.

1.2 Detection of the other LHON mutations

The other primary LHON mutations and the secondary mutations were determined either by RFLP analysis or direct sequencing in one individual from each LHON family. The result of LHON mutation detection in the LHON patients was shown in the Table 7. The secondary LHON mtDNA mutation C3497T and G3316A were found in two samples, F11 and F19, respectively. No other primary and secondary LHON mutations were found in the group of LHON samples.

The G11778A LHON patients and their maternal relatives were also analyses. A total of 152 cases in 30 G11778A LHON families were observed. The detail of clinical manifestation and mutation load of each sample were shown in Appendix D. The overall of their clinical manifestation and mutation load were analysed in 7 below.

The statistical analysis of G11778A patients and their maternal relatives who do or do not have secondary mutation were showed in Table 8. Of the G11778A with secondary mutation G3316A and C3497T family members, the frequency of affected persons were 57.1% (4/7) and 85.7% (6/7), respectively. While the affected persons found in the other G11778A families were 39.9% (55/138). There was statistical significant difference between the frequency of affected persons in the G11778A samples who do or do not have secondary mutation either G3316A or C3497T (p-value=0.042).

Table 7. The result of primary and secondary LHON mutation detection in 30 unrelated LHON patients.

Subject no.	Primary mutation					Secondary mutation																							
	G11778A	G13460A	G14459A	T14484C	G15245A	G3460A	T3394C	G3394T	C3497T	G3635A	A4136G	T4160C	C4171A	T4216C	A4917G	G5244A	G7444A	G9738T	G9804A	G13708A	G13730A	C14487A	C14484A	A14495G	T14498C	C15612T	A15908G	G15812A
F1	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F2	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F3	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F4	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F5	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F6	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F7	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F8	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F9	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F10	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F11	+	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F12	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F13	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F14	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F15	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F16	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F17	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F18	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F19	+	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F20	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F21	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F22	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F23	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F24	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F25	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F26	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F27	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F28	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F29	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
F30	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Table 8. The clinical manifestation and mutation load compared between the G11778A patients and their maternal relatives with or without secondary mutation either G3316A or C3497T.

Factors	Secondary mutation			p-value
	No secondary mutation (Total=138)	G3316A (Total=7)	C3497T (Total=7)	
Affected status (N) :				
Affected cases (N, %)	55 (39.9%)	4 (57.1%)	6 (85.7%)	0.042*
Unaffected cases (N, %)	83 (60.1%)	3 (42.9%)	1 (14.3%)	
Affected group :				
Mutant mtDNA status :				
Homoplasmy (N, %)	50 (90.9%)	0 (0%)	6 (100%)	>0.001*
Heteroplasmy (N, %)	5 (9.1%)	4 (100%)	0 (0%)	
Age of onset :				
Total (N)	48	4	6	0.124
Median (years)	20	14.5	13	
Min-Max (years)	6-53	10-20	8-33	
Final Visual Acuity (VA) :				
Total (N, no. of eyes)	46 (91 eyes)	4 (8 eyes)	5 (10 eyes)	0.239
Median (logMAR)	2.00	2.00	1.51	
Min-Max (logMAR)	0.00-3.00	1.30-3.00	0.70-2.00	
Unaffected group :				
Mutant mtDNA status :				
Homoplasmy (N, %)	50 (60.2%)	1 (33.3%)	1 (100%)	0.460
Heteroplasmy (N, %)	33 (39.8%)	2 (66.7%)	0 (0%)	

* p-value<0.05 and considered significant.

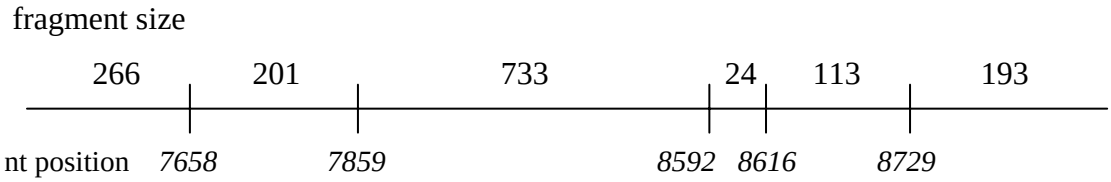
In the affected group (Table 8), all of G11778A with secondary mutation G3316A individuals were heteroplasmy whereas none of G11778A with secondary mutation C3497T individuals were heteroplamy. The heteroplasmic persons found in the G11778A without secondary mutation group were 9.1% (5/55). There was significantly different between the heteroplasmic persons found in the G11778A with and without secondary mutation G3316A and C3497T individuals. The age of onset ranged from 10 to 20 years (median=14.5 years) in the G11778A with G3316A individuals, from 8 to 33 years (median=13 years) in the G11778A with C3497T individuals and from 6 to 53 years (median=20 years) in the G11778A without secondary mutation. No significantly different in the age of onset among these 3 groups. The final visual acuity (VA) ranged from 1.30 to 3.00 logMAR (median=2.00 logMAR, Snellen visual acuity=6/600) in the G11778A with G3316A group and from 0.70 to 2.00 logMAR (median=1.51 logMAR, Snellen visual acuity=6/192) in the G11778A with C3497T group whereas from 0.00 to 3.00 logMAR (median=2.00 logMAR, Snellen visual acuity=6/600) in the G11778A without secondary mutation group. As in the age of onset, the final VA between 3 groups were not statistical significantly different.

In the unaffected group, all of G11778A with C3497T secondary mutation individuals were homoplasmy whereas the heteroplasmy individuals found in the G11778A with secondary mutation G3316A and without secondary mutation were 66.7% (2/3) and 39.8% (33/83), respectively. There was no significantly different between the heteroplasmy of 3 groups (p-value=0.460).

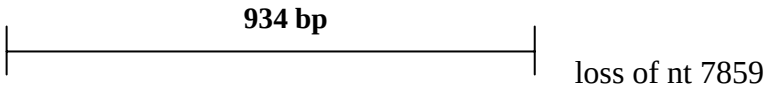
2. Determination of mtDNA haplotypes and haplogroups by Restriction Fragment Length Polymorphism (RFLP)

In this study, approximately 22% (600 restriction sites) of the whole mitochondrial sequences were screened using the high-resolution of 18 restriction endonuclease digestion (RFLP). The presence and absence of the restriction sites of all restriction enzymes used in each sample are in Appendix C. An example of mitochondrial variant was shown in Figure 5. The total of 145 polymorphisms in the recognition sites of the restriction enzymes were found in these samples. These high-resolution restriction analysis revealed 88 haplotypes among 100 normal controls

A.



B.



C.

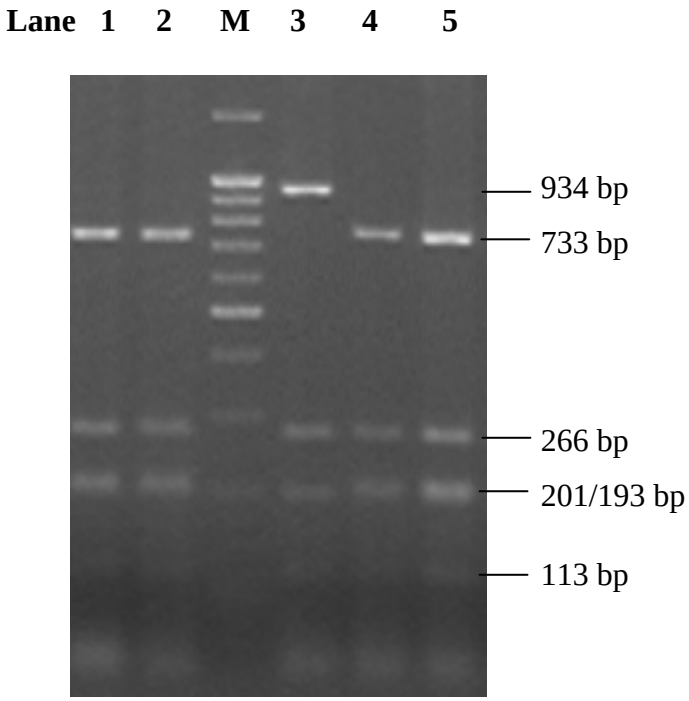


Figure 5A-C. The polymorphism of the *Mbo*I site at nucleotide (nt) 7859. A. The restriction pattern of the 1530 bp PCR product from nt 7392-8921 digested with *Mbo*I. The numbers (above the horizontal line) indicated the fragment sizes which were 733, 266, 201, 193, 113 and 24 bp, respectively and the italics number (below the vertical line) indicated the first nucleotide of the recognition sequence of *Mbo*I relative to the rCRS. **B.** The additional 934 bp fragment and the absence of 733 and 201 bp fragment in size were found when the 7859 site was lost. **C.** 2% agarose gel showed the *Mbo*I variants at nt 7859. Lane M was the 100 bp ladder. Lane 1, 2, 4 and 5 showed the presence of the *Mbo*I restriction site at nt position 7859. Lane 3 showed the absence of the *Mbo*I restriction site at nt position 7859.

(C1,... C59, C61,…C77, C79, C80, C81, C84,…C102, C104, C105) and 27 haplotypes among 30 LHON individuals (F1-F30). The frequencies of each polymorphism found were shown in Table 9. Many polymorphisms found in the LHON samples were not much difference in the normal controls while many polymorphisms found in the LHON showed some different compared to normal controls. The frequency difference of the RFLP polymorphisms in the LHON samples which were equal and more 10% of the normal controls were -3534*Hae*III (17%), -3537*Dde*I (17%), -6957*Hae*III (14%), -7013*Rsa*I (10%), +9820*Hin*fI (12%), +10394*Dde*I (26%), +10397*Alu*I (14%), -14859*Hha*I (11%), -15234*Hin*fI (11%) and +15590*Xho*II (13%) (10 positions). The frequency difference of polymorphisms found equal and more than 10% in the normal controls than in the LHON samples were the -9052*Hae*II (15%), -9053*Hha*I (15%), -12406*Hin*cII (16%) and -12406*Hpa*I (16%) (4 positions). These 14 RFLP polymorphisms were also tested different in the frequency between the normal controls and LHON individuals and showed in Table 10. There were significantly different only in the -3534*Hae*III, -3537*Dde*I, -7013*Rsa*I, +10394*Dde*I, -12406*Hin*cII, -12406*Hpa*I, -14859*Hha*I and +15590*Xho*II polymorphisms between normal controls and LHON individuals and their p-value were 0.040, >0.001, 0.012, 0.012, 0.043, 0.043, 0.042 and 0.041, respectively.

The haplogroup (haplotype grouping) of all the samples in this study were determined by both RFLP and 9-bp deletion information according to the criteria in Table 1. The haplogroup of each sample was shown in Table 11. Eight haplogroups; A, B, B*, C, D, G, F and M were found in our samples. Some of our samples can be classified into two haplogroups in one individual. These haplogroup was A/B in one sample C28 (1% in normal controls). The haplogroup distribution of the studied samples was in Table 12. The frequency of the samples carrying mitochondrial haplogroup A, B, B*, C, D, G, F and M determined by RFLP and 9-bp deletion information in the normal controls were 3%, 11%, 9%, 1%, 1%, 1%, 15% and 43%, respectively. The frequency of haplogroup A, B, B*, C, D, G, F and M determined by RFLP pattern and 9-bp deletion information in the LHON individual were 0%, 10%, 20% 0%, 0%, 0%, 0% and 57%, respectively. The most common haplogroup in both of normal controls and the LHON samples was haplogroup M which were 43% and 57%, respectively. Haplogroup A, C, D, G and F were not found in the LHON

Table 9. The frequency of each variant in the recognition sites of restriction endonuclease in 100 normal controls and 30 LHON subjects.

RFLP variants			Controls (N, %)	LHON (N, %)	Frequency difference (%LHON)-(%controls)
+	663	*Hae*III	4 (4%)	0 (0%)	-4
-	675	*Alu*I	7 (7%)	1 (3%)	-4
-	951	*Mbo*I	2 (2%)	0 (0%)	-2
-	971	*Alu*I	1 (1%)	0 (0%)	-1
-	1004	*Hinc*II	5 (5%)	0 (0%)	-5
+	1229	*Taq*I	1 (1%)	0 (0%)	-1
+	2349	*Mbo*I	1 (1%)	0 (0%)	-1
-	2758	*Rsa*I	2 (2%)	0 (0%)	-2
-	3315	*Hae*III	0 (0%)	1 (3%)	3
+	3391	*Hae*III	1 (1%)	0 (0%)	-1
-	3534	*Dde*I	10 (10%)	8 (27%)	17
-	3537	*Alu*I	0 (0%)	5 (17%)	17
-	4310	*Alu*I	1 (1%)	0 (0%)	-1
-	4341	*Hinf*I	0 (0%)	2 (7%)	7
-	4685	*Alu*I	1 (1%)	0 (0%)	-1
+	4793	*Hae*III	4 (4%)	0 (0%)	-4
+	4830	*Hae*II	1 (1%)	0 (0%)	-1
+	4831	*Hha*I	2 (2%)	0 (0%)	-2
-	4848	*Hae*III	5 (5%)	0 (0%)	-5
+	4965	*Alu*I	1 (1%)	0 (0%)	-1
+	4886	*Dde*I	2 (2%)	0 (0%)	-2
-	5054	*Rsa*I	4 (4%)	0 (0%)	-4
-	5176	*Alu*I	1 (1%)	1 (3%)	2
+	5260	*Ava*II	0 (0%)	1 (3%)	3
-	5261	*Hae*III	1 (1%)	0 (0%)	-1
+	5351	*Hha*I	5 (5%)	2 (7%)	2
+	5370	*Taq*I	4 (4%)	0 (0%)	-4
-	5644	*Alu*I	0 (0%)	1 (3%)	3
+	5818	*Dde*I	4 (4%)	0 (0%)	-4
-	6211	*Hinf*I	1 (1%)	0 (0%)	-1
-	6260	*Hae*III	1 (1%)	0 (0%)	-1
-	6377	*Dde*I	2 (2%)	0 (0%)	-2
+	4901	*Mbo*I	1 (1%)	0 (0%)	-1
-	6850	*Hpa*II	1 (1%)	0 (0%)	-1
-	6867	*Alu*I	0 (0%)	2 (7%)	7
-	6957	*Hae*III	9 (9%)	7 (23%)	14
-	7013	*Rsa*I	0 (0%)	3 (10%)	10
+	7241	*Rsa*I	1 (1%)	0 (0%)	-1
+	7570	*Mbo*I	1 (1%)	0 (0%)	-1
-	7598	*Hha*I	2 (2%)	0 (0%)	-2
+	7828	*Hha*I	5 (5%)	0 (0%)	-5
-	7853	*Hinc*II	11 (11%)	4 (13%)	2
-	7859	*Mbo*I	6 (6%)	0 (0%)	-6
+	8078	*Rsa*I	1 (1%)	0 (0%)	-1
+	8148	*Hae*III	6 (6%)	0 (0%)	-6
+	8165	*Hae*III	1 (1%)	0 (0%)	-1
+	8198	*Alu*I	1 (1%)	0 (0%)	-1
+	8249	*Ava*II	1 (1%)	0 (0%)	-1
+	8090	*Hae*III	1 (1%)	0 (0%)	-1
-	8250	*Hae*III	4 (4%)	0 (0%)	-4

Table 9 (continued). The frequency of each variant in the recognition sites of restriction endonuclease in 100 normal controls and 30 LHON subjects.

RFLP variants			Controls (N, %)	LHON (N, %)	Frequency difference (%LHON)-(%controls)
-	8303	*Alu*I	1 (1%)	0 (0%)	-1
-	8572	*Hae*III	1 (1%)	0 (0%)	-1
+	8678	*Alu*I	1 (1%)	0 (0%)	-1
+	8714	*Dde*I	1 (1%)	0 (0%)	-1
-	9020	*Pst*I	1 (1%)	0 (0%)	-1
-	9025	*Hae*III	2 (2%)	1 (3%)	1
-	9052	*Hae*II	15 (15%)	0 (0%)	-15
-	9053	*Hha*I	15 (15%)	0 (0%)	-15
+	9253	*Hae*III	0 (0%)	1 (3%)	3
-	9380	*Hha*I	1 (1%)	0 (0%)	-1
-	9438	*Hae*III	1 (1%)	1 (3%)	2
-	9553	*Hae*III	0 (0%)	1 (3%)	3
-	9641	*Dde*I	1 (1%)	0 (0%)	-1
-	9644	*Alu*I	1 (1%)	1 (3%)	2
+	9118	*Rsa*I	1 (1%)	0 (0%)	-1
+	9820	*Hin*fI	5 (5%)	5 (17%)	12
+	10028	*Alu*I	1 (1%)	0 (0%)	-1
+	10054	*Hin*fI	1 (1%)	0 (0%)	-1
-	10232	*Alu*I	0 (0%)	1 (3%)	3
+	10252	*Taq*I	1 (1%)	0 (0%)	-1
-	10254	*Mbo*I	2 (2%)	0 (0%)	-2
-	10256	*Xba*I	1 (1%)	0 (0%)	-1
+	10394	*Dde*I	57 (57%)	25 (83%)	26
+	10397	*Alu*I	46 (46%)	18 (60%)	14
+	10325	*Rsa*I	0 (0%)	1 (3%)	3
+	10407	*Rsa*I	1 (1%)	0 (0%)	-1
-	10631	*Dde*I	0 (0%)	1 (3%)	3
+	10636	*Hae*III	0 (0%)	1 (3%)	3
+	10806	*Hin*fI	2 (2%)	0 (0%)	-2
+	8719	*Ava*II	1 (1%)	0 (0%)	-1
+	11002	*Hha*I	1 (1%)	0 (0%)	-1
+	11074	*Dde*I	0 (0%)	2 (7%)	7
+	10517	*Taq*I	1 (1%)	0 (0%)	-1
+	10535	*Mbo*I	1 (1%)	0 (0%)	-1
-	11421	*Taq*I	1 (1%)	0 (0%)	-1
+	11892	*Alu*I	1 (1%)	0 (0%)	-1
+	11624	*Xba*I	0 (0%)	1 (3%)	3
+	11949	*Hin*fI	1 (1%)	0 (0%)	-1
+	12185	*Hae*III	1 (1%)	0 (0%)	-1
-	12282	*Alu*I	1 (1%)	0 (0%)	-1
+	12345	*Rsa*I	0 (0%)	1 (3%)	3
-	12406	*Hinc*II	16 (16%)	0 (0%)	-16
-	12406	*Hpa*I	16 (16%)	0 (0%)	-16
-	12629	*Ava*II	1 (1%)	0 (0%)	-1
+	12629	*Mbo*I	1 (1%)	0 (0%)	-1
+	12729	*Alu*I	1 (1%)	0 (0%)	-1
+	12763	*Alu*I	2 (2%)	0 (0%)	-2
+	12810	*Rsa*I	1 (1%)	0 (0%)	-1
-	12891	*Dde*I	1 (1%)	0 (0%)	-1

Table 9 (continued). The frequency of each variant in the recognition sites of restriction endonuclease in 100 normal controls and 30 LHON subjects.

RFLP variants			Controls (N, %)	LHON (N, %)	Frequency difference (%LHON)-(%controls)
+	12940	*Hha*I	1 (1%)	0 (0%)	-1
+	12949	*Hae*II	1 (1%)	0 (0%)	-1
-	13051	*Hae*III	0 (0%)	1 (3%)	3
+	13104	*Mbo*I	1 (1%)	0 (0%)	-1
-	13259	*Hin*cII	5 (5%)	1 (3%)	-2
+	13262	*Alu*I	1 (1%)	0 (0%)	-1
+	13542	*Rsa*I	1 (1%)	0 (0%)	-1
-	13634	*Hin*cII	1 (1%)	0 (0%)	-1
+	13707	*Hae*III	1 (1%)	0 (0%)	-1
-	14015	*Alu*I	1 (1%)	0 (0%)	-1
-	14258	*Bam*HI	1 (1%)	0 (0%)	-1
+	14749	*Hae*III	1 (1%)	0 (0%)	-1
+	14749	*Mbo*I	2 (2%)	0 (0%)	-2
-	14858	*Hae*II	1 (1%)	1 (3%)	2
-	14859	*Hha*I	2 (2%)	4 (13%)	11
-	14869	*Mbo*I	1 (1%)	0 (0%)	-1
+	14899	*Alu*I	0 (0%)	2 (7%)	7
-	14976	*Hin*fI	0 (0%)	1 (3%)	3
-	15047	*Hae*III	1 (1%)	0 (0%)	-1
-	15152	*Hae*III	2 (2%)	0 (0%)	-2
-	15234	*Hin*fI	12 (12%)	7 (23%)	11
+	15235	*Mbo*I	11 (11%)	6 (20%)	9
+	15595	*Hae*III	2 (2%)	0 (0%)	-2
+	15727	*Dde*I	1 (1%)	0 (0%)	-1
-	15883	*Hae*III	2 (2%)	1 (3%)	1
-	15925	*Hpa*II	1 (1%)	0 (0%)	-1
-	15996	*Dde*I	1 (1%)	0 (0%)	-1
-	16000	*Hin*fI	1 (1%)	0 (0%)	-1
-	16049	*Rsa*I	2 (2%)	0 (0%)	-2
-	16065	*Hin*fI	1 (1%)	0 (0%)	-1
+	16145	*Mbo*I	3 (3%)	1 (3%)	0
-	16156	*Rsa*I	6 (6%)	0 (0%)	-6
-	16208	*Rsa*I	5 (5%)	4 (13%)	8
+	16242	*Pst*I	2 (2%)	0 (0%)	-2
+	16275	*Rsa*I	1 (1%)	0 (0%)	-1
-	16303	*Rsa*I	17 (17%)	2 (7%)	-10
+	16318	*Hae*III	3 (3%)	0 (0%)	-3
-	16380	*Dde*I	2 (2%)	2 (7%)	5
+	15590	*Xho*II	4 (4%)	5 (17%)	13
+	16389	*Hin*fI	3 (3%)	3 (10%)	7
-	16390	*Ava*II	4 (4%)	2 (7%)	3
+	16398	*Hae*III	3 (3%)	0 (0%)	-3
+	16398	*Mbo*I	2 (2%)	0 (0%)	-2
+	16494	*Hpa*II	1 (1%)	0 (0%)	-1
+	16528	*Dde*I	1 (1%)	0 (0%)	-1
+	16517	*Hae*III	67 (67%)	1 (3%)9	-4

Table 10. The RFLP and HVS-1 polymorphisms found 10% or higher in different frequency of 100 normal controls and 30 LHON individuals and their p-value of comparison between controls and LHON.

Polymorphisms			Normal controls (N=100)	LHON (N=30)	%LHON-%Controls	p-value
RFLP:						
-	3534	*Dde*I	10 (10%)	8 (27%)	17	0.040*
-	3537	*Alu*I	0 (0%)	5 (17%)	17	>0.001*
-	6957	*Hae*III	9 (9%)	7 (23%)	14	0.083
-	7013	*Rsa*I	0 (0%)	3 (10%)	10	0.012*
-	9052	*Hae*II	15 (15%)	0 (0%)	-15	0.054
-	9053	*Hha*I	15 (15%)	0 (0%)	-15	0.054
+	9820	*Hin*fI	5 (5%)	5 (17%)	12	0.078
+	10394	*Dde*I	57 (57%)	25 (83%)	26	0.012*
+	10397	*Alu*I	46 (46%)	18 (60%)	14	0.256
-	12406	*Hin*cII	16 (16%)	0 (0%)	-16	0.043*
-	12406	*Hpa*I	16 (16%)	0 (0%)	-16	0.043*
-	14859	*Hha*I	2 (2%)	4 (13%)	11	0.042*
-	15234	*Hin*fI	12 (12%)	7 (23%)	11	0.229
+	15590	*Xho*II	4 (4%)	5 (17%)	13	0.041*
HVS-1 sequence:						
C	16140	T	10 (10%)	6 (20%)	10	0.252
C	16172	T	18 (18%)	1 (3%)	-15	0.080
C	16182	A	12 (12%)	8 (27%)	15	0.088
C	16183	A	27 (27%)	13 (43%)	16	0.150
C	16304	T	23 (23%)	0 (0%)	-23	0.009*
C	16362	T	20 (20%)	1 (3%)	-17	0.052

* p-value<0.05 and considered significant.

Table 11. The definite haplogroup determined by at least 3 of 4 criteria which were the polymorphisms in RFLP and 9-bp deletion information and their phylogenetic tree and HVS-1 sequence data and their phylogenetic tree in 100 normal controls and 30 LHON individuals.

Subject no.	RFLP haplogroup		HVS-1 haplogroup		Definite haplogroup
	From criteria	From phylogenetic tree	From criteria	From phylogenetic tree	
C1	B*	B*	B*	B*	**B***
C2	A9	A9	M	M	
C3	B	B	B	B	**B**
C4	B*	B*	B*	B*	**B***
C5	F	F	F	F	**F**
C6	M	M	M	M	**M**
C7					
C8	F	F	F	F	**F**
C9	F	F	F	F	**F**
C10	M	M	D	D	**M**
C11	B	B	B,B*	B	**B**
C12			D	M	
C13			F	F	
C14	M	F	D	D	**M**
C15			M	M	
C16	B*	B*	B*	B*	**B***
C17			M	M	
C18	M	M	D	D	**M**
C19	M	M	M	M	**M**
C20	F	F	F	F	**F**
C21	B	B	B	B	**B**
C22			D	D	
C23	M	M	C	C	**M**
C24	B	B	B	B	**B**
C25	M	M	M	M	**M**
C26	B*	B*	B*	B*	**B***
C27	M	M	M	M	**M**
C28	A9,B	A	M	M	
C29	F	F	F	F	**F**
C30	M	M	M	M	**M**
C31	B*	B*	B*	B*	**B***
C32	M	M	M	M	**M**
C33	M	M	M	M	**M**
C34	M	M	M	M	**M**
C35					
C36		B*	B*	B*	**B***
C37	A1	A1	A	A	**A**
C38	M	M	D	D	**M**

Table 11 (continued). The definite haplogroup determined by at least 3 of 4 criteria which were the polymorphisms in RFLP and 9-bp deletion information and their phylogenetic tree and HVS-1 sequence data and their phylogenetic tree in 100 normal controls and 30 LHON individuals.

Subject no.	RFLP haplogroup		HVS-1 haplogroup		Definite haplogroup
	From criteria	From phylogenetic tree	From criteria	From phylogenetic tree	
C39	M	M	M	M	**M**
C40	M	M	F, M	M	**M**
C41	B	B	B,B*	B	**B**
C42	F	F		F	**F**
C43	F	F	F	F	**F**
C44	M	M	M	M	**M**
C45	F	F	F	F	**F**
C46	M	M	M	M	**M**
C47			F	F	
C48	M	M	M, P	M	**M**
C49	M	M	D	D	**M**
C50	M	M	M	M	**M**
C51	A9	A9	M	M	
C52	M	M	M	M	**M**
C53	M	M	D	D	**M**
C54	F	F	F	F	**F**
C55	M	M	M	M	**M**
C56	M	M	M	M	**M**
C57	B	B	B	B	**B**
C58	M	M	D	D	**M**
C59			F	F	
C61	M	M	M	M	**M**
C62	M	M	F, M	M	**M**
C63	M	M	M	M	**M**
C64	M	M	D	D	**M**
C65	B	B			
C66	B*	B*	B*	B*	**B***
C67	M	M	M	M	**M**
C68	M	M	M	M	**M**
C69	M	M	M	M	**M**
C70	M	M	F, M	M	**M**
C71	M	M	M	M	**M**
C72	F	F	F	F	**F**
C73	F	F	F	F	**F**
C74	M	M	D	D	**M**
C75		M	M, P	M	**M**
C76	G	M	D	D	**M**

Table 11 (continued). The definite haplogroup determined by at least 3 of 4 criteria which were the polymorphisms in RFLP and 9-bp deletion information and their phylogenetic tree and HVS-1 sequence data and their phylogenetic tree in 100 normal controls and 30 LHON individuals.

Subject no.	RFLP haplogroup		HVS-1 haplogroup		Definite haplogroup
	From criteria	From phylogenetic tree	From criteria	From phylogenetic tree	
C77	M	M	M	M	**M**
C79	B	B	B	B	**B**
C80	M	M	M	M	**M**
C81	M	M	M	M	**M**
C84	B*	B*	B*	B*	**B***
C85			F	F	
C86	B	B	B	B	**B**
C87	F	F	F	F	**F**
C88	M	M	M	M	**M**
C89		B	M	M	
C90	B	B	B	B	**B**
C91	B*	B*			
C92	M	M	M	M	**M**
C93	D	D	D	D	**D**
C94	M	M	M	M	**M**
C95	C	C	C	C	**C**
C96			F	F	
C97	F	F	F	F	**F**
C98	M	M	M	M	**M**
C99	F	F	F	F	**F**
C100	M	M	M	M	**M**
C101	B*	B*			
C102			F	F	
C104	F	F	F	F	**F**
C105	B	B	B	B	**B**
F1	M	M	M	M	**M**
F2	B*	B*	B*	B*	**B***
F3	B*	B*			
F4	M	M		M	**M**
F5	M	M	M	M	**M**
F6		M	M	M	**M**
F7	B	B		B	**B**
F8	M	M	D	D	**M**
F9	M	M	M	M	**M**
F10	B	B		B	**B**
F11	B	B	B,B*	B	**B**
F12					

Table 11 (continued). The definite haplogroup determined by at least 3 of 4 criteria which were the polymorphisms in RFLP and 9-bp deletion information and their phylogenetic tree and HVS-1 sequence data and their phylogenetic tree in 100 normal controls and 30 LHON individuals.

Subject no.	RFLP haplogroup		HVS-1 haplogroup		Definite haplogroup
	From criteria	From phylogenetic tree	From criteria	From phylogenetic tree	
F13	M	M	M	M	**M**
F14		B*	B*	B*	**B***
F15	M	M	M	M	**M**
F16	M	M	M	M	**M**
F17	M	M	M	M	**M**
F18	M	M	M	M	**M**
F19	B*	B*		B	
F20	M	M	M	M	**M**
F21	M	M		M	**M**
F22	B*	B*	B*	B*	**B***
F23	M	M	M	M	**M**
F24		M			
F25	M	M	M	M	**M**
F26	M	M	M	M	**M**
F27	B*	B*		B	
F28	M	M	M	M	**M**
F29	B*	B*	B*	B*	**B***
F30	M	M	M	M	**M**

Table 12. The distribution of haplogroups determined by RFLP and 9-bp deletion data and HVS-1 sequence data in 100 normal controls and 30 LHON patients.

Haplogroup	N	A	B	B*	F	M	C	D	G	A/B	B/B*	F/M	M/P	Unclassified
determined by														
RFLP and 9-bp deletion														
Controls (N, %)	100	3 (3%)	11 (11%)	9 (9%)	15 (15%)	43 (43%)	1 (1%)	1 (1%)	1 (1%)	1 (1%)	-	-	-	15 (15%)
LHON (N, %)	30	-	3 (10%)	6 (20%)	-	17 (57%)	-	-	-	-	-	-	-	4 (13%)
HVS-1 sequence														
Controls (N, %)	100	1 (1%)	8 (8%)	8 (8%)	20 (20%)	35 (35%)	2 (2%)	13 (13%)	-	-	2 (2%)	3 (3%)	2 (2%)	6 (6%)
LHON (N, %)	30	-	-	4 (13%)	-	15 (50%)	-	1 (3%)	-	-	-	-	-	10 (33.3%)

individuals. The known mitochondrial haplogroups were not able to be classified by RFLP and 9-bp information in 15 normal controls (15%) and 4 LHON individuals (13%). The haplogroup J was found in none of the studied samples.

3. Detection of the 9-bp COII/tRNA^{Lys} deletion

All of the samples in this study were screened for the 9-bp deletion (Figure 6). The results of all samples were presented in Table 13. The 9-bp deletion was found in 23 controls (23% of controls) and 10 LHON individuals (33.3% of LHON samples). The comparison of 9-bp deletion found in the normal controls different from LHON individuals was showed in Table 14. No significantly different between the 9-bp deletion found in the normal controls and LHON individuals (p-value=0.367).

4. Determination of the mitochondrial Control region (D-loop)

The hypervariable segment 1 (HVS-1) from nucleotide 16024-16383 (360 bp) in the mitochondrial control region was also determined. The polymorphisms in the HVS-1 sequence of each sample were shown in Table 15. The total of 108 polymorphisms in the HVS-1 sequences were found in these samples. The 90 haplotypes and 27 haplotypes were found among these 100 normal controls and 30 LHON individuals, respectively. The frequency of each polymorphism was shown in Table 16. Many polymorphisms found in the LHON samples were not more difference than in the normal controls while many polymorphism found in the LHON were equal or higher 10% difference of the normal controls. These polymorphisms were C16140T (10%), C16182A (15%) and C16183A (16%) whereas the polymorphisms found equal or higher than 10% of frequency difference in the normal controls to the LHON samples were C16172T (15%), C16304T (23%) and C16362T (17%). The comparison of these six HVS-1 polymorphisms found in normal controls different from LHON individuals were also showed in Table 10. The statistical analysis was presented significant only in the C16304T mutation (p-value=0.009).

The C to T at nt 16223 mutation was the most found in both normal controls (N=56, 56%) and LHON subjects (N=16, 53%). In addition, the second most common mutation in the HVS-1 in these controls was T16189C whereas this mutation was the

Figure 6. The detection of 9-bp deletion in COII/tRNA^{Lys} between nt 8272 and 8289. The PCR product from nucleotide position 8211-8311 of both the 101 bp of the normal length and 92 bp of the sample harboring 9-bp deletion were shown in 4% Nusieve® 3:1 agarose gel. Lane M was the 100 bp Ladder. Lane 1 was the PCR product of the 101 bp in size of the normal and lane 2 was the PCR product of the 92 bp in size of the sample harboring the 9-bp deletion.

Table 13. The detection result of each sample including the 9-bp deletion, T16189C mutation and length heteroplasmy in 100 normal controls and 30 LHON individuals.

Subject no.	9-bp deletion	T16189C	Length heteroplasmy
C1	+	+	+
C2	-	-	-
C3	+	+	+
C4	+	+	+
C5	-	-	-
C6	-	-	-
C7	-	-	-
C8	-	-	-
C9	-	-	-
C10	-	-	-
C11	+	+	+
C12	-	-	-
C13	-	-	-
C14	-	-	-
C15	-	-	-
C16	+	+	+
C17	-	-	-
C18	-	-	-
C19	-	-	-
C20	-	-	-
C21	+	+	+
C22	-	+	+
C23	+	-	-
C24	+	+	+
C25	-	-	-
C26	+	+	+
C27	-	+	+
C28	+	-	-
C29	-	-	-
C30	-	-	-
C31	+	+	+
C32	-	-	-
C33	-	+	+
C34	-	-	-
C35	-	-	-
C36	+	+	+
C37	-	-	-
C38	-	-	-
C39	-	-	-
C40	-	-	-
C41	+	+	+
C42	-	-	-
C43	-	-	-

Table 13 (continued). The detection result of each sample including the 9-bp deletion, T16189C mutation and length heteroplasmy in 100 normal controls and 30 LHON individuals.

Subject no.	9-bp deletion	T16189C	Length heteroplasmy
C44	-	+	-
C45	-	-	-
C46	-	+	-
C47	-	+	+
C48	-	-	-
C49	-	-	-
C50	-	+	-
C51	-	-	-
C52	-	+	+
C53	-	-	-
C54	-	-	-
C55	-	-	-
C56	-	-	-
C57	+	+	+
C58	-	-	-
C59	-	-	-
C61	-	-	-
C62	-	-	-
C63	-	-	-
C64	-	+	+
C65	+	+	+
C66	+	+	+
C67	-	-	-
C68	-	+	-
C69	-	+	+
C70	-	-	-
C71	-	-	-
C72	-	-	-
C73	-	-	-
C74	-	-	-
C75	-	-	-
C76	-	-	-
C77	-	-	-
C79	+	+	-
C80	-	-	-
C81	-	-	-
C84	+	+	+
C85	-	-	-
C86	+	+	+
C87	-	+	+
C88	-	-	-
C89	-	-	-
C90	+	+	+

Table 13 (continued). The detection result of each sample including the 9-bp deletion, T16189C mutation and length heteroplasmy in 100 normal controls and 30 LHON individuals.

Subject no.	9-bp deletion	T16189C	Length heteroplasmy
C91	+	+	+
C92	-	-	-
C93	-	-	-
C94	-	-	-
C95	-	-	-
C96	-	+	+
C97	-	-	-
C98	-	-	-
C99	-	-	-
C100	-	-	-
C101	+	+	-
C102	-	-	-
C104	-	-	-
C105	+	+	+
F1	-	-	-
F2	+	+	+
F3	+	-	-
F4	-	+	+
F5	-	+	+
F6	-	+	+
F7	+	+	+
F8	-	-	-
F9	-	-	-
F10	+	+	-
F11	+	+	+
F12	-	-	-
F13	-	-	-
F14	+	+	+
F15	-	-	-
F16	-	-	-
F17	-	-	-
F18	-	-	-
F19	+	+	+
F20	-	-	-
F21	-	-	-
F22	+	+	+
F23	-	-	-
F24	-	-	-
F25	-	-	-
F26	-	-	-
F27	+	+	+
F28	-	-	-
F29	+	+	+
F30	-	-	-

Table 14. The association of 9-bp deletion, T16189C mutation and length heteroplasmy between 100 normal controls and 30 LHON individuals.

Factors	Number of cases (%)		p-value
	Normal (N=100)	LHON (N=30)	
9-bp deletion	23 (23%)	10 (33.3%)	0.367
T16189C	34 (34%)	12 (40%)	0.700
Length heteroplasmy	28 (28%)	11 (36.7%)	0.496

Table 15. Nucleotide variants in the HVS-1 sequence from nt 16024 to nt 16383 of the 100 normal controls and 30 LHON patients.

subject	Nuclotide Position																																																																																																				
	16024	16038	16051	16059	16067	16069	16078	16085	16086	16092	16093	16104	16108	16124	16126	16129	16130	16134	16140	16145	16147	16148	16154	16162	16167	16169	16172	16175	16176	16181	16182	16183	16184	16188	16189	16192	16193	16203	16209	16213	16214	16215	16217	16218	16223	16224	16232	16234	16235	16239	16243	16249	16256	16257	16259	16260	16261	16263	16266	16267	16271	16272	16274	16275	16278	16286	16289	16290	16291	16292	16293	16294	16295	16296	16297	16298	16299	16304	16305	16311	16316	16317	16318	16319	16323	16325	16327	16334	16335	16342	16343	16352	16353	16354	16355	16356	16357	16362	16368	16381
rCRS	T	A	A	A	C	C	A	C	T	T	T	C	C	T	T	G	G	C	T	G	C	C	T	A	C	C	T	A	C	A	A	A	C	C	T	C	C	A	T	G	C	A	T	C	C	T	C	C	A	C	T	T	C	C	C	C	C	T	C	C	T	A	G	A	C	C	A	C	C	C	A	C	C	C	T	T	A	T	A	T	A	A	A	G	T	T	C	T	A	T	A	T	C	C	C	T	T	T	T	T
C1	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	C	C	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C2	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C3	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	C	C	.	.	C	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
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C42	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	A	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C43	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	G	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C44	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C45	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	A	.	.	.	.	.	.	.	G	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Table 15 (continued). Nucleotide variants in the HVS-1 sequence from nt 16024 to nt 16383 of the 100 normal controls and 30 LHON patients.

Nuclotide Position

subject	16024	16038	16051	16059	16067	16069	16078	16085	16086	16092	16093	16104	16108	16124	16126	16129	16130	16134	16140	16145	16147	16148	16154	16162	16167
rCRS	**T**	**A**	**A**	**A**	**C**	**C**	**A**	**C**	**T**	**T**	**T**	**C**	**C**	**T**	**T**	**G**	**G**	**C**	**T**	**G**	**C**	**C**	**T**	**A**	**C**
C46	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C47	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C48	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C49	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C50	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.
C51	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C52	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C53	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C54	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C55	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C56	.	.	.	.	T	.	.	.	C	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C57	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C58	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C59	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C61	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C62	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C63	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C64	.	.	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C65	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C66	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.
C67	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C68	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.
C69	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C70	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.
C71	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C72	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	A	.	.	.	.	.	.	.	G	.
C73	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C74	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C75	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C76	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C77	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	A	.	.	.	.	.	.	.	.	.
C79	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.
C80	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C81	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C84	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.
C85	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T
C86	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C87	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C88	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.
C89	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C90	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

subject	16169	16172	16175	16176	16181	16182	16183	16184	16188	16189	16192	16193	16203	16209	16213	16214	16215	16217	16218	16223	16224	16232	16234	16235	16239
rCRS	**C**	**T**	**A**	**C**	**A**	**A**	**A**	**C**	**C**	**T**	**C**	**C**	**A**	**T**	**G**	**C**	**A**	**T**	**C**	**C**	**T**	**C**	**C**	**A**	**C**
C46	.	.	.	.	.	.	.	T	.	C	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C47	.	.	.	.	.	.	C	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C48	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C49	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C50	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C51	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	T	.	.
C52	.	.	.	.	.	.	C	.	.	C	.	.	.	C	.	.	.	.	.	T	.	.	.	.	.
C53	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C54	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C55	T	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C56	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	T	.	.	.	.	.
C57	.	.	.	.	C	C	C	.	.	C	.	.	.	.	A	.	.	C	.	.	.	.	.	.	.
C58	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C59	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C61	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	T	.	.	.	.	.
C62	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	T	.	.	.	.	.
C63	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	T	.	.
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C66	.	.	.	.	.	C	C	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C67	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C68	.	.	.	.	.	.	.	T	.	C	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C69	.	.	.	.	.	.	C	.	.	C	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C70	.	.	.	.	G	.	.	.	.	.	T	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C71	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C72	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C73	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C74	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	T	.	.
C75	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C76	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C77	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	T	.	.
C79	.	.	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	C	.	.	.	.	.	G	.
C80	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	C	.	.	.	.
C81	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	G	.	.	T	.	.	.	.	.
C84	.	.	.	.	.	C	C	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.
C85	.	.	.	.	.	.	.	.	.	.	.	.	G	.	.	.	.	.	.	.	.	.	.	.	.
C86	.	.	.	.	.	.	C	.	.	C	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.
C87	.	.	.	.	.	.	C	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C88	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	T	.	.
C89	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C90	.	.	.	.	.	.	C	.	.	C	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.

subject	16243	16249	16256	16257	16259	16260	16261	16263	16266	16267	16271	16272	16274	16275	16278	16286	16289	16290	16291	16292	16293	16294	16295	16296	16297
rCRS	**T**	**T**	**C**	**C**	**C**	**C**	**C**	**T**	**C**	**C**	**T**	**A**	**G**	**A**	**C**	**C**	**A**	**C**	**C**	**C**	**A**	**C**	**C**	**C**	**T**
C46	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C47	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C48	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C49	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.
C50	.	C	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.
C51	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	T	.	.	C	.	.	.	.
C52	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C53	.	.	.	.	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.
C54	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C55	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.
C56	.	.	.	.	.	.	.	.	.	.	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.
C57	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C58	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C59	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
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C66	.	.	.	.	.	.	T	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C67	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	T	.	.
C68	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C
C69	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C
C70	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.
C71	C	.	.	.	.	.	.	.	.	.	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.
C72	.	.	.	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C73	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C74	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C75	.	.	.	.	.	.	.	C	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.
C76	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.
C77	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.
C79	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C80	.	.	.	.	.	.	.	C	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.
C81	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C84	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C85	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C86	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C87	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C88	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.
C89	.	.	.	A	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.
C90	.	.	.	.	.	.	T	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

subject	16298	16299	16304	16305	16311	16316	16317	16318	16319	16323	16325	16327	16334	16335	16342	16343	16352	16353	16354	16355	16356	16357	16362	16368	16381
rCRS	**T**	**A**	**T**	**A**	**T**	**A**	**A**	**G**	**T**	**T**	**C**	**T**	**A**	**T**	**A**	**T**	**C**	**C**	**C**	**T**	**T**	**T**	**T**	**T**	**T**
C46	C	.	.	.	C	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C47	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C48	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	.
C49	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.
C50	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.
C51	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C52	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C53	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	C
C54	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.
C55	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C56	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C57	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.
C58	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	N	C
C59	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C61	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C62	.	.	C	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C63	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C64	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.
C65	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.	T	.	.	.	.	.
C66	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C67	.	.	.	.	.	.	.	.	.	.	.	.	.	G	.	.	.	.	.	.	.	.	.	.	.
C68	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C69	.	.	.	.	.	.	.	.	.	.	.	T	.	.	.	.	.	.	.	T	.	.	.	.	.
C70	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C71	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C72	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C73	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C74	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	C	.	.
C75	.	.	.	.	C	.	.	C	.	.	.	.	.	.	.	G	.	.	.	.	.	C	.	.	.
C76	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	C	.	.
C77	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C79	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C80	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C81	.	.	.	.	.	G	.	.	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C84	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C85	.	.	C	.	.	.	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C86	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C87	.	.	C	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C88	.	.	.	.	.	.	.	.	A	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C89	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.
C90	.	G	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.

Table 15 (continued). Nucleotide variants in the HVS-1 sequence from nt 16024 to nt 16383 of the 100 normal controls and 30 LHON patients.

subject	Nuclotide Position
	16024 16035 16055 16067 16089 16090 16222 16233 16244 16246 16290 16402 16405 16427 16429 16457 16483 16519 16524 16527 16528 16529 16530 16531 16532 16533 16534 16535 16536 16537 16538 16539 16540 16541 16542 16543 16544 16545 16546 16547 16548 16549 16550 16551 16552 16553 16554 16555 16556 16557 16558 16559 16560 16561 16562 16563 16564 16565 16566 16567 16568 16569 16570 16571 16572 16573 16574 16575 16576 16577 16578 16579 16580 16581 16582 16583 16584 16585 16586 16587 16588 16589 16590 16591 16592 16593 16594 16595 16596 16597 16598 16599 16600 16601 16602 16603 16604 16605 16606 16607 16608 16609 16610 16611 16612 16613 16614 16615 16616 16617 16618 16619 16620 16621 16622 16623 16624 16625 16626 16627 16628 16629 16630 16631 16632 16633 16634 16635 16636 16637 16638 16639 16640 16641 16642 16643 16644 16645 16646 16647 16648 16649 16650 16651 16652 16653 16654 16655 16656 16657 16658 16659 16660 16661 16662 16663 16664 16665 16666 16667 16668 16669 16670 16671 16672 16673 16674 16675 16676 16677 16678 16679 16680 16681 16682 16683 16684 16685 16686 16687 16688 16689 16690 16691 16692 16693 16694 16695 16696 16697 16698 16699 16700 16701 16702 16703 16704 16705 16706 16707 16708 16709 16710 16711 16712 16713 16714 16715 16716 16717 16718 16719 16720 16721 16722 16723 16724 16725 16726 16727 16728 16729 16730 16731 16732 16733 16734 16735 16736 16737 16738 16739 16740 16741 16742 16743 16744 16745 16746 16747 16748 16749 16750 16751 16752 16753 16754 16755 16756 16757 16758 16759 16760 16761 16762 16763 16764 16765 16766 16767 16768 16769 16770 16771 16772 16773 16774 16775 16776 16777 16778 16779 16780 16781 16782 16783 16784 16785 16786 16787 16788 16789 16790 16791 16792 16793 16794 16795 16796 16797 16798 16799 16800 16801 16802 16803 16804 16805 16806 16807 16808 16809 16810 16811 16812 16813 16814 16815 16816 16817 16818 16819 16820 16821 16822 16823 16824 16825 16826 16827 16828 16829 16830 16831 16832 16833 16834 16835 16836 16837 16838 16839 16840 16841 16842 16843 16844 16845 16846 16847 16848 16849 16850 16851 16852 16853 16854 16855 16856 16857 16858 16859 16860 16861 16862 16863 16864 16865 16866 16867 16868 16869 16870 16871 16872 16873 16874 16875 16876 16877 16878 16879 16880 16881 16882 16883 16884 16885 16886 16887 16888 16889 16890 16891 16892 16893 16894 16895 16896 16897 16898 16899 16900 16901 16902 16903 16904 16905 16906 16907 16908 16909 16910 16911 16912 16913 16914 16915 16916 16917 16918 16919 16920 16921 16922 16923 16924 16925 16926 16927 16928 16929 16930 16931 16932 16933 16934 16935 16936 16937 16938 16939 16940 16941 16942 16943 16944 16945 16946 16947 16948 16949 16950 16951 16952 16953 16954 16955 16956 16957 16958 16959 16960 16961 16962 16963 16964 16965 16966 16967 16968 16969 16970 16971 16972 16973 16974 16975 16976 16977 16978 16979 16980 16981 16982 16983 16984 16985 16986 16987 16988 16989 16990 16991 16992 16993 16994 16995 16996 16997 16998 16999 17000 17001 17002 17003 17004 17005 17006 17007 17008 17009 17010 17011 17012 17013 17014 17015 17016 17017 17018 17019 17020 17021 17022 17023 17024 17025 17026 17027 17028 17029 17030 17031 17032 17033 17034 17035 17036 17037 17038 17039 17040 17041 17042 17043 17044 17045 17046 17047 17048 17049 17050 17051 17052 17053 17054 17055 17056 17057 17058 17059 17060 17061 17062 17063 17064 17065 17066 17067 17068 17069 17070 17071 17072 17073 17074 17075 17076 17077 17078 17079 17080 17081 17082 17083 17084 17085 17086 17087 17088 17089 17090 17091 17092 17093 17094 17095 17096 17097 17098 17099 17100 17101 17102 17103 17104 17105 17106 17107 17108 17109 17110 17111 17112 17113 17114 17115 17116 17117 17118 17119 17120 17121 17122 17123 17124 17125 17126 17127 17128 17129 17130 17131 17132 17133 17134 17135 17136 17137 17138 17139 17140 17141 17142 17143 17144 17145 17146 17147 17148 17149 17150 17151 17152 17153 17154 17155 17156 17157 17158 17159 17160 17161 17162 17163 17164 17165 17166 17167 17168 17169 17170 17171 17172 17173 17174 17175 17176 17177 17178 17179 17180 17181 17182 17183 17184 17185 17186 17187 17188 17189 17190 17191 17192 17193 17194 17195 17196 17197 17198 17199 17200 17201 17202 17203 17204 17205 17206 17207 17208 17209 17210 17211 17212 17213 17214 17215 17216 17217 17218 17219 17220 17221 17222 17223 17224 17225 17226 17227 17228 17229 17230 17231 17232 17233 17234 17235 17236 17237 17238 17239 17240 17241 17242 17243 17244 17245 17246 17247 17248 17249 17250 17251 17252 17253 17254 17255 17256 17257 17258 17259 17260 17261 17262 17263 17264 17265 17266 17267 17268 17269 17270 17271 17272 17273 17274 17275 17276 17277 17278 17279 17280 17281 17282 17283 17284 17285 17286 17287 17288 17289 17290 17291 17292 17293 17294 17295 17296 17297 17298 17299 17300 17301 17302 17303 17304 17305 17306 17307 17308 17309 17310 17311 17312 17313 17314 17315 17316 17317 17318 17319 17320 17321 17322 17323 17324 17325 17326 17327 17328 17329 17330 17331 17332 17333 17334 17335 17336 17337 17338 17339 17340 17341 17342 17343 17344 17345 17346 17347 17348 17349 17350 17351 17352 17353 17354 17355 17356 17357 17358 17359 17360 17361 17362 17363 17364 17365 17366 17367 17368 17369 17370 17371 17372 17373 17374 17375 17376 17377 17378 17379 17380 17381 17382 17383
rCRS	T A A A C C A C T T T C C T T G G C T G C C T A C C T A C A A A C C T C C A T G C A T C C T C C A C T T C C C C C T C C T A G A C C A C C C A C C C T T A T A T A A A G T T C T A T A T C C C T T T T T
C91	. . . . . C . . C . . . . . T . . . . . A . . . . .
C92	. . . . C . . . A . . . . . C . . . . . T . . . . . G . . . . . G . . . . .
C93	. . . . . T . . . . . T . . . . . T . . . A . . . . . C .
C94	. . . . . A . . . . . C . . . . . T . . . . . T . . . G . . . . .
C95	. . . . . T . . . . . C . . . . . T . . . . .
C96	. . . . . A . . . . . C . . G . . . . . C . . . . .
C97	. . . . . A A . . . . . C . . . . . C . . . . .
C98	. . . . . T . . . . . T . . . . . T . . . . .
C99	. . . . . T . A . . . . . C . . . . . T . . . . . C . . . . .
C100	. . . . . T . . . . . C . . . . . T . . . . .
C101	. . . . . T C . . . . . A . . . . .
C102	. . . . . C A . . . . . T . . . . . C . . . . .
C104	. . . . . T . A . . . . G . C . . . . . T . . . . . C . . . . .
C105	. . . . . C C . C . . . . . C . . . . . T . . . . . T . . . . .
F1	. . . . . A . . . . . T . . . . . T . . . . .
F2	. . . . . C . . . . . C C . C . . . . .
F3	. . . . . C . . . . . C . . . . .
F4	. . . . . T . . . . . C . C . C . . . . . C . . . . .
F5	. . . . . C . C . C . . . . T . . . . .
F6	. . . . . T . C C . C . . . . T . . . . .
F7	. . . . . C C . C . . . . .
F8	. . . . . A . . . . . T . . . . . C . .
F9	. . . . . T . . . . . C . . . . . T . . . . .
F10	. . . . . T . . . . . C A . C . . . . .
F11	. . . . C . . . . . C . . . . . C C . C . . . . . C . . . A . . T . . . . . C . . . . .
F12	. . . . . A . . . . . T . . C . . . . .
F13	. . . . . T . . . . .
F14	. . . . . C . . . . . C C . C . . . . .
F15	. . . . . T . . . . . T G . . . . .
F16	. . . . . A . . . . . T . . . . . C . . . . .
F17	. . . . . T . . . . . T . . . . .
F18	. . . . . A . . . . . T . . . . .
F19	. . . . . C C . C . . . . . C . . . T . . . T . . . . .
F20	. . . . . T . . . . . T . . . . .
F21	. . . . . C . . C . . . . .
F22	. . . . . C . . . . . C . C . . . . .
F23	. . . . . C . . . . . T C
F24	. . . . . C . . . . .
F25	. . . . . C . . . . . T . . . . . T . . . . . C . . . . .
F26	. . . . . C . . . . . T C
F27	. . . . . C C . C . . . . . A . . . . .
F28	. . . . . C . . . A . . . . . C . . . . . T . . . . . G . . . . .
F29	. . . . . C . . . . . C C . C . . . . . T A . . . . .
F30	. . . . . A . . . . . T . . . . . T . . . . .

Table 16. The frequency of each polymorphism in the hypervariable segment 1 (HVS-1) of control region in 100 normal controls and 30 LHON patients.

HVS-1 variants	Controls (N, %)	LHON (N, %)	Frequency difference (% LHON)-(% Controls)
G 16024 T	1 (1%)	0 (0%)	-1
G 16038 A	1 (1%)	0 (0%)	-1
G 16051 A	1 (1%)	0 (0%)	-1
G 16059 A	1 (1%)	0 (0%)	-1
T 16067 C	4 (4%)	0 (0%)	-4
T 16069 C	1 (1%)	0 (0%)	-1
C 16078 A	1 (1%)	0 (0%)	-1
T 16085 C	0 (0%)	1 (3%)	3
C 16086 T	5 (5%)	3 (10%)	5
A 16092 T	1 (1%)	0 (0%)	-1
C 16092 T	0 (0%)	1 (3%)	3
C 16093 T	5 (5%)	0 (0%)	-5
T 16104 C	1 (1%)	0 (0%)	-1
T 16108 C	7 (7%)	0 (0%)	-7
C 16124 T	1 (1%)	0 (0%)	-1
C 16126 T	3 (3%)	0 (0%)	-3
A 16129 G	28 (28%)	6 (20%)	-8
A 16130 G	1 (1%)	0 (0%)	-1
T 16134 C	1 (1%)	0 (0%)	-1
C 16140 T	10 (10%)	6 (20%)	10
A 16145 G	2 (2%)	0 (0%)	-2
A 16147 C	0 (0%)	1 (3%)	3
T 16147 C	3 (3%)	1 (3%)	0
T 16148 C	1 (1%)	0 (0%)	-1
C 16154 T	2 (2%)	0 (0%)	-2
G 16162 A	6 (6%)	0 (0%)	-6
T 16167 C	1 (1%)	0 (0%)	-1
T 16169 C	3 (3%)	0 (0%)	-3
C 16172 T	18 (18%)	1 (3%)	-15
C 16175 A	1 (1%)	0 (0%)	-1
A 16176 C	1 (1%)	0 (0%)	-1
T 16176 C	0 (0%)	1 (3%)	3
C 16181 A	1 (1%)	0 (0%)	-1
G 16181 A	2 (2%)	0 (0%)	-2
C 16182 A	12 (12%)	8 (27%)	15
G 16182 A	1 (1%)	0 (0%)	-1
C 16183 A	27 (27%)	13 (43%)	16
A 16184 C	0 (0%)	1 (3%)	3
T 16184 C	2 (2%)	0 (0%)	-2
T 16188 C	2 (2%)	0 (0%)	-2
C 16189 T	34 (34%)	12 (40%)	6
T 16192 C	4 (4%)	2 (7%)	3
T 16193 C	1 (1%)	0 (0%)	-1
G 16203 A	2 (2%)	0 (0%)	-2
C 16209 T	5 (5%)	3 (10%)	5
A 16213 G	1 (1%)	0 (0%)	-1
T 16214 C	3 (3%)	0 (0%)	-3
G 16215 A	1 (1%)	0 (0%)	-1
C 16217 T	10 (10%)	1 (3%)	-7
T 16218 C	2 (2%)	0 (0%)	-2
T 16223 C	56 (56%)	16 (53%)	-3
C 16224 T	1 (1%)	1 (3%)	2
T 16232 C	0 (0%)	1 (3%)	3
T 16234 C	7 (7%)	0 (0%)	-7

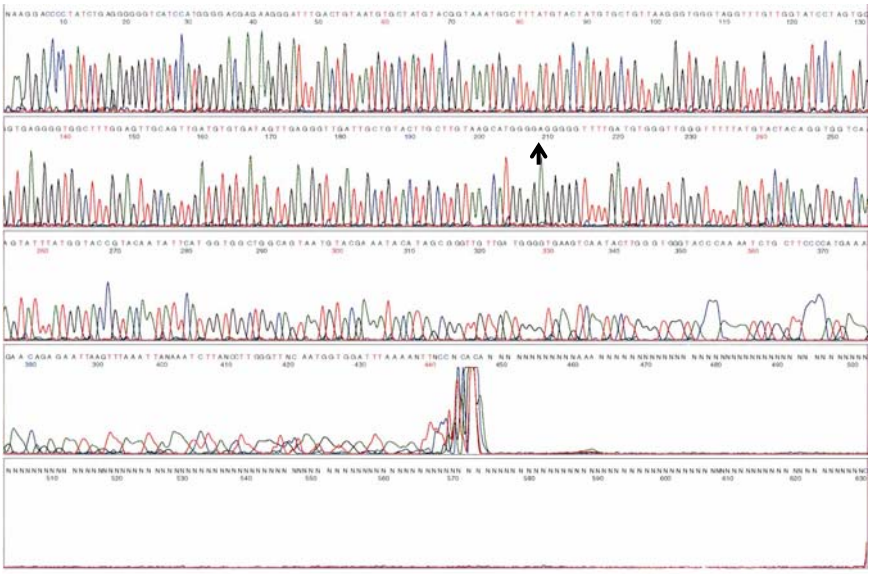
Table 16 (continued). The frequency of each polymorphism in the hypervariable segment 1 (HVS-1) of control region in 100 normal controls and 30 LHON patients.

HVS-1 variants	Controls (N, %)	LHON (N, %)	Frequency difference (% LHON)-(% Controls)
G 16235 A	2 (2%)	0 (0%)	-2
T 16239 C	2 (2%)	0 (0%)	-2
C 16243 T	1 (1%)	0 (0%)	-1
C 16249 T	1 (1%)	1 (3%)	2
T 16256 C	1 (1%)	0 (0%)	-1
A 16257 C	1 (1%)	0 (0%)	-1
T 16259 C	1 (1%)	0 (0%)	-1
T 16260 C	2 (2%)	0 (0%)	-2
T 16261 C	8 (8%)	2 (7%)	-1
C 16263 T	3 (3%)	1 (3%)	0
A 16266 C	10 (10%)	1 (3%)	-7
T 16266 C	2 (2%)	0 (0%)	-2
A 16267 C	0 (0%)	1 (3%)	3
C 16271 T	1 (1%)	0 (0%)	-1
G 16272 A	4 (4%)	1 (3%)	-1
T 16272 A	0 (0%)	1 (3%)	3
A 16274 G	5 (5%)	1 (3%)	-2
G 16275 A	1 (1%)	0 (0%)	-1
T 16278 C	11 (11%)	1 (3%)	-8
T 16286 C	0 (0%)	1 (3%)	3
G 16289 A	0 (0%)	1 (3%)	3
T 16290 C	7 (7%)	2 (7%)	0
T 16291 C	8 (8%)	1 (3%)	-5
T 16292 C	2 (2%)	0 (0%)	-2
C 16293 A	1 (1%)	0 (0%)	-1
T 16294 C	2 (2%)	0 (0%)	-2
T 16295 C	2 (2%)	0 (0%)	-2
T 16296 C	1 (1%)	0 (0%)	-1
C 16297 T	7 (7%)	0 (0%)	-7
C 16298 T	5 (5%)	1 (3%)	-2
G 16299 A	2 (2%)	0 (0%)	-2
C 16304 T	23 (23%)	0 (0%)	-23
T 16305 A	1 (1%)	0 (0%)	-1
C 16311 T	17 (17%)	4 (13%)	-4
G 16316 A	2 (2%)	0 (0%)	-2
G 16317 A	1 (1%)	0 (0%)	-1
C 16318 A	1 (1%)	0 (0%)	-1
G 16318 A	2 (2%)	0 (0%)	-2
A 16319 G	7 (7%)	0 (0%)	-7
C 16323 T	0 (0%)	1 (3%)	3
C 16325 T	2 (2%)	0 (0%)	-2
T 16327 C	6 (6%)	1 (3%)	-3
C 16334 T	1 (1%)	0 (0%)	-1
G 16335 A	3 (3%)	0 (0%)	-3
C 16342 T	0 (0%)	1 (3%)	3
G 16343 A	1 (1%)	0 (0%)	-1
C 16352 T	2 (2%)	0 (0%)	-2
T 16353 C	1 (1%)	0 (0%)	-1
T 16354 C	1 (1%)	0 (0%)	-1
T 16355 C	3 (3%)	0 (0%)	-3
C 16356 T	2 (2%)	0 (0%)	-2
C 16357 T	2 (2%)	0 (0%)	-2
C 16362 T	20 (20%)	1 (3%)	-17
C 16381 T	2 (2%)	2 (7%)	5

third most common mutation in the LHON samples and the second most mutation in HVS-1 sequence of the LHON individuals was C16183A. The T to C mutation at nt 16189 was found in 34 controls (34% of controls) and 12 LHON individuals (40% of LHON samples). The comparison of T16189C mutation in the normal controls and LHON individuals was showed in Table 14. There was no significantly different in the T16189C mutation between 100 normal controls and 30 LHON individuals (p-value=0.700). Length heteroplasmy between nucleotide 16184 to 16193 was found in 28% of normal controls (28/100) and 37% of LHON individuals (11/30). Length heteroplasmy was found approximately 82% and 92% in the normal controls (28/34) and in the LHON individuals (11/12) who harbor T16189C mutation, respectively. The comparison of length heteroplasmy in normal controls and LHON samples was also presented in Table 14. No significantly different between the normal controls and LHON samples (p-value=0.496). Length heteroplasmy was not found in individual carrying 16189T. The length heteroplasmy in the T16189C mutation sample was shown in Figure 7. The T16189C mutation and length heteroplasmy information of each sample were also shown in Table 13. The association of length heteroplasmy and the T16189C mutation was also performed the statistical analysis that demonstrated in Table 17. These presented that length heteroplasmy was significantly associated with the T16189C mutation (p-value<0.001).

The 9-bp deletion was also found in 62% of normal controls harboring the T16189C mutation (21/34) and 75% of LHON individuals harboring the T16189C mutation (9/12). The 9-bp deletion was also found in 56% of normal controls carrying length heteroplasmy (19/34) and in 67% of LHON individuals carrying length heteroplasmy (8/12). The individuals who harboring all of the 9-bp deletion, T16189C mutation and length heteroplasmy in one individual were found in 19% of normal controls (19/100) and 27% of LHON individuals (8/30). The information of the T16189C mutation, length heteroplasmy and 9-bp deletion were shown in Figure 8. The association of 9-bp deletion with T16189C, length heteroplasmy and T16189C with length heteroplasmy were showed in Table 18. The statistical analysis showed associated significant of 9-bp deletion with all of T16189C (p-value<0.001), length heteroplasmy (p-value<0.001) and T16189C with length heteroplasmy (p-value<0.001).

A.



B.

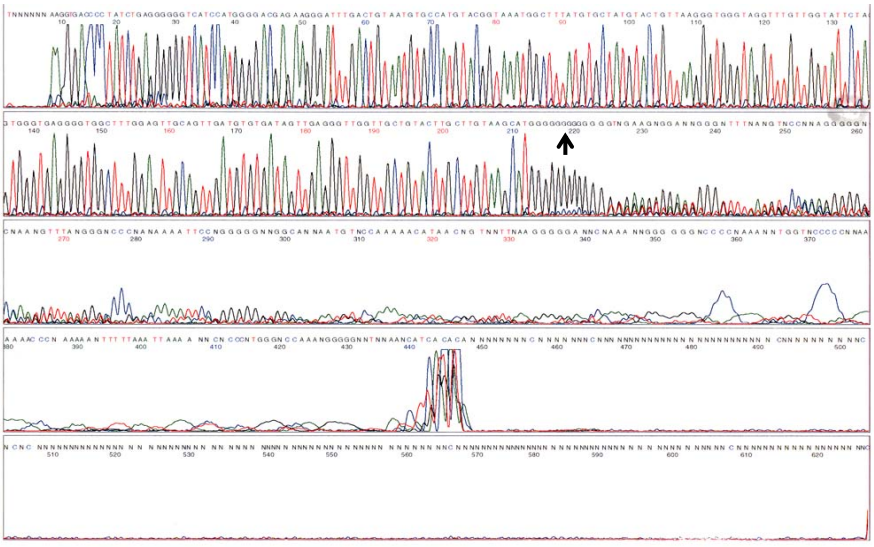


Figure 7A-B. The T16189C and length heteroplasmy in the HVS-1 region (nt 16024 to 16383). A. The 16189T in the HVS-1 region (arrow). **B.** The T16189C mutation and length heteroplasmy between nt 16184 to 16193 in the sequencing of the HVS-1 region (arrow).

Table 17. The association of T16189C mutation and length heteroplasmy in the studied samples.

Factor	T16189C mutation		p-value
	Normal (16189T) (N=84)	T16189C (N=46)	
Normal	84 (100%)	7 (15.22%)	<0.001*
Length Heteroplasmy	0 (0%)	39 (84.78%)	

* p-value<0.05 and considered significant.

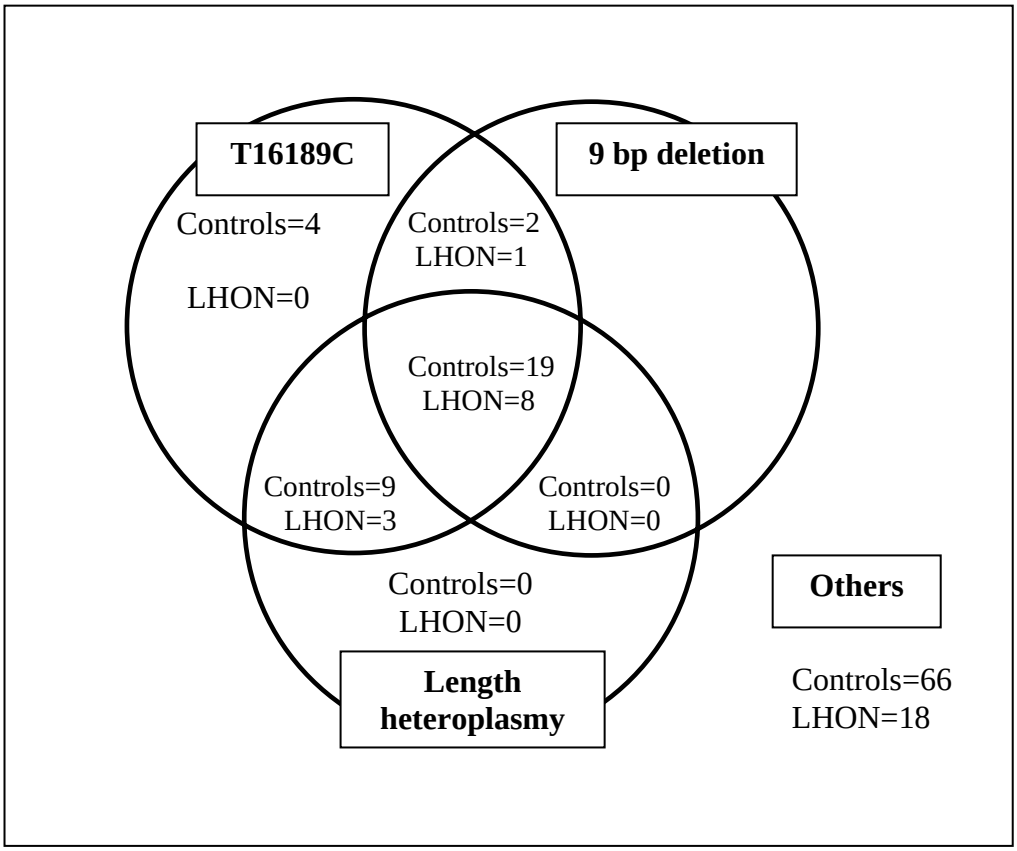


Figure 8. The frequency of T16189C mutation in the HVS-1 sequence, length heteroplasmy and 9-bp deletion in 100 normal controls and 30 LHON patients.

Table 18. The association of 9-bp deletion in COII/tRNA^{Lys} with either T16189C mutation or length heteroplasmy, or T16189C with length heteroplasmy in all studied samples.

Factors	9-bp deletion status		p-value
	Non 9-bp deletion (N=97)	9-bp deletion (N=33)	
T16189C mutation :			
16189T	81 (83.5%)	3 (9.1%)	<0.001*
T16189C	16 (16.5%)	30 (90.91%)	
Length heteroplasmy status :			
Normal	85 (87.6%)	6 (18.2%)	<0.001*
Length heteroplasmy	12 (12.4%)	27 (81.8%)	
T16189C plus Length heteroplasmy :			
Normal	81 (83.5%)	3 (9.1%)	
T16189C no length heteroplasmy	4 (4.1%)	3 (9.1%)	<0.001*
T16189C plus length heteroplasmy	12 (12.4%)	27 (81.8%)	

* p-value<0.05 and considered significant.

Mitochondrial DNA haplogroups were also determined by HVS-1 sequences according to the criteria in Table 1. Seven haplogroups; A, B, B*, C, D, F and M, were detected in these samples. The HVS-1 haplogroup was also represented in Table 11. The frequency of the HVS-1 haplogroup A, B, B*, C, D, F and M in the normal controls were 1%, 8%, 8%, 2%, 13%, 20% and 35%, respectively whereas the frequency of these haplogroups in the LHON individual were 0%, 0%, 13%, 0%, 3%, 0% and 50%, respectively. Some of our samples can be classified into two haplogroups in one individual, determined by HVS-1 sequence. These haplogroups were B/B*, F/M and M/P. The frequencies of these HVS-1 haplogroups were 2%, 3% and 2%, respectively. The most common haplogroup, determined by HVS-1 sequence, in the normal controls and LHON samples was haplogroup M which were 35% and 50%, respectively. Haplogroup A, B, C and F determined by HVS-1 sequence were not found in the LHON individuals. The known HVS-1 mitochondrial haplogroups were not able to be classified in 6 normal controls (6%) and 9 LHON individuals (30%).

5. Phylogenetic analysis

Phylogenetic tree was constructed with the PAUP* program using the distance method. Both RFLP and 9-bp deletion data and HVS-1 sequence data were used in this analysis. The outgroup of both trees was Khwe (GenBank no. AY195777), the haplogroup L, which was downloaded from the Complete Human Mitochondrial Sequence website (http://www.genpat.uu.se/mtDB/sequence.php).

5.1 Phylogenetic tree constructed from the RFLP and 9-bp deletion information

From the unroot of the Neighbor-Joining (NJ) tree constructed from the RFLP and 9-bp deletion information, the branches in the RFLP unroot tree were divided into main 5 groups. Each RFLP haplogroup was clustered together in the tree (Figure 9). Haplogroup A, B and F were located within one branch of the tree whereas haplogroup B* and M were more than one branch. None of the unclassified samples were in the haplogroup A and F clusters while there was one unclassified sample, C89, in the haplogroup B cluster. Haplogroup B* were located in 2 branches and there were 2 unclassified samples, C36 and F14, in their cluster. Haplogroup M can be

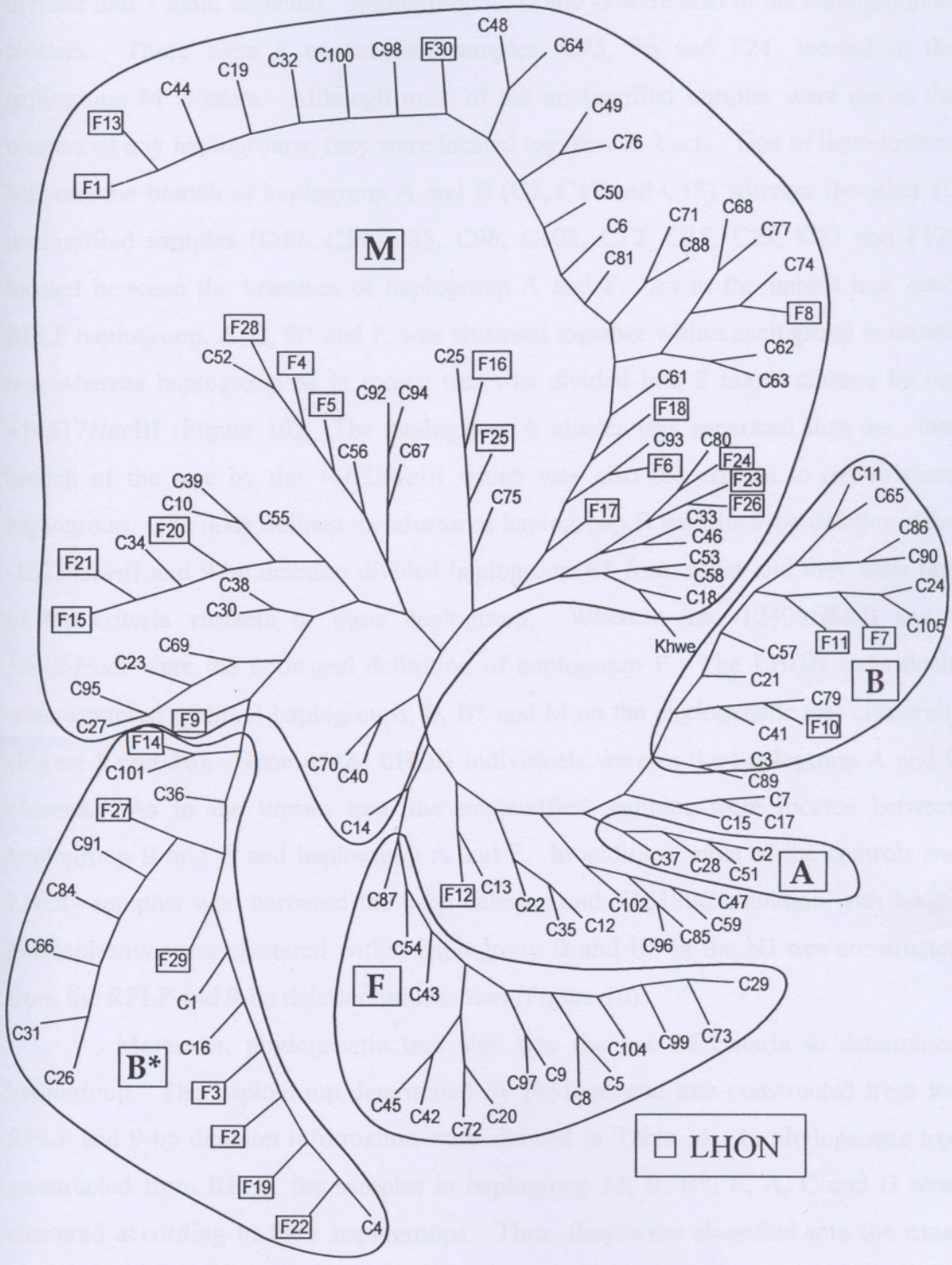


Figure 9. The Neighbor-Joining unroot tree constructed from the RFLP and 9-bp deletion information of 100 normal controls (C1,…C59, C61,…C77, C79, C80, C81, C84,…C102, C104, C105) and 30 LHON individuals (F1-F30).

divided into 3 main branches. Haplogroup C, D and G were also in the haplogroup M clusters. There were 3 unclassified samples, C75, F6 and F24, located in the haplogroup M clusters. Although most of the unclassified samples were not in the clusters of any haplogroups, they were located together in 2 sets. One of them located between the branch of haplogroup A and B (C7, C17 and C15) whereas the other 10 unclassified samples (C47, C59, C85, C96, C102, C12, C35, C22, C13 and F12) located between the branches of haplogroup A and F. As in the unroot tree, each RFLP haplogroup, A, B, B* and F, was clustered together within each group in rooted tree whereas haplogroup M in rooted tree was divided into 2 major clusters by the +16517*Hae*III (Figure 10). The haplogroup A cluster was separated into the other branch of the tree by the +663*Hae*III which was also the criteria to define these haplogroup. The node defined the cluster of haplogroup B was the 9-bp deletion. The -15234*Hin*fI and 9-bp deletion divided haplogroup B* from other and they were one of the criteria variants of these haplogroup. Whereas the -12406*Hin*cII and -12406*Hpa*I were the node and definition of haplogroup F. The LHON individuals were scattered within 3 haplogroups; B, B* and M on the phylogenetic tree clustering (Figure 9 and 10). None of the LHON individuals were in the haplogroup A and F clusters. As in the unroot tree, the unclassified samples were located between haplogroup B and A and haplogroup A and F. In addition, most of the controls and LHON samples who harbored the 9-bp deletion and T16189C mutation with length heteroplasmy were clustered within haplogroup B and B* in the NJ tree constructed from the RFLP and 9-bp deletion information (Figure 10).

Moreover, phylogenetic tree also was the one of criteria to determined haplogroup. The haplogroup determined by phylogenetic tree constructed from the RFLP and 9-bp deletion information were showed in Table 11. In phylogenetic tree constructed from RFLP, the samples in haplogroup M, B, B*, F, A, C and D were clustered according to their haplogroups. Thus, they were classified into the same haplogroup determined by RFLP criteria. The sample, C28, who classified into haplogroup A9 and B by RFLP criteria was located together with haplogroup A in the tree. Therefore, this sample was haplogroup A determined by RFLP tree. For the unclassified sample, C89, was located in haplogroup B cluster therefore this sample could be classified to haplogroup B determined by phylogenetic tree. The unclassified

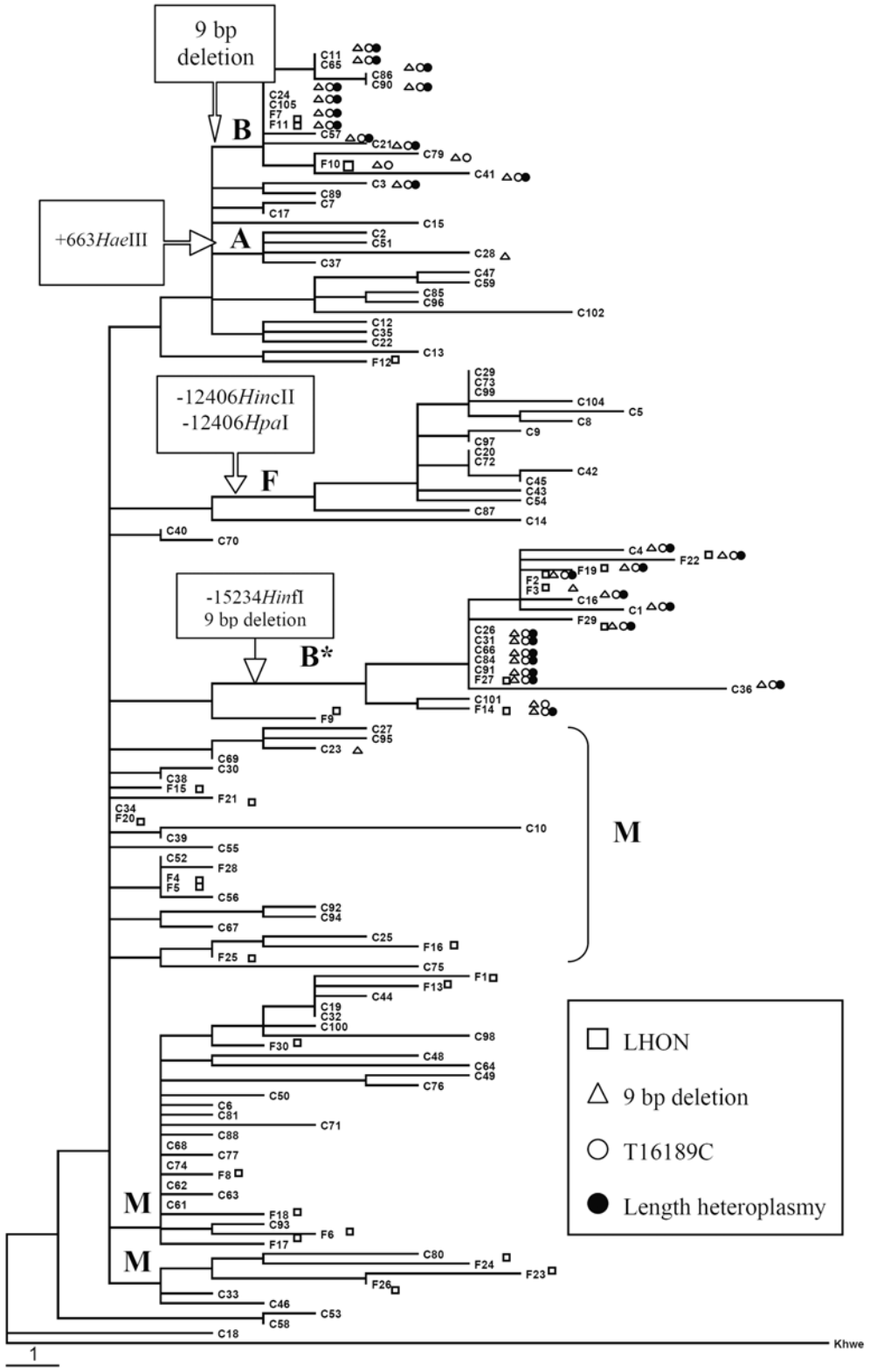


Figure 10. The Neighbor-Joining root tree constructed from the RFLP and 9-bp deletion information of 100 normal controls (C1,…C59, C61,…C77, C79, C80, C81, C84,…C102, C104, C105) and 30 LHON individuals (F1-F30).

samples, C36 and F14, were clustered in haplogroup B* thus they were haplogroup B* and the other unclassified samples, C75, F6 and F24, were in the haplogroup M clusters which classified them into haplogroup M determined by RFLP tree. Thirteen unclassified samples (C7, C17, C15, C47, C59, C85, C96, C102, C12, C35, C22, C13 and F12) were still unable to be classified either by RFLP criteria or phylogenetic tree constructed from RFLP and 9-bp deletion information.

5.2 Phylogenetic tree constructed from HVS-1 sequence

The same as in the tree constructed from the RFLP and 9-bp deletion information, most of the mitochondrial haplogroups defined by HVS-1 sequence criteria were clustered in the tree while the haplogroup M was divided into 3 branches (Figure 11 and 12). Two of them were located in the same main branch of tree whereas one of them was located between haplogroup F and B*. Most of the unclassified samples were scattered in the tree. Haplogroup C was clustered within one of the haplogroup M main branches where as haplogroup D was clustered between the haplogroup M clusters (Figure 11). In the root HVS-1 tree, the cluster of haplogroup C and D were located between the cluster of haplogroup M (Figure 12). The T16140C mutation was separated haplogroup B* out of haplogroup B. Haplogroup F was grouped by the T16304C mutation in HVS-1 sequence which also was the HVS-1 haplogroup F criteria. The mitochondrial DNA haplogroup of LHON individuals defined by HVS-1 sequence were scattered within 3 haplogroups; B, B* and M on the phylogenetic tree (Figure 11 and 12). None of the LHON individuals were found in haplogroup F cluster. As in the normal controls, the unclassified LHON subjects were also dispersed into many haplogroup clusters (Figure 11 and 12). The unclassified LHON subjects, F19, F7 and F27, were clustered in haplogroup B whereas the other unclassified LHON subjects, F21, F24 and F12 were dispersed along the main branch of haplogroup M and F3, F4 and F10 were in the haplogroup M cluster which located between haplogroup F and B*. As in tree constructed from the RFLP and 9-bp deletion information (Figure 10), most of controls and LHON samples who harbored the 9-bp deletion and T16189C mutation with length heteroplasmy were clustered within haplogroup B and B* (Figure 12).

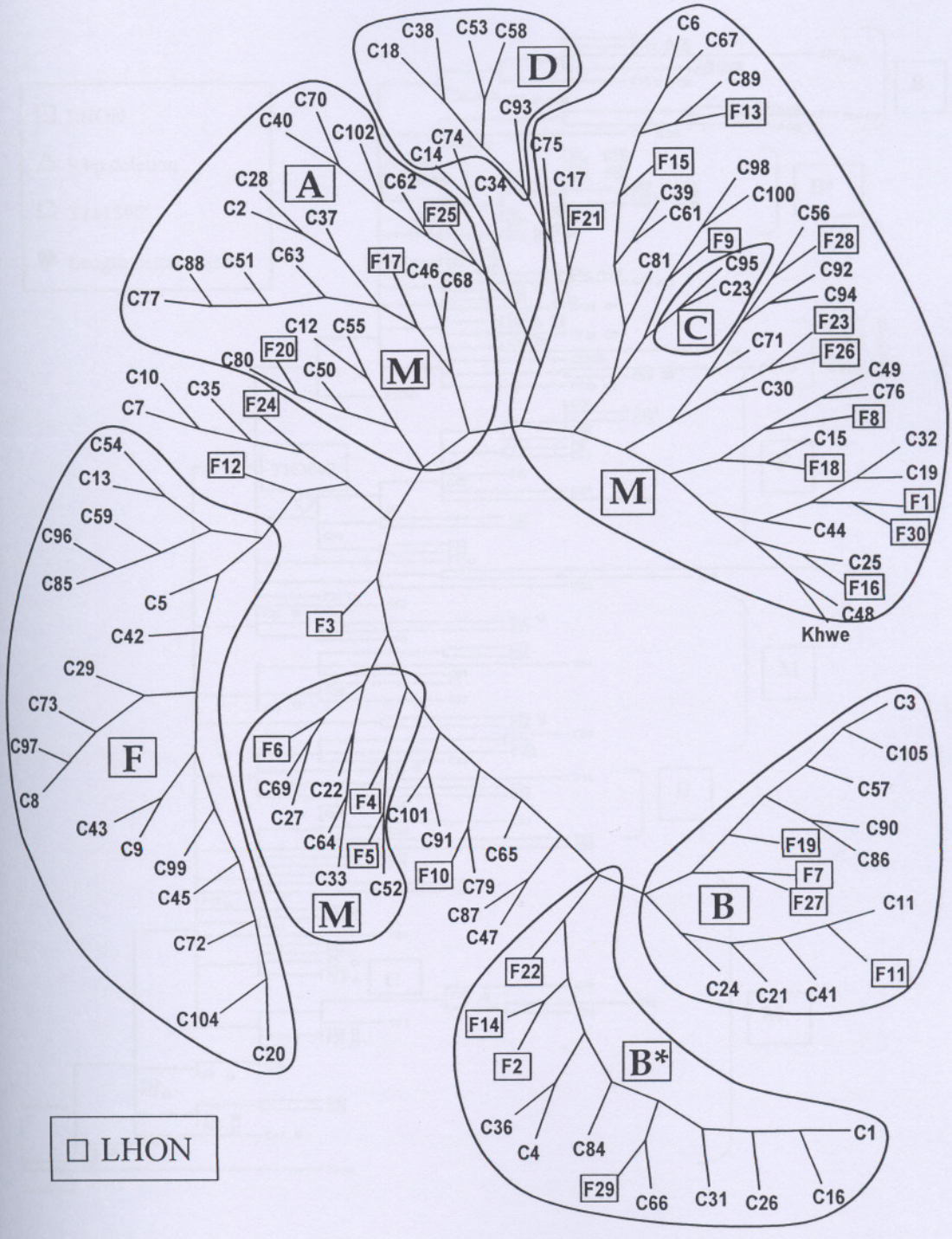


Figure 11. The Neighbor-Joining unroot tree constructed from the HVS-1 sequence of 100 normal controls (C1,...C59, C61,...C77, C79, C80, C81, C84,...C102, C104, C105) and 30 LHON individuals (F1-F30).

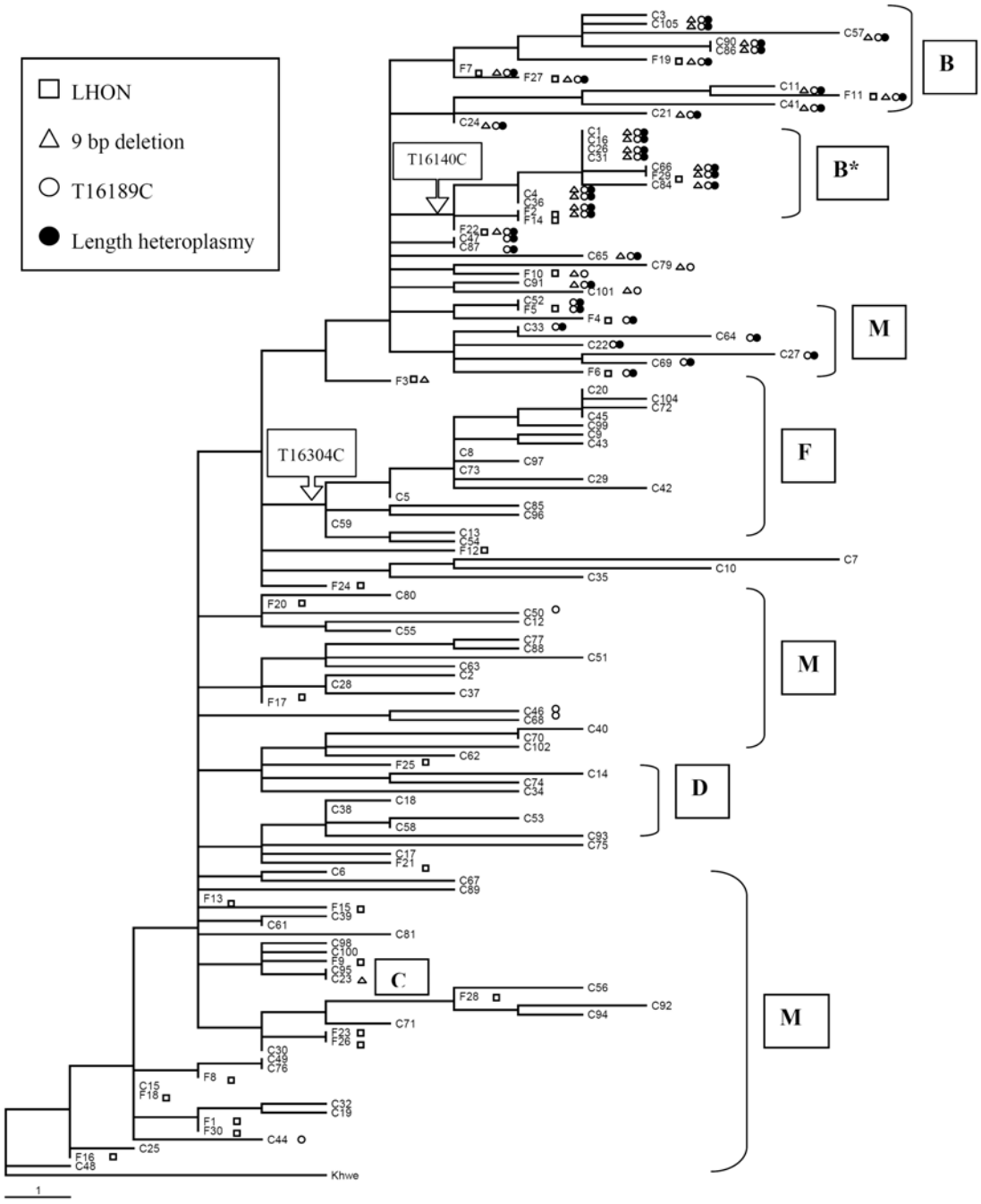


Figure 12. The Neighbor-Joining root tree constructed from the HVS-1 sequence of 100 normal controls (C1,…C59, C61,…C77, C79, C80, C81, C84,…C102, C104, C105) and 30 LHON individuals (F1-F30).

The HVS-1 tree was also the criteria to determined haplogroup. The unclassified samples, F19, F7 and F27, were clustered in the haplogroup B thus they could be classified to haplogroup B determined by HVS-1 tree. The other unclassified samples, F4 and F21, were scattered in the haplogroup M cluster therefore they could be classified to haplogroup M. And the unclassified sample, F10, was located in the same branch of haplogroup B sample thus this sample were haplogroup B defined by HVS-1 tree. Whereas C42 was the unclassified sample located in haplogroup F, this sample could be classified to haplogroup F. There were some samples, C40, C62 and C70, were assigned to haplogroup F and M by HVS-1 sequence criteria. They located in the haplogroup M cluster thus they could be classified to haplogroup M. The other samples, C11, C41 and F11, could be classified to both haplogroup B and B*. Their location were scattered in the haplogroup B cluster thus they could be classified to haplogroup B. Whereas the samples, C48 and C75 were classified to both haplogroup M and P, they located in the haplogroup M cluster. Therefore they could be classified to haplogroup M defined by HVS-1 tree.

5.3 Phylogenetic analysis of both tree constructed from RFLP and 9-bp deletion information and HVS-1 sequence

All of classified samples were clustered according to their haplogroups in both phylogenetic tree constructed from RFLP information and HVS-1 sequence (Figure 9-12). Haplogroup B, B* and F were in the one main branch whereas haplogroup M was in the many branches of both tree. Haplogroup either C or D samples were clustered together with haplogroup M samples. Whereas haplogroup A samples, C2, C51 and C28, classified to haplogroup A determined by RFLP criteria and tree, they were classified to haplogroup M in the HVS-1 criteria and clustered in both RFLP and HVS-1 tree with haplogroup A, C37, determined by both of RFLP and HVS-1 criteria. Moreover, the haplogroup B* samples, F19 and F27, determined by RFLP information were belonging to haplogroup B determined by HVS-1 sequence. While the unclassified sample, C89, determined by RFLP criteria which was clustered in haplogroup B in RFLP tree, C89 was haplogroup M determined by HVS-1 sequence and also located in haplogroup M. Some of unclassified samples determined by RFLP criteria were the known haplogroup determined by HVS-1 criteria. The unclassified RFLP haplogroup samples, C12, C15 and C17, were belonging to haplogroup M

determined by HVS-1 and clustered according to their HVS-1 haplogroup in HVS-1 tree. The other RFLP unclassified sample, C22, was haplogroup D and located within it. Moreover there were the unclassified samples determined by RFLP, C13, C47, C59, C85, C96 and C102, were belonging to HVS-1 haplogroup F and clustered in these haplogroup in the HVS-1 tree. In contrast, the unclassified samples, C91, C101 and F3, determined by HVS-1 were haplogroup B* determined by RFLP information. The other HVS-1 unclassified sample, C65, was haplogroup B determined by RFLP and clustered in it.

6. The determination of definite haplogroup by at least 3 of 4 criteria which were RFLP and 9-bp deletion information and their phylogenetic tree and HVS-1 sequence and their phylogenetic tree.

The criteria to determine the mitochondrial DNA haplogroup were RFLP and 9-bp deletion information and their phylogenetic tree and HVS-1 sequence and their phylogenetic tree. At least 3 of them were assigned the definite haplogroup. The definite haplogroup of each sample was showed in Table 11. Seven definite haplogroups, M, B, B*, F, A, C and D found in this study. The frequency of haplogroup M, B, B*, F, A, C and D found in 100 normal controls were 45% (45/100), 10% (10/100), 8% (8/100), 15% (15/100), 1% (1/100), 1% (1/100) and 1% (1/100), respectively. While only 3 haplogroups, M, B and B* were found in 30 LHON individuals. Their frequency found in LHON individuals were 60% (18/30), 10% (3/30) and 13.3% (4/30), respectively. None of LHON individuals were haplogroup F, A, C and D. The unclassified samples found 19% (19/100) in normal controls whereas 16.7% (5/30) in LHON individuals. The distribution of each haplogroup found in normal controls and LHON individuals was presented in Table 19.

To test statistically whether the definite haplogroups distribution of the G11778A LHON individuals and normal controls defined by at least 3 of 4 criteria which were RFLP and 9-bp deletion data and their phylogenetic tree and the HVS-1 sequence and their phylogenetic tree, the Chi-square testing was used. The statistical analysis of the frequency found in each haplogroup of the normal controls and the LHON individuals were also shown in Table 19. The p-value of the frequency difference among the LHON individuals and the normal controls of definite

Table 19. The distribution of definite haplogroup found in 100 normal controls and 30 LHON individuals and their statistical comparison between 100 normal controls and 30 LHON individuals.

Subjects	Total	Haplogroup							
		M	B	B*	F	A	C	D	Unclassified
Normal control (N, %)	100	45 (45%)	10 (10%)	8 (8%)	15 (15%)	1 (1%)	1 (1%)	1 (1%)	19 (19%)
LHON (N, %)	30	18 (60%)	3 (10%)	4 (13.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (16.7%)
p-value		0.217	0.729	0.637	0.053	0.521	0.521	0.521	0.9836

haplogroup M, B, B*, F, A, C and D were 0.217, 0.729, 0.637, 0.053, 0.521 and 0.521, respectively. The results indicated no significant difference between the LHON samples and the normal controls ($p>0.05$). Interesting that the frequency of haplogroup F in the normal controls and the LHON individuals was nearly significantly different ($p=0.053$). The unclassified haplogroup were also test the statistical analysis which found no significantly different in the unclassified samples between the normal controls and LHON individuals (p-value=0.984).

7. The statistical analysis of clinical manifestation and mutation load of G11778A LHON families

7.1 Comparison of the clinical manifestation and mutation load between the affected and unaffected samples of 30 G11778A LHON families.

To investigate the different between affected and unaffected samples in 30 LHON families, the maternal relatives were also included in this analysis. The variables were gender and the degree of mutant mtDNA and comparing using Chi-Square testing. The information and their statistical analysis were presented in Table 20. For the comparison of gender, male were found in the affected group (72.3%) higher than in the unaffected group (34.5%). There was significantly different of gender between affected and unaffected group (p-value<0.001). For the comparison of degree of mutant mtDNA, the homoplasmic cases were found in the affected group (86.2%) greater than in the unaffected group (59.8%). There was significantly different of degree of mutant mtDNA between affected and unaffected group (p-value=0.001).

For comparison of the clinical manifestation and mutation load between haplogroup M, B and B* found in 30 LHON families, the variables used in this study were affected status, gender, final visual acvity, age of onset and degree of mutant mtDNA. All of them were comparing using Chi-Square analysis except for the final visual acvity and age of onset using Kruskal-Wallis analysis. The statistical analysis of each variable between the definite haplogroup in the LHON families was shown in Table 21. The frequency of affected cases found in haplogroup B (80%) were higher than in haplogroup M (40.9%) and B* (57.1%). There was significantly different between 3 haplogroups (p-value=0.047).

Table 20. Comparison of gender and mutation load between affected and unaffected cases in 30 G11778A LHON families.

Factors	All cases (Total=152)	Affected Status		p-value
		Affected (Total=65)	Unaffected (Total=87)	
Sex :				
Male (M) (N, %)	77 (50.7%)	47 (72.3%)	30 (34.5%)	>0.001*
Female (F) (N, %)	75 (49.3%)	18 (27.7%)	57 (65.5%)	
Ratio M : F	1.03:1	2.61:1	0.53:1	
Mutant mtDNA status :				
Homoplasmy (N, %)	108 (71.1%)	56 (86.2%)	52 (59.8%)	0.001*
Heteroplasmy (N, %)	44 (28.9%)	9 (13.8%)	35 (40.2%)	

* p-value<0.05 and considered significant.

Table 21. Comparison of clinical manifestation and mutation load between haplogroup M, B and B*.

Factors	All cases (Total=152)	Haplogroup			p-value
		M (Total=110)	B (Total=10)	B* (Total=7)	
Affected status (N) :					
Affected cases (N, %)	65	45 (40.9%)	8 (80%)	4 (57.1%)	0.047*
Unaffected cases (N, %)	87	65 (59.1%)	2 (20%)	3 (42.9%)	
Affected group :					
Sex :					
Male (M) (N, %)	47 (72.3%)	31 (68.9%)	6 (75%)	4 (100%)	0.406
Female (F) (N, %)	18 (27.7%)	14 (31.1%)	2 (25%)	0 (0%)	
Ratio M : F	2.6:1	2.21:1	3:1		
Mutant mtDNA status :					
Homoplasmy (N, %)	56 (86.2%)	41 (91.1%)	8 (100%)	3 (75%)	0.352
Heteroplasmy (N, %)	9 (13.8%)	4 (8.9%)	0 (0%)	1 (25%)	
Age of onset :					
Total (N)	58	39	8	4	
Mean ± SD (years)	22.59±11.65	22.46±10.90	25.25±17.39	22.25±13.33	
Median (years)	19.5	20	23	17	0.944
Min-Max (years)	6-53	6-45	8-53	13-42	
Final Visual Acuity (VA) :					
Total (N, no. of eyes)	55 (109 eyes)	38 (76 eyes)	7 (13 eyes)	3 (6 eyes)	
Mean + SD (logMAR)	1.70±0.76	1.66±0.80	1.68±0.76	1.50±0.77	
Median (logMAR)	2.00	2.00	1.51	2.00	0.933
Min-Max (logMAR)	0.00-3.00	0.00-3.00	0.70-3.00	0.50-2.00	
Unaffected group :					
Sex (N) :					
Male (M) (N, %)	30 (34.5%)	19 (29.2%)	1 (50%)	2 (66.7%)	0.334
Female (F) (N, %)	57 (65.5%)	46 (70.8%)	1 (50%)	1 (33.3%)	
Ratio M : F	0.53:1	0.41:1	1:01	0.5:1	
Mutant mtDNA status :					
Homoplasmy (N, %)	52 (59.8%)	44 (67.7%)	2 (100%)	2 (66.7%)	0.623
Heteroplasmy (N, %)	35 (40.2%)	21 (32.3%)	0 (0%)	1 (33.3%)	

* p-value<0.05 and considered significant.

In the affected group (Table 21), overall male were 72.3% of samples whereas male found in haplogroup M, B and B* were 68.9%, 75% and 100%, respectively. No significantly different in the gender between affected samples of haplogroup M, B and B* (p-value=0.406). For the degree of mutant mtDNA, the homoplasmic samples found in 86.2% of all affected cases. The homoplasmic samples found in the affected cases of haplogroup M, B and B* were 91.1%, 100% and 75%, respectively. There was no significantly different between the homoplasmic samples in 3 haplogroups (p-value=0.352). The age of onset ranged from 6 to 53 years of overall affected cases (median=19.5 years) while ranged from 6 to 45 years in haplogroup M (median=20 years), from 8 to 53 in haplogroup B (median=23 years) and from 13 to 42 in haplogroup B* (median=17 years). Although the median of age of onset in haplogroup B* was less than in haplogroup M and B, the statistical analysis was no significantly different between 3 haplogroups (p-value=0.944). The final visual acuity (VA) ranged from 0.00 to 3.00 logMAR in overall affected samples (median=2.00 logMAR, Snellen visual acuity=6/600 or counting fingers), ranged from 0.00 to 3.00 logMAR in haplogroup M (median=2.00 logMAR), from 0.70 to 3.00 logMAR in haplogroup B (median=1.51 logMAR, Snellen visual acuity=6/192) and from 0.50 to 2.00 logMAR in haplogroup B* (median=2.00 logMAR). There was also no significantly different in the final visual acuity between 3 haplogroups (p-value=0.933).

In the unaffected group (Table 21), overall male were 34.5% of samples whereas the male found in haplogroup M, B and B* were 29.2%, 50% and 66.7%, respectively. No significantly different in the gender between unaffected samples of haplogroup M, B and B* (p-value=0.334). For the degree of mutant mtDNA, the homoplasmic samples found in 59.8% of all affected cases. The homoplasmic samples found in the unaffected cases of haplogroup M, B and B* were 67.7%, 100% and 67.7%, respectively. There was no significantly different between the homoplasmy of unaffected samples in 3 haplogroups (p-value=0.623).

7.2 Comparisons of the clinical manifestation and mutation load between male and female of 30 G11778A LHON families.

The clinical manifestation and mutation load compared between male and female was demonstrated in Table 22. The affected cases were observed in 61% of

Table 22. Comparison of clinical manifestation and mutation load between male and female in 30 G11778A LHON families.

Factors	Sex		p-value
	Male (Total=77)	Female (Total=75)	
Affected status (N) :			
Affected cases (N, %)	47 (61%)	18 (24%)	>0.001*
Unaffected cases (N, %)	30 (39%)	57 (76%)	
Affected group :			
Mutant mtDNA status :			
Homoplasmy (N, %) :	41 (87.2%)	15 (83.3%)	0.995
Heteroplasmy (N, %) :	6 (12.8%)	3 (16.7%)	
Age of onset :			
Total (N)	44	14	
Mean ± SD (years)	20.66±10.01	28.64±14.56	
Median (years)	19	30	0.073
Min-Max (years)	6-44	10-53	
Final Visual Acuity (VA) :			
Total (N, no. of eyes)	40 (79 eyes)	15 (30 eyes)	
Mean ± SD (logMAR)	1.66±0.73	1.83±0.84	
Median (logMAR)	2.00	2.00	0.540
Min-Max (logMAR)	0.00-3.00	0.00-3.00	
Unaffected group :			
Mutant mtDNA status :			
Homoplasmy (N, %)	20 (66.7%)	32 (56.1%)	0.470
Heteroplasmy (N, %)	10 (33.3%)	25 (43.9%)	

* p-value<0.05 and considered significant.

male whereas in 24% of female. There was significantly different in the affected cases between male and female (p-value<0.001). In the affected group, the homoplasmic samples found in male and female were 87.2% and 83.3%, respectively. No significantly different of degree of mutant mtDNA between sex (p-value=0.995). The age of onset in male ranged from 6 to 44 years (median=19 years) while in female ranged from 10 to 53 years (median=30 years). Although the median of age of onset in male and female seem slightly different, there was no significantly different in age of onset between male and female (p-value=0.073). The final VA ranged from 0.00 to 3.00 logMAR in both male and female (median=2.00 logMAR, Snellen visual acuity=6/600 or counting fingers). There was no significantly different in the final VA between male and female (p-value=0.540). In the unaffected group, the homoplasmic samples found in male were 66.7% and found in female were 56.1%. There was also no significantly different in the homoplasmy between unaffected male and female (p-value=0.470).

For information of male between haplogroups (Table 23), the affected male found in haplogroup M, B and B* were 62%, 85.7% and 66.7%, respectively. There was no significantly different in the frequency of affected male between 3 haplogroups (p-value=0.466). In the affected male, the homoplasmic samples found in haplogroup M, B and B* were 90.3%, 100% and 75%, respectively. No significantly different between 3 haplogroups (p-value=0.426). The age of onset of male ranged from 6 to 44 years in haplogroup M (median=19 years), ranged from 8 to 44 years in haplogroup B (median=13 years) and ranged from 13 to 42 years in haplogroup B* (median=17 years). No significantly different between 3 haplogroups (p-value=0.775). The final VA of male ranged from 0.00 to 3.00 logMAR in haplogroup M (median=2.00 logMAR, Snellen visual acuity=6/600 or counting fingers), ranged from 0.70 to 2.00 logMAR in haplogroup B (median=1.50 logMAR, approximately Snellen visual acuity=6/192) and ranged from 0.50 to 2.00 logMAR in haplogroup B* (median=2.00 logMAR). There was no significantly different in the final VA of affected male between 3 haplogroups (p-value=0.635). In the unaffected male, the homoplasmic cases were found in 73.7% of haplogroup M, 100% of both haplogroup B and B*. There was no significantly different in the homoplasmic unaffected male between haplogroup M, B and B* (p-value=0.600).

Table 23. Comparison of clinical manifestation and mutation load of male between haplogroup M, B and B*.

Factors	Male			p-value
	Haplogroup M (Total=50)	**Haplogroup B** (Total=7)	**Haplogroup B*** (Total=6)	
Affected status (N) :				
Affected cases (N, %)	31 (62%)	6 (85.7%)	4 (66.7%)	0.466
Unaffected cases (N, %)	19 (38%)	1 (14.3%)	2 (33.3%)	
Affected group :				
Mutant mtDNA status :				
Homoplasmy (N, %) :	28 (90.3%)	6 (100%)	3 (75%)	0.426
Heteroplasmy (N, %) :	3 (9.7%)	0 (0%)	1 (25%)	
Age of onset :				
Total (N)	29	6	4	0.775
Mean ± SD (years)	20.03±9.05	19.83±15.16	22.25±13.33	
Median (years)	19	13	17	
Min-Max (years)	6-44	8-44	13-42	
Final Visual Acuity (VA) :				
Total (N, no. of eyes)	26 (52 eyes)	6 (11 eyes)	3 (6 eyes)	0.635
Mean ± SD (logMAR)	1.63±0.80	1.44±0.53	1.50±0.77	
Median (logMAR)	2.00	1.50	2.00	
Min-Max (logMAR)	0.00-3.00	0.70-2.00	0.50-2.00	
Unaffected group :				
Mutant mtDNA status :				
Homoplasmy (N, %)	14 (73.7%)	1 (100%)	2 (100%)	0.600
Heteroplasmy (N, %)	5 (26.3%)	0 (0%)	0 (0%)	

For information of female between haplogroup (Table 24), the affected female found in haplogroup M, B and B* were 23.3% (14/60), 66.7% (2/3) and 0% (0/1), respectively. There was no significantly different in the frequency of affected female between 3 haplogroups (p-value=0.202). In the affected female, the homoplasmic samples found in haplogroup M, B and B* were 92.9%, 100% and 0%, respectively. No significantly different between 3 haplogroups (p-value=0.875). The age of onset of female ranged from 10 to 45 years in haplogroup M (median=32.5 years), ranged from 30 to 53 years in haplogroup B (median=41.5 years) whereas female in haplogroup B* had not this information because none of them was the affected cases. No significant different between 3 haplogroups (p-value=0.331). The final VA of female ranged from 0.00 to 3.00 logMAR in haplogroup M (median=1.90 logMAR, Snellen visual acuity=6/480) whereas all of affected eyes in haplogroup B had the final VA was 3.00 logMAR (Snellen visual acuity=6/6000 or hand motion) As in the age of onset, none of female in haplogroup B* was the affected cases. There was significantly different between 3 haplogroups (p-value=0.049). In the unaffected female, the homoplasmic cases were found in 65.2% of haplogroup M, 100% of haplogroup B and 0% of haplogroup B*. There was no significantly different in homoplasmic unaffected cases between female in haplogroup M, B and B* (p-value=0.304).

7.3 Comparisons of the clinical manifestation and mutation load between homoplasmic and heteroplasmic samples of 30 G11778A LHON families.

In 30 LHON families, the heteroplasmy G11778A were found in 12 families (40%) which contained at least one individual with heteroplasmy. The clinical manifestation and mutation load of homoplasmic and heteroplasmic samples and their statistical analysis were also presented in Table 25. The affected samples of homoplasmy (51.9%) were higher than those of heteroplasmy (20.5%). The statistical analysis showed the significantly different in the frequency of affected cases between homoplasmy and heteroplasmy (p-value=0.001). In the affected group, 73.2% of homoplasmic samples were male (41/56) while 66.7% of heteroplasmic samples were male (6/9). There was no significantly different in the gender between homoplasmic and heteroplasmic samples (p-value=0.995). The age of onset ranged from 6 to 53 years in the homoplasmic samples (median=19.5 years) and from 10 to 42 in the

Table 24. Comparison of clinical manifestation and mutation load of female between haplogroup M, B and B*.

Factors	Female			p-value
	Haplogroup M (Total=60)	Haplogroup B (Total=3)	Haplogroup B* (Total=1)	
Affected status (N) :				
Affected cases (N, %)	14 (23.3%)	2 (66.7%)	0 (0%)	0.202
Unaffected cases (N, %)	46 (76.7%)	1 (33.3%)	1 (100%)	
Affected group :				
Mutant mtDNA status :				
Homoplasmy (N, %) :	13 (92.9%)	2 (100%)	0 (0%)	0.875
Heteroplasmy (N, %) :	1 (7.1%)	0 (0%)	0 (0%)	
Age of onset :				
Total (N)	10	2	0	
Mean ± SD (years)	29.50±13.17	41.50±16.26		
Median (years)	32.5	41.5		0.331
Min-Max (years)	10-45	30-53		
Final Visual Acuity (VA) :				
Total (N, no. of eyes)	12 (24 eyes)	1 (2 eyes)	0	
Mean ± SD (logMAR)	1.72±0.82	3.00±0.00		
Median (logMAR)	1.90	3.00		0.049*
Min-Max (logMAR)	0.00-3.00	3.00-3.00		
Unaffected group :				
Mutant mtDNA status :				
Homoplasmy (N, %)	30 (65.2%)	1 (100%)	0 (0%)	0.304
Heteroplasmy (N, %)	16 (34.8%)	0 (0%)	1 (100%)	

* p-value<0.05 and considered significant.

Table 25. Comparison of clinical manifestation of homoplasmic and heteroplasmic samples in 30 G11778A LHON families.

Factors	Mutation load		p-value
	Homoplasmy (Total=108)	Heteroplasmy (Total=44)	
Affected status (N) :			
Affected cases (N, %)	56 (51.9%)	9 (20.5%)	0.001*
Unaffected cases (N, %)	52 (48.1%)	35 (79.5%)	
Affected group :			
Sex :			
Male (M) (N, %)	41 (73.2%)	6 (66.7%)	0.995
Female (F) (N, %)	15 (26.8%)	3 (33.3%)	
Ratio M:F	2.73:1	2:01	
Age of onset :			
Total (N)	50	8	
Mean ± SD (years)	22.82±11.94	21.13±10.30	
Median (years)	19.5	19	0.795
Min-Max (years)	6-53	10-42	
Final Visual Acuity (VA) :			
Total (N, no. of eyes)	47 (93 eyes)	8 (16 eyes)	
Mean ± SD (logMAR)	1.71±0.76	1.66±0.84	
Median (logMAR)	2.00	2.00	0.871
Min-Max (logMAR)	0.00-3.00	0.20-3.00	
Unaffected group :			
Sex :			
Male (M) (N, %)	20 (38.5%)	10 (28.6%)	0.470
Female (F) (N, %)	32 (61.5%)	25 (71.4%)	
Ratio M:F	0.63:1	0.4:1	

* p-value<0.05 and considered significant.

heteroplasmic samples (median=19 years). No significantly different in the age of onset between the homoplasmic and heteroplasmic affected samples (p-value=0.795). The final VA ranged from 0.00 to 3.00 logMAR in the homoplasmic samples (median=2.00 logMAR, Snellen visual acuity=6/600 or counting fingers) and from 0.20 to 3.00 logMAR in the heteroplasmic samples (median=2.00 logMAR). There was also no significantly different in the final VA between homoplasmic and heteroplasmic samples (p-value=0.871). In the unaffected group, male were 38.5% of homoplasmic samples (20/52) whereas those were 28.6% of heteroplasmic samples (10/35). There was no significantly different in the gender between the homoplasmic and heteroplasmic unaffected samples (p-value=0.470).

For the homoplasmic group (Table 26), the affected cases found in haplogroup M, B and B* were 48.2% (41/85), 80% (8/10) and 60% (3/5), respectively. No significantly different in the affected homoplasmy cases between 3 haplogroups (p-value=0.487). The age of onset in the homoplasmic samples ranged from 6 to 45 years in haplogroup M (median=19.5 years), from 8 to 53 years in haplogroup B (median=23 years) and from 13 to 18 years in haplogroup B* (median=16 years). Although the median of age of onset in haplogroup B* was less than in haplogroup M and B, there was no significantly different between 3 haplogroups (p-value=0.577). The final VA of homoplasmic samples ranged from 0.00 to 3.00 logMAR in haplogroup M (median=2.00 logMAR, Snellen visual acuity=6/600 or counting fingers) and ranged from 0.70 to 3.00 logMAR in haplogroup B (median=1.51 logMAR, Snellen visual acuity=6/192). All of haplogroup B* had the final VA 2.00 logMAR. There was no significantly different in the final VA of homoplasmic samples between 3 haplogroups (p-value=0.533). In the unaffected group, 31.8%, 50% and 60% of homplasmic cases were male in haplogroup M, B and B*, respectively. The statistical analysis showed no significantly different in unaffected homoplasmy between 3 haplogroups (p-value=0.130).

For the heteroplasmic group (Table 27), the affected cases were 16% in the haplogroup M (4/25) and 50% in haplogroup B* (1/2). None of haplogroup B was heteroplasmy. There was no significantly different in the affected heteroplasmic cases between 3 haplogroups (p-value=0.342). In the affected group, male found in 75% of haplogroup M (3/4) and 100% in haplogroup B* (1/1). There was no significantly

Table 26. Comparison of clinical manifestation of homoplasmic samples between haplogroup M, B and B*.

Factors	Homoplasmy			p-value
	Haplogroup M (Total=85)	Haplogroup B (Total=10)	Haplogroup B* (Total=5)	
Affected status (N) :				
Affected cases (N, %)	41 (48.2%)	8 (80%)	3 (60%)	0.153
Unaffected cases (N, %)	44 (51.8%)	2 (20%)	2 (40%)	
Affected group :				
Sex :				
Total (N)				
Male (M) (N, %)	28 (68.3%)	6 (75%)	3 (100%)	0.487
Female (F) (N, %)	13 (31.7%)	2 (25%)	0 (0%)	
Ratio M:F	2.15:1	3:1	3:0	
Age of onset :				
Total (N)	36	8	3	
Mean ± SD (years)	22.44±11.26	25.25±17.39	15.67±2.52	
Median (years)	19.5	23	16	0.577
Min-Max (years)	6-45	8-53	13-18	
Final Visual Acuity (VA) :				
Total (N, no. of eyes)	35 (70 eyes)	7 (13 eyes)	2 (4 eyes)	
Mean ± SD (logMAR)	1.68±0.80	1.68±0.76	2.00±0.00	
Median (logMAR)	2.00	1.51	2.00	0.533
Min-Max (logMAR)	0.00-3.00	0.70-3.00	2.00-2.00	
Unaffected group :				
Sex :				
Male (M) (N, %)	14 (31.8%)	1 (50%)	2 (100%)	0.130
Female (F) (N, %)	30 (68.2%)	1 (50%)	0 (0%)	
Ratio M:F	0.47:1	1:1	2:0	

Table 27. Comparison of clinical manifestation of heteroplasmic samples between haplogroup M, B and B*.

Factors	Heteroplasmy			p-value
	Haplogroup M (Total=25)	Haplogroup B (Total=0)	Haplogroup B* (Total=2)	
Affected status (N) :				
Affected cases (N, %)	4 (16%)	0 (0%)	1 (50%)	0.342
Unaffected cases (N, %)	21 (84%)	0 (0%)	1 (50%)	
Affected group :				
Sex :				
Total (N)				
Male (M) (N, %)	3 (75%)	0 (0%)	1 (100%)	0.800
Female (F) (N, %)	1 (25%)	0 (0%)	0 (0%)	
Ratio M:F				
Age of onset :				
Total (N)	3	0	1	
Mean ± SD (years)	22.67±6.43		42.00±0.00	
Median (years)	20		42	0.180
Min-Max (years)	18-30		42-42	
Final Visual Acuity (VA) :				
Total (N, no. of eyes)	3 (6 eyes)	0	1 (2 eyes)	
Mean ± SD (logMAR)	1.48±0.82		0.50±0.00	
Median (logMAR)	2.00		0.50	0.153
Min-Max (logMAR)	0.20-2.00		0.50-0.50	
Unaffected group :				
Sex :				
Total (N)				
Male (M) (N, %)	5 (23.8%)	0 (0%)	0 (0%)	0.773
Female (F) (N, %)	16 (76.2%)	0 (0%)	1 (100%)	
Ratio M:F	0.31:1	0	0:1	

different between 3 haplogroups (p-value=0.800). The age of onset in the heteroplasmic samples ranged from 18 to 30 years in haplogroup M while the age of onset in haplogroup B* was 42 years. There was no significant in the age of onset in the heteroplasmic samples between 3 haplogroups (p-value=0.180). The final VA of the heteroplasmic samples ranged from 0.20 to 2.00 logMAR in haplogroup M (median=2.00 logMAR, Snellen visual acuity=6/600 or counting fingers). In haplogroup B*, the final VA of the heteroplasmic samples was 0.50 logMAR (Snellen visual acuity=6/18.9). No significantly different in the final VA of heteroplasmic samples betweeen 3 haplogroups (p-value=0.153). In the unaffected group, the heteroplasmic male were 23.8% in haplogroup M (5/21). None of haplogroup B (0/0) and B* (0/1) were heteroplasmic unaffected male. There was no significantly different in the gender of unaffected heteroplasmic samples between 3 haplogroups (p-value=0.773).

CHAPTER V
DISCUSSION

LHON has a strict maternal inheritance. The risk of developing the disease is inherited solely from the mother. Therefore pathogenic mtDNA mutations are recognized as the primary cause and the predominant risk factor. However LHON is characterized by incomplete penetrance and males are preferentially affected. So other factors seem to be required for the clinical manifestation and modification of the disease. These factors may include other genetic factors such as mitochondrial DNA heteroplasmy, secondary mtDNA mutation, mitochondrial background, mutations in nuclear genes, or environmental factors, but have not yet been discovered.

In our study, the mitochondrial genetic background was focus on, including the heteroplasmy of G11778A mutation in the mitochondrial genome, the secondary mtDNA mutation and the mitochondrial DNA haplogroup-specific polymorphism which could be associated with the expression of the G11778A mutation in Thai LHON samples.

1. Heteroplasmy and secondary mutation in 30 Thai LHON families

Heteroplasmy of the LHON mutation has been reported to influence the expression of disease (8). Forty percent of Thai LHON families contained at least one individual with heteroplasmy of G11778A mutation (12/30). Although in the affected persons, the homoplasmy individuals were higher than the heteroplasmic individuals statistically significant (p-value=0.001), 20.5% of heteroplasmic persons were affected. In the affected group, the clinical manifestation including age of onset and final VA and gender were not significantly different between homoplasmic and heteroplasmic persons (p-value>0.05). The result indicated that the heteroplasmy affected samples was not different in the clinical manifestation with the homoplasmy affected persons in these Thai LHON population.

In addition to the primary mutations, the secondary mutations have been suggested to act synergistically with each other and/or with the primary mutations and increase the risk of disease expression (1, 32). Two secondary mutations of LHON, G3316A and C3497T, have been found in 30 Thai LHON families. The G to A mutation at nt 3316, changed the amino acid alanine to threonine at the fourth amino acid residue of the ND1 subunit of complex I. One family (F19) was found to have this mutation together with G11778A mutation. The C3497T secondary mutation changed the amino acid alanine to valine at amino acid residue 64 of the ND1 subunit as well. Of 30 families with G11778A LHON in this study, one family (F11) carried this C3497T mutation. The number of affected persons in LHON families who carried G11778A with either G3316A (57.1%) or C3497T (85.7%) was more than the affected persons in other families that do not have these secondary mutations (39.9%) significantly (p-value=0.042). The secondary mutations, G3316A and C3497T, were then suggested to be associated with the expression of disease in Thai LHON. The significantly different in the number of affected persons among the G11778A patients who do or do not have the secondary mutation were probably caused from the small numbers of family members of the LHON families who carried G11778A and secondary mutation. All of the secondary G3316A affected persons carried heteroplasmic G11778A while homoplasmy of G11778A mtDNA was found in all affected persons of the other secondary mutation C3497T and the G11778A patients who do not have secondary mutation (p-value<0.001). The clinical manifestation, age of onset and final VA were not different between the G11778A patients who do or do not have the secondary mutation (p-value>0.05).

2. Variation of mitochondrial polymorphism including RFLP and HVS-1 polymorphisms, 9-bp deletion, T16189C and length heteroplasmy in Thai LHON individuals and normal controls

For the RFLP analysis, 145 polymorphisms were found in 30 LHON individuals and 100 normal controls. Fourteen polymorphisms were found more than 10% difference between LHON individuals and normal controls. Ten of these 14 polymorphisms were found in the LHON samples more than in the normal controls; -3534*Hae*III, -3537*Dde*I, -6957*Hae*III, -7013*Rsa*I, +9820*Hin*fI, +10394*Dde*I,

+10397*Alu*I, -14859*Hha*I, -15234*Hin*fI and +15590*Xho*II with percentage of difference; 17%, 17%, 14%, 10%, 12%, 26%, 14%, 11%, 11% and 13%, respectively. Three of these 10 polymorphisms, -3534*Hae*III, -3537*Dde*I and -15234*Hin*fI, were the polymorphism criteria of haplogroup B* which was one of 3 major haplogroups found in the LHON individual in a higher frequency than in normal controls. Furthermore, 2 of these 10 polymorphisms, +10394*Dde*I and +10397*Alu*I, were the polymorphism criteria of haplogroup M which was the most common haplogroup found in the LHON individuals greater than normal controls. The -6957*Hae*III and +9820*Hin*fI were in the COX I and COX III subunits in the respiratory chain, respectively. While the –7013*Rsa*I was also in COX I subunit and the +15590*Xho*II was in the Cy *b* of complex III. These polymorphisms, -6957*Hae*III, –7013*Rsa*I, +9820*Hin*fI, +10397*Alu*I and +15590*Xho*II did not changed the amino acid residue in their subunits whereas the +10394*Dde*I changed the amino acid threonine to alanine in the ND3 subunit of respiratory complex I. The -14859*Hha*I changed the amino acid glutamine to serine in the Cy *b* of complex III. All of these 10 polymorphisms were statistical different between normal controls and LHON individuals. The -3534*Hae*III, -3537*Dde*I, -7013*Rsa*I, +10394*Dde*I, -14859*Hha*I and +15590*Xho*II were found significantly to be associated with LHON individuals. From above reasons, 3 of these polymorphisms, -3534*Hae*III, -3537*Dde*I and +10394*Dde*I, were the haplogroup determination criteria and -7013*Rsa*I and +16383*Xho*II site did not change the amino acid. Therefore only the -14859*Hha*I site was probably associated with the Thai LHON patients. Other 4 polymorphisms found in normal controls more than LHON samples were the -9052*Hae*II, -9053*Hha*I, -12406*Hin*cII and -12406*Hpa*I, the different percentage of frequency were 15%, 15%, 16% and 16%, respectively. Two of these 4 polymorphisms, -12406*Hin*cII and -12406*Hpa*I, were the haplogroup F criteria which was not found in the LHON individuals. Another 2 polymorphisms, -9052*Hae*II and -9053*Hha*I, were in the ATP6 subunit and changed the amino acid serine to glutamine. These 4 polymorphisms, -9052*Hae*II, -9053*Hha*I, -12406*Hin*cII and -12406*Hpa*I, were different between normal controls and LHON samples which found only -12406*Hin*cII and -12406*Hpa*I were significant (p-value<0.05). These 2 polymorphisms changed the amino acid valine to isoleucine in the ND5 subunit. These results suggested that these 2 polymorphisms, -12406*Hin*cII and -12406*Hpa*I,

did not shared the common ancestor with the G11778A mutation in Thai population and also were probably not associated with the expression in Thai LHON.

For the HVS-1 sequence, 108 variants were found in 30 LHON individuals and 100 normal controls. Six polymorphisms were found more than 10% difference between LHON individuals and normal controls. Three of them were found in the LHON samples more than the normal controls; C16140T, C16182A and C16183A, the different percentage of frequency were 10%, 15% and 16%, respectively. These 2 variations, C16182A and C16183A, were close to the homopolymeric tract of 10 cytosines which cause length heteroplasmy. Thus, they probably associated with length heteroplasmy which was found in the LHON individuals (36%) more than in the normal controls (28%) (p-value=0.496). The C16140T were one of haplogroup B* criteria which was found in LHON individuals higher than in normal controls. The other 3 polymorphisms were found in normal controls more than LHON samples; C16172T, C16304T and C16362T, and their frequency different were 15%, 23% and 17%, respectively. One of them, C16304T, was the criteria variation of haplogroup F which was found only in the normal controls whereas the other variant, C16362T, was one of the criteria of haplogroup D which was the haplogroup found in the normal controls more than the LHON individuals. All of them were tested for statistical different between normal controls and LHON individuals. The statistical analysis found that only the C16304T mutation was significantly different (p-value=0.009). These result suggested that the C16304T mutation did not share the common ancestor with the G11778A mutation in these Thai population and may occurred with none disease expression.

Furthermore, the sample harbored the T16189C mutation in the HVS-1 sequence also had the length heteroplasmy in the sequencing result. Bendall and Sykes (1995) found the T16189C mutation results in an unstable homopolymeric tract of ten cytosines, and length variation of the poly [C] (pattern of length heteroplasmy) was observed in the individuals in a heteroplasmic manner. The length heteroplasmy was also found in the most cases who harboring the T16189C mutation in both Thai normal controls (82%) and LHON individuals (92%). These finding confirmed that length heteroplasmy was associated with the T to C mutation at nucleotide position 16189 in Thai samples (p-value<0.001). The frequency of either T16189C mutation

or length heteroplasmy or T16189C with length heteroplasmy between normal controls and LHON individual were not significant different (p-value<0.05). These results demonstrated that the T16189C mutation and length heteroplasmy and T16189C with length heteroplasmy were not specific with the expression of LHON in Thai families.

The 9-bp deletion between the COII and $tRNA^{Lys}$ genes in the mitochondrial DNA was the one of the marker defining haplogroup B and was also very common in Asians and populations of Asian ancestry (63, 66). In this study, the 9-bp deletion was found in 25% of the studied samples whereas 93% in Polynesia, 19% in Japanese, 20% in Chinese, 14% in coastal New Guineans (70). The 9-bp deletion was found in normal controls (23%) and LHON individuals (33.3%) and was not significantly different (p-value=0.367). In this study, most of mtDNA harboring the 9-bp deletion also had the T16189C mutation in the HVS-1 (90.91%) as similar in the Amerinds, and East Asians (70, 71). Furthermore, the individual harboring 9-bp deletion also harbor T16189C and length heteroplasmy (81.8%) significantly (p-value<0.001). These indicated that the 9-bp deletion was associated with T16189C and length heteroplasmy as reported in the previous study (72).

3. Phylogenetic analysis of 30 Thai LHON samples and 100 normal controls

In all unroot and root phylogenetic trees constructed from the RFLP and 9-bp deletion information (Figure 9 and 10, respectively) and HVS-1 sequence (Figure 11 and 12, respectively), the LHON samples were dispersed in many branches of the trees but clustered in haplogroup M, B and B*. The scattering of G11778A LHON samples in different mtDNA backgrounds suggested that the G11778A mutation have arisen several independent times in the Thai LHON population. None of LHON individuals were in the haplogroup F cluster.

In all trees constructed from the RFLP and 9-bp deletion information (unroot tree in Figure 9 and root tree in Figure 10) and HVS-1 sequence (unroot tree in Figure 11 and root tree in Figure 12), the haplogroup B, B* and F samples were clustered in one branch while haplogroup M samples were divided in many branches of these trees. These demonstrated that haplogroup M in our population have the higher mitochondrial DNA diversity within group than haplogroup B, B* and F.

Eleven of 96 controls and 1 LHON samples were haplogroup C or D or G which shared the +10394*Dde*I and +10397*Alu*I in the RFLP information and the C to T at nucleotide 16223 in the HVS-1 sequence as in haplogroup M. They also clustered in haplogroup M in both phylogenetic tree constructed from the RFLP and 9-bp deletion information (Figure 9) and HVS-1 sequence (Figure 11). These result supported previous study that haplogroup C and D were the subhaplogroup of haplogroup M (27, 28).

Both of phylogenetic trees constructed form either RFLP and 9-bp deletion (Figure 10) or HVS-1 sequence (Figure 12) also supported the individual harboring 9-bp deletion constituted a group of mtDNA defined by the T16189C mutation in the studied samples. Both LHON samples and normal individuals who harboring 9-bp deletion with T16189C and length heteroplasmy were clustered together especially in haplogroup B and B*. The T16189C mutation and 9-bp deletion were the HVS-1 and RFLP criteria of both haplogroup B and B*, respectively.

Some samples belong to 2 haplogroups in one individual. Three samples, C11, C41 and F11, were defined as haplogroup B and B* from HVS-1 criteria but they clustered with haplogroup B samples. They were defined as haplogroup B as determined by RFLP and located according to their RFLP haplogroup in RFLP tree. All results supported that C11, C41 and F11 were truly haplogroup B. While one sample, C28, were both haplogroup A9 and B determined by RFLP and 9-bp deletion information, this sample was clustered with haplogroup A in the RFLP tree. Therefore C28 shared the maternal ancestor with haplogroup A. Two samples, C48 and C75, were defined as haplogroup M and P in one individual as determined by HVS-1 sequence, while they were located in haplogroup M cluster in the HVS-1 and RFLP tree. Thus they were truly haplogroup M. Three samples, C40, C62 and C70, belong to haplogroup F and M as determined by the HVS-1 criteria but they were in haplogroup M cluster in the HVS-1 tree. These results showed that they shared the common ancestor with haplogroup M.

In the phylogenetic tree constructed from RFLP and 9-bp deletion, there were two unclassified samples (C36 and F14) clustered in haplogroup B* defined by the RFLP and 9-bp deletion information (Figure 10) and they were also haplogroup B* determined by HVS-1 sequence and clustered in this haplogroup in HVS-1 tree

(Figure 12). They also harbored the 9-bp deletion and T16189C mutation with length heteroplasmy in the HVS-1 sequence as same as most of haplogroup B* samples. These evidence assumed that they shared the common maternal ancestor with haplogroup B* but they do not have the mutation(s) in the nucleotide(s) that defined the RFLP haplogroup B*. The normal control, C36, has the +15234*Hin*fI and the -16517*Hae*III which made C36 not to be classified in haplogroup B* whereas LHON sample, F14, has the +15234*Hin*fI and the -15235*Mbo*I which made F14 not to be classified in haplogroup B*. In the RFLP unclassified LHON individual, F6, was haplogroup M determined by both HVS-1 criteria and their tree. This sample lost the 10394*Dde*I site which was the one of RFLP haplogroup M criteria. This LHON sample also located with haplogroup M in the tree constructed by RFLP. Thus this sample shared the common ancestor with haplogroup M in both coding and non-coding region. This result indicated that the LHON sample, F6, were truly haplogroup M. In contrast, 2 samples, C42 and F4, were the unclassified samples determined by HVS-1 but they were in haplogroup F and M clusters, respectively. The RFLP criteria and their phylogenetic tree also supported this result. Finally, these samples, C42 and F4 were truly haplogroup F and M, respectively supported by all of results. All of the results indicated that the phylogenetic tree was one of the good tool to determine the haplogroup of unclassified samples determined by only polymorphic criteria.

While the RFLP haplogroup A, C2, C28 and C51, were clustered according to their haplogroup in the RFLP tree, they were haplogroup M determined by HVS-1 sequence criteria and clustered within their haplogroup but located near haplogroup A, C37, defined by both RFLP and HVS-1 criteria. These results suggested that they still share common ancestor with haplogroup A but they do not have the T16362C mutation which was one of HVS-1 haplogroup A criteria. This suggested that the HVS-1 sequence criteria of haplogroup A were probably not suitable to determine this haplogroup in the studied samples.

In the phylogenetic tree constructed from HVS-1 sequence, 4 unclassified LHON individuals, F7, F10, F19 and F27, were clustered with haplogroup B. It was assumed that these samples shared the common ancestor with the HVS-1 haplogroup B samples. Moreover, these LHON samples also shared the T16189C mutation in the HVS-1 sequence and length heteroplasmy and 9-bp deletion as the other haplogroup B

samples within the same branch of the HVS-1 tree (Figure 12). All of them carried the 16189T and 16217T mutation which made them not to be haplogroup B. Only F7 and F10 were the RFLP haplogroup B and clustered with this haplogroup in the RFLP tree, therefore they were truly haplogroup B. Although the HVS-1 tree defined 2 samples, F19 and F27 as haplogroup B, they were haplogroup B* determinined by RFLP criteria thus RFLP criteria distinguished them out of haplogroup B. The other one, C89, was the unclassified sample located in the haplogroup B cluster in the RFLP tree. This sample was classified as haplogroup M and located in this haplogroup cluster in the phylogenetic tree constructed by HVS-1 sequence. Thus C89 was not either haplogroup B or M.

There were some samples that could be classified by RFLP criteria but they were unclassified determined by HVS-1 sequence. Four samples, C9, C91, C101 and F3, were the RFLP haplogroup B* but they were the HVS-1 unclassified samples and also not clustered in any known haplogroup. As those 4 samples, the HVS-1 unclassified sample, C65, was the RFLP haplogroup B therefore they were also not haplogroup B determined by HVS-1 criteria and their tree.

Some of haplogroup M or D (C12, C15, C17 and C22) and haplogroup F (C13, C47, C59, C85, C96 and C102) determined by HVS-1 criteria were the RFLP unclassified haplogroups. Therefore RFLP criteria was the tool for distinguish them out of haplogroup M, D and F, respectively. All of these results suggested that the RFLP criteria and their tree together with the HVS-1 criteria and their tree were the good tool for determination the haplogroup in the samples.

However, there were 2 normal controls, C7 and C35, and 1 LHON individual, F12, which could not be classified into any haplogroup by any criteria. These results demonstrated that these 3 samples do not have the relationship with the known haplogroup samples defined by RFLP and HVS-1 criteria and also do not share the common ancestor with the other samples.

4. Distribution of mitochondrial DNA haplogroups in 30 LHON families and 100 normal controls in Thai population

In the studied samples, most of the haplogroup determined by the RFLP and 9-bp deletion information was similar to the haplogroup determined by HVS-1 sequence in

the same individual (81% in the normal controls and 83.3% in the LHON individuals). These results indicated that the RFLP and HVS-1 criteria were the quite good criteria to defined haplogroup in these Thai population.

To determine the definite mitochondrial DNA haplogroup, at least 3 of 4 criteria, high-resolution RFLP and 9-bp deletion information, and their phylogenetic tree, and HVS-1 sequence data, and their phylogenetic tree, were used in this study. The classified samples were found in 83.3% of LHON individuals. Three definite haplogroup, M, B and B*, were found in the LHON samples. The frequencies of these haplogroups in the LHON individuals were 60%, 10% and 13.3%, respectively. In this study, the classified samples were found in 81% of all normal controls. Seven mitochondrial DNA haplogroups were found in our 100 normal controls, M, B, B*, F, A, C and D. The frequency of these haplogroups in the normal controls were 45%, 10%, 8%, 15%, 1%, 1% and 1%, respectively. The most common haplogroups in the normal Asian population were M, F and B (27, 28, 44, 73) as same as in our Thai normal controls and LHON families.

The most common haplogroups in our normal controls were M and F whereas the most common haplogroups in the LHON samples were M and B*. Although the frequency of haplogroup M and B* in LHON individuals were more than normal controls but they were not statistical significance (p-value>0.05). The results indicated that haplogroup M and B* were not associated with the disease expression in Thai LHON. Interestingly, haplogroup F was found only in the normal controls. This result suggested that the G11778A mutation was not shared the maternal ancestor with haplogroup F and their haplogroup-determined polymorphisms in Thai LHON families.

In the previous study, haplogroup J was associated with the LHON Caucasian (32). Haplogroup J was not found in our studied samples. The result was the same as in the Iranian LHON patients which were not associated with haplogroup J (74).

Moreover, the LHON samples in this study included one Indian, who was Thai habitat, was classified in haplogroup M which was not the same as the common haplogroup, N, in the Indian population (75).

5. The clinical manifestation and mutation load correlation in these 30 Thai LHON families

All maternal relatives of 30 LHON families available were included in this study. For all samples analysed, male were affected more than female and the homoplasmy were found in the affected persons higher than in the unaffected persons. The statistical analysis showed that gender and mutation load were associated with the LHON expression (p-value=0.001 and <0.001, respectively). Although almost of the affected persons were homoplasmy, there were highly percent of heteroplasmic G11778A person in the affected group. Thus the heteroplasmy of G11778A was one of the factors involve in pathogenic role in Thai LHON population. The clinical manifestation and heteroplasmy in 30 Thai LHON families between the mitochondrial DNA haplogroups were also analysed. These clinical variables used in this study were affected status, gender, age of onset, and final visual acuity. The affected persons were found in most of LHON haplogroup B (80%) whereas about half of haplogroup M (59.1%) and B* (42.9%) were the unaffected persons. The statistical significant was also supported the different in the affected frequency between those 3 haplogroups, M, B and B* (p-value=0.047). Thus the frequency of the affected persons found in haplogroup B was higher than haplogroup B* and M, respectively. In the affected group, no clinical features different between haplogroups among LHON patients (p-value>0.05). As in the unaffected group, the gender and the mutation load were not significant different between the LHON haplogroups (p-value>0.05). This result indicated that the clinical manifestation and mutation load of either affected or unaffected persons between 3 haplogroups were not different.

The bias penetrance of LHON expression in male was found in this study. The clinical manifestation and mutation load between male and female of all maternal Thai LHON relatives were also compared. No clinical feature and mutation load different between male and female in these Thai LHON families (p-value>0.05). In the comparison of clinical manifestation and mutation load in male between haplogroups, the statistical analysis found no different between 3 haplogroups (p-value>0.05). In comparison of male, no different in the clinical manifestation and degree of mutation load of female except for the final visual acuity which was significantly different

between haplogroups. Less of visual loss (visual acuity) was found in haplogroup M more than haplogroup B while none of the female affected cases were haplogroup B*.

The clinical manifestation of either homoplasmy or heteroplasmy of G11778A mutation between LHON haplogroups were also analysed. For the homoplasmic group, none of clinical manifestation were different between haplogroups (p-value>0.05). As in the homoplasmic group, the clinical feature in the heteroplasmic persons between 3 haplogroups found in LHON families were not significantly different (p-value>0.05).

In conclusion, the number of affected persons and the final VA in affected female were different among haplogroup M, B and B* in Thai LHON families. Haplogroup B was found in the highest frequency of affected persons than haplogroup B* and M. Moreover the affected female in haplogroup B also have more visual loss than haplogroup M and none of haplogroup B* female were affected.

CHAPTER VI
CONCLUSION

In this study, the mitochondrial genetic background was analysed in order to identify the polymorphisms in the mitochondrial DNA that may be associated with the LHON expression in Thai families. The RFLP and 9-bp deletion and HVS-1 sequence data of 100 normal controls and 30 Thai families with the G11778A LHON were used in this study. Approximately 24% of the whole mitochondrial sequences were screened using both methods. Haplogroup A, B, B*, C, D, F and M were found in our normal controls whereas only haplogroup M, B and B* were found in these 30 LHON families. None of haplogroups were associated with these LHON families compared with the normal controls except for haplogroup F which tend to have the bias of none association with the LHON G11778A expression. For these Thai LHON families, no significant clinical correlation between haplogroups and 30 LHON families except for the frequency of affected persons found in haplogroup B were higher than haplogroup M and B*. The clinical manifestation of each sex was also not different between 3 haplogroups except for the final VA in female of haplogroup B was higher than haplogroup M and none of haplogroup B* female were affected. The clinical manifestation of the homoplasmic and heteroplasmic persons between haplogroup M, B and B* in these Thai LHON families were not different.

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APPENDIX

APPENDIX A

Appendix A: The mitochondrial mutations reported to be associated with Leber Hereditary Optic Neuropathy (44).

Locus	Disease	Allele	Nucleotide Position	Nucleotide Change	Amino Acid Change	Homoplasmy	Heteroplasmy
MTND1	LHON	3460A	3460	G-A	A-T	+	+
MTND1	LHON	4216C	4216	T-C	Y-H	+	-
MTND2	LHON	4917G	4917	A-G	N-D	+	-
MTND4	LHON	11778A	11778	G-A	R-H	+	+
MTND6	LDYT / Leigh Disease	14459A	14459	G-A	A-V	+	+
MTND6	LHON	14482G	14482	C-G	M-I	+	+
MTND6	LHON	14484C	14484	T-C	M-V	+	+
MTND1	LHON	3635A	3635	G-A	S-N	+	-
MTND1	LHON	4136G	4136	A-G	Y-C	+	-
MTND1	LHON	4160C	4160	T-C	L-P	+	-
MTND1	LHON	4171A	4171	C-A	L-M	+	+
MTND2	LHON	4640A	4640	C-A	I-M	+	-
MTND2	LHON	5244A	5244	G-A	G-S	-	+
MTCO1	LHON; SNHL	7444A	7444	G-A	Ter-K	+	-
MTATP6	LHON	9101C	9101	T-C	I-T	+	-
MTCO3	LHON	9438A	9438	G-A	G-S	+	-
MTCO3	LHON	9738T	9738	G-T	A-S	+	-
MTCO3	LHON	9804A	9804	G-A	A-T	+	-

Appendix A (continued): The mitochondrial mutations reported to be associated with Leber Hereditary Optic Neuropathy (44).

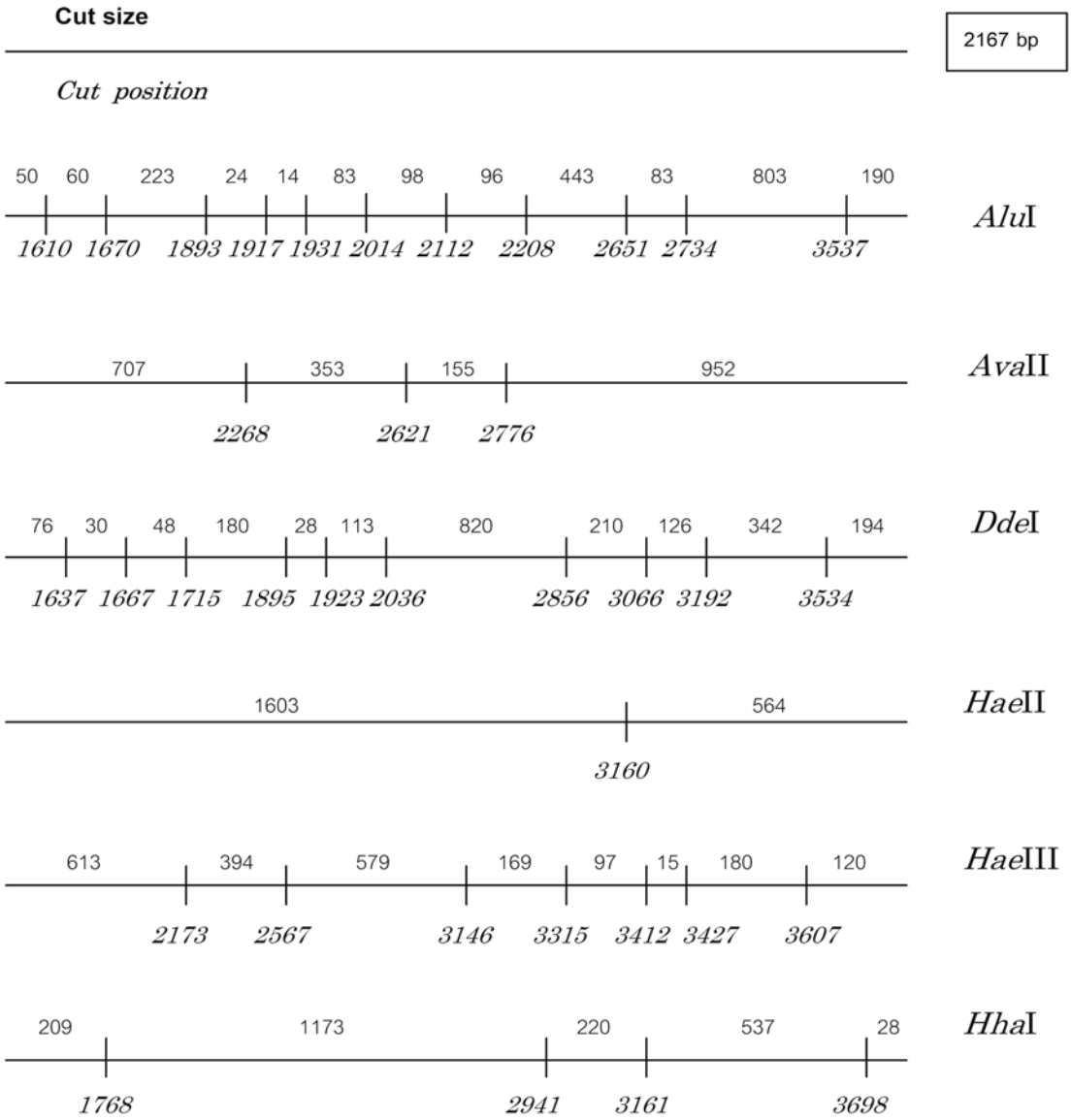
Locus	Disease	Allele	Nucleotide Position	Nucleotide Change	Amino Acid Change	Homoplasmy	Heteroplasmy
MTND4L	LHON	10663C	10663	T-C	V-A	+	-
MTND4	LHON	11696A	11696	G-A	V-I	-	+
MTND5	MELAS / LHON / Leigh overlap syndrome	13045C	13045	A-C	M-L	-	+
MTND5	LHON-like	13528G	13528	A-G	T-A	+	-
MTND5	LHON	13730A	13730	G-A	G-E	-	+
MTND6	LHON	14482A	14482	C-A	M-I	+	+
MTND6	LHON	14495G	14495	A-G	L-S	-	+
MTND6	LHON	14498C	14498	T-C	Y-C	+	+
MTND6	LHON	14568T	14568	C-T	G-S	+	-
MTND6	LHON	14596T	14596	A-T	I-M	+	-
MTND1	LHON	3496T	3496	G-T	A-S	+	-
MTND1	LHON	3497T	3497	C-T	A-V	+	-
MTND1	NIDDM; LHON; PEO	3316A	3316	G-A	A-T	+	-
MTND1	LHON; NIDDM	3394C	3394	T-C	Y-H	+	-
MTND5	LHON	13708A	13708	G-A	A-T	+	-
MTCYB	LHON	15257A	15257	G-A	D-N	+	-
MTCYB	LHON	15812A	15812	G-A	V-M	+	-

APPENDIX B

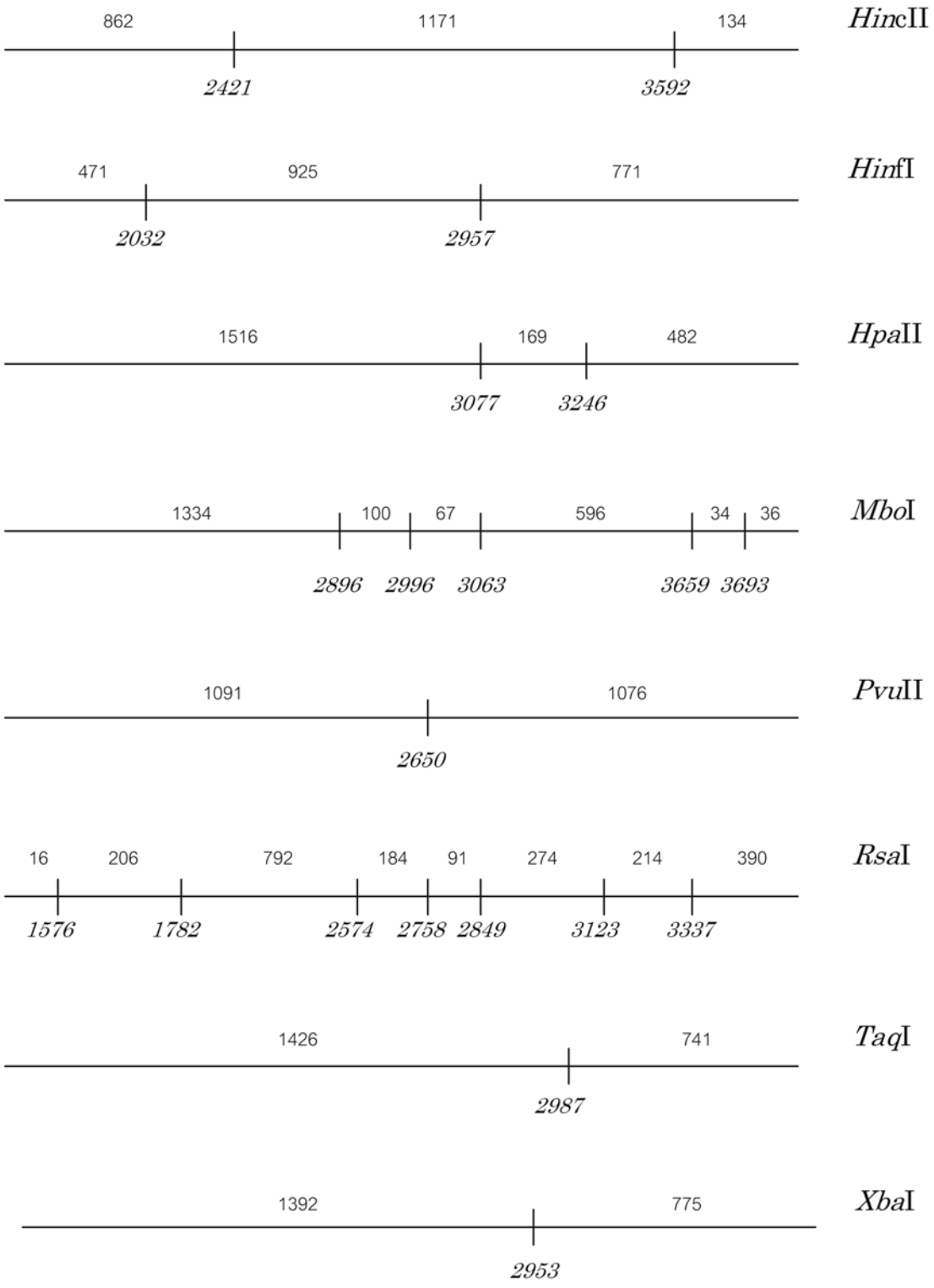
Restriction map

Primer pair 1 : L1562 – H3728 = 2167 bp

None of recognition site was found when using these restriction enzymes, *Bam*HI, *Hpa*I, *Pst*I, *Xho*II, with PCR product from this primer pair.

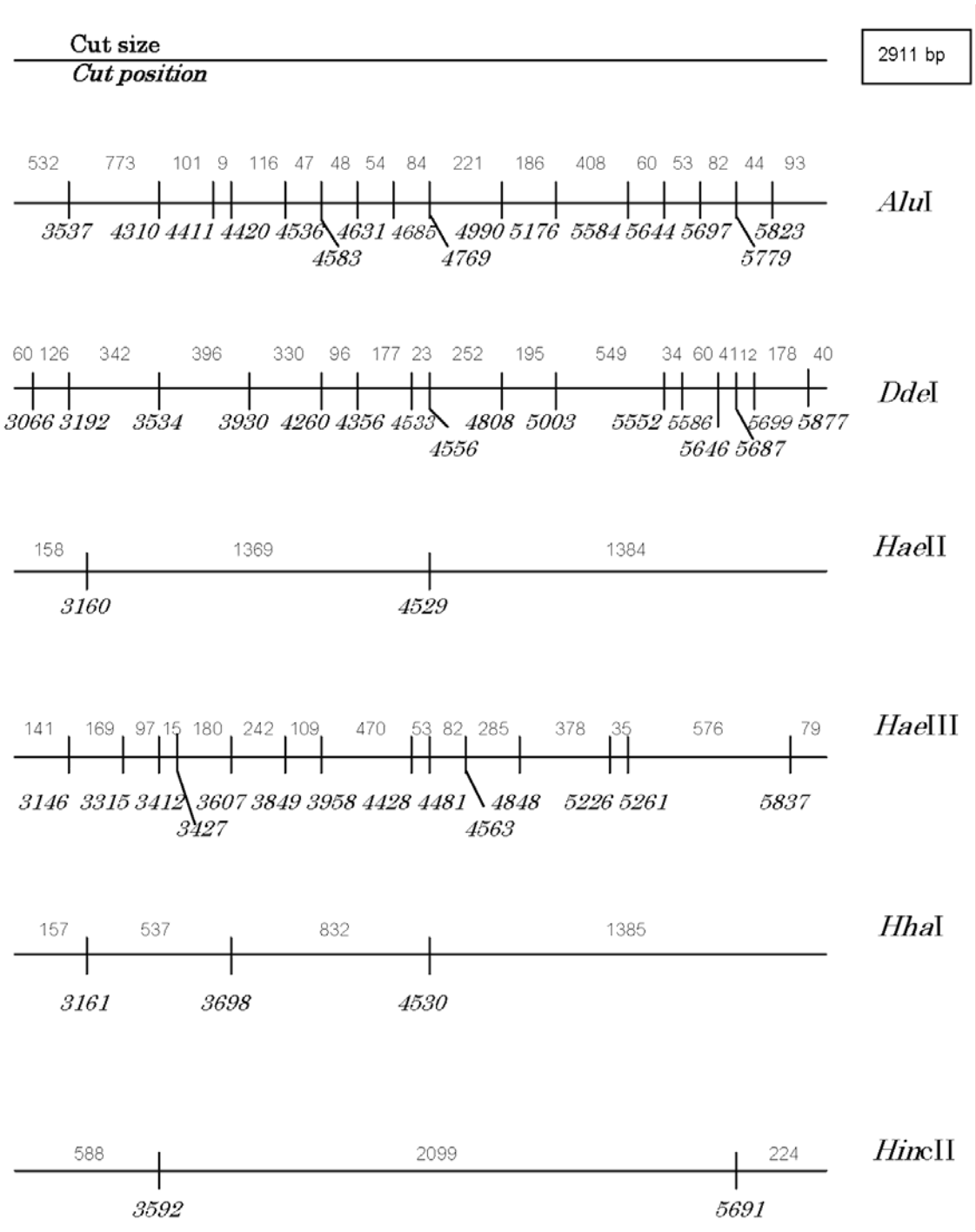


***Primer pair 1 : L1562 – H3728 = 2167 bp* (continued)**

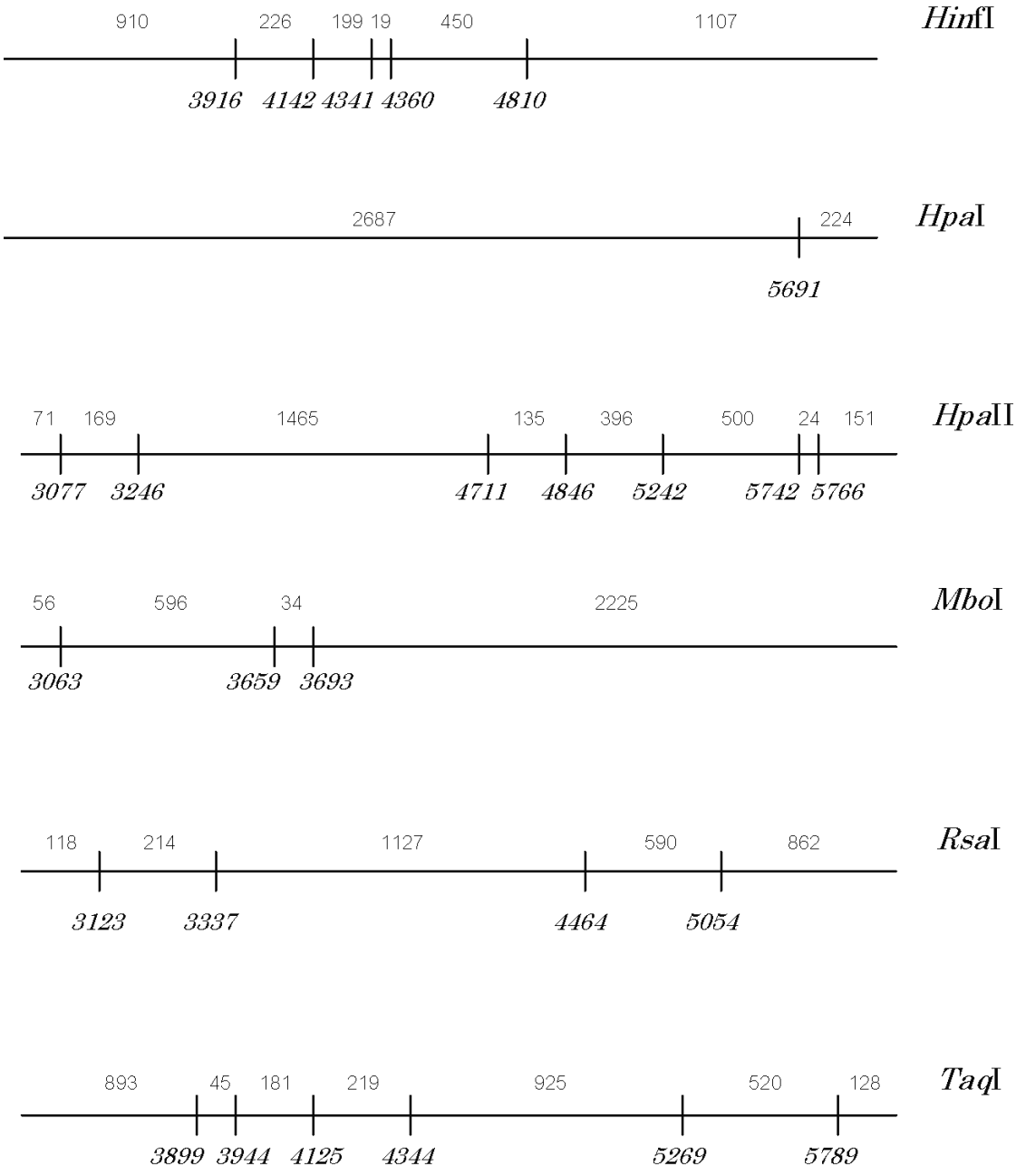


Primer pair 2 : L3007 – H5917 = 2911 bp

None of recognition site was found when using these restriction enzymes, *Ava*II, *Bam*HI, *Pst*I, *Pvu*II, *Xba*I, *Xho*II, with PCR product from this primer pair.

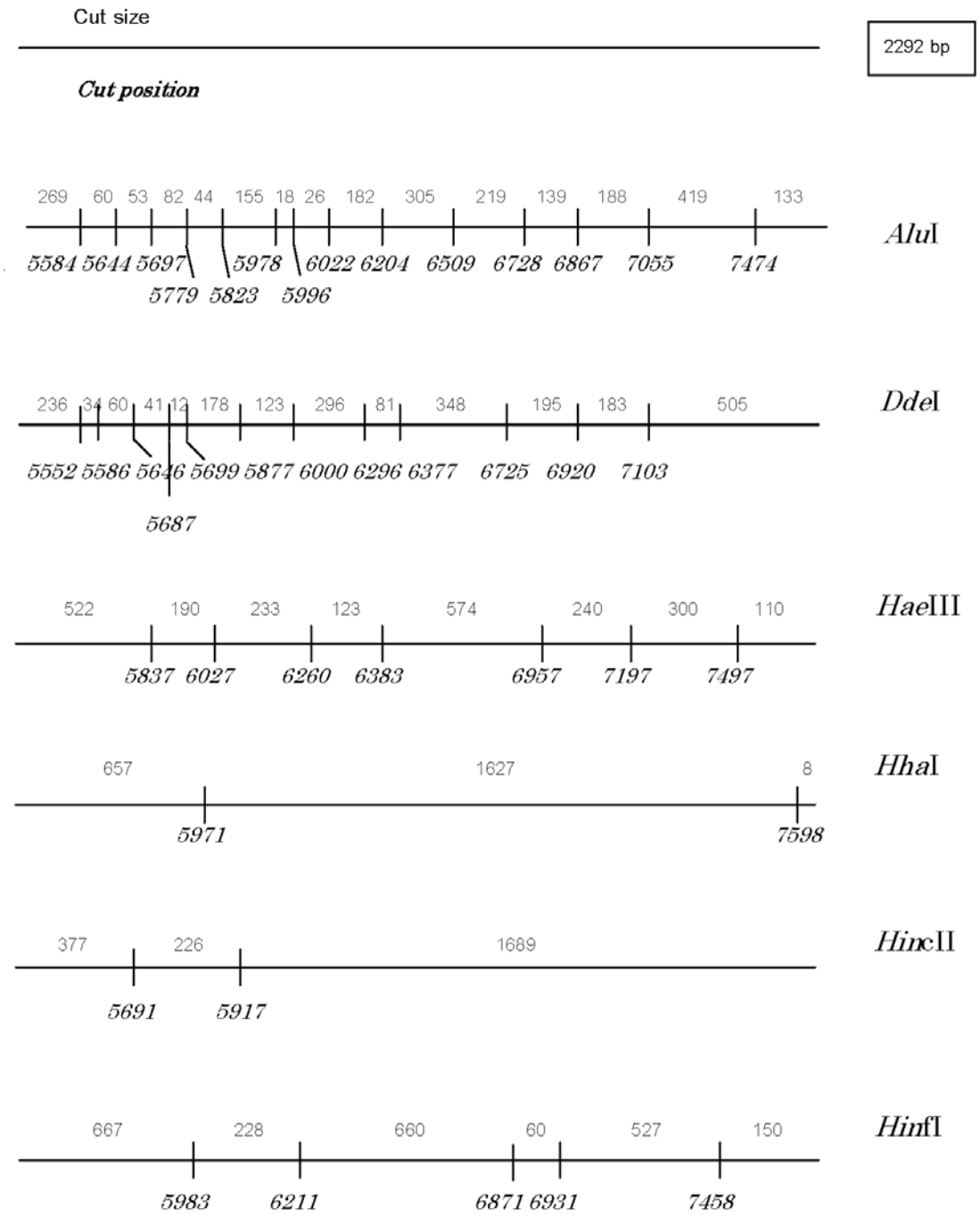


***Primer pair 2 : L3007 – H5917 = 2911 bp* (continued)**

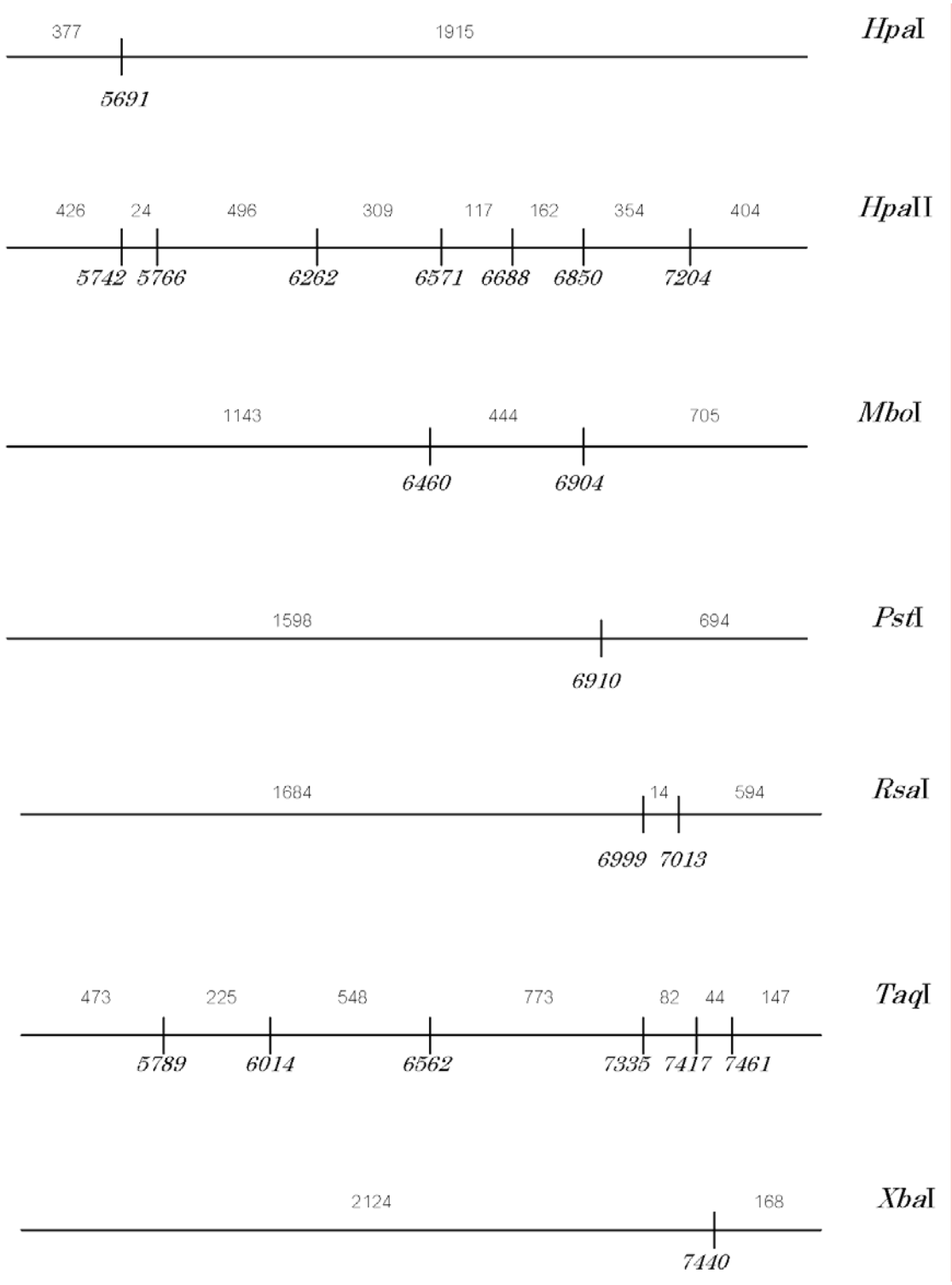


Primer pair 3 : L5317 – H 7608 = 2292 bp

None of recognition site was found when using these restriction enzymes, *Ava*II, *Bam*HI, *Hae*II, *Pvu*II, *Xho*II, with PCR product from this primer pair.

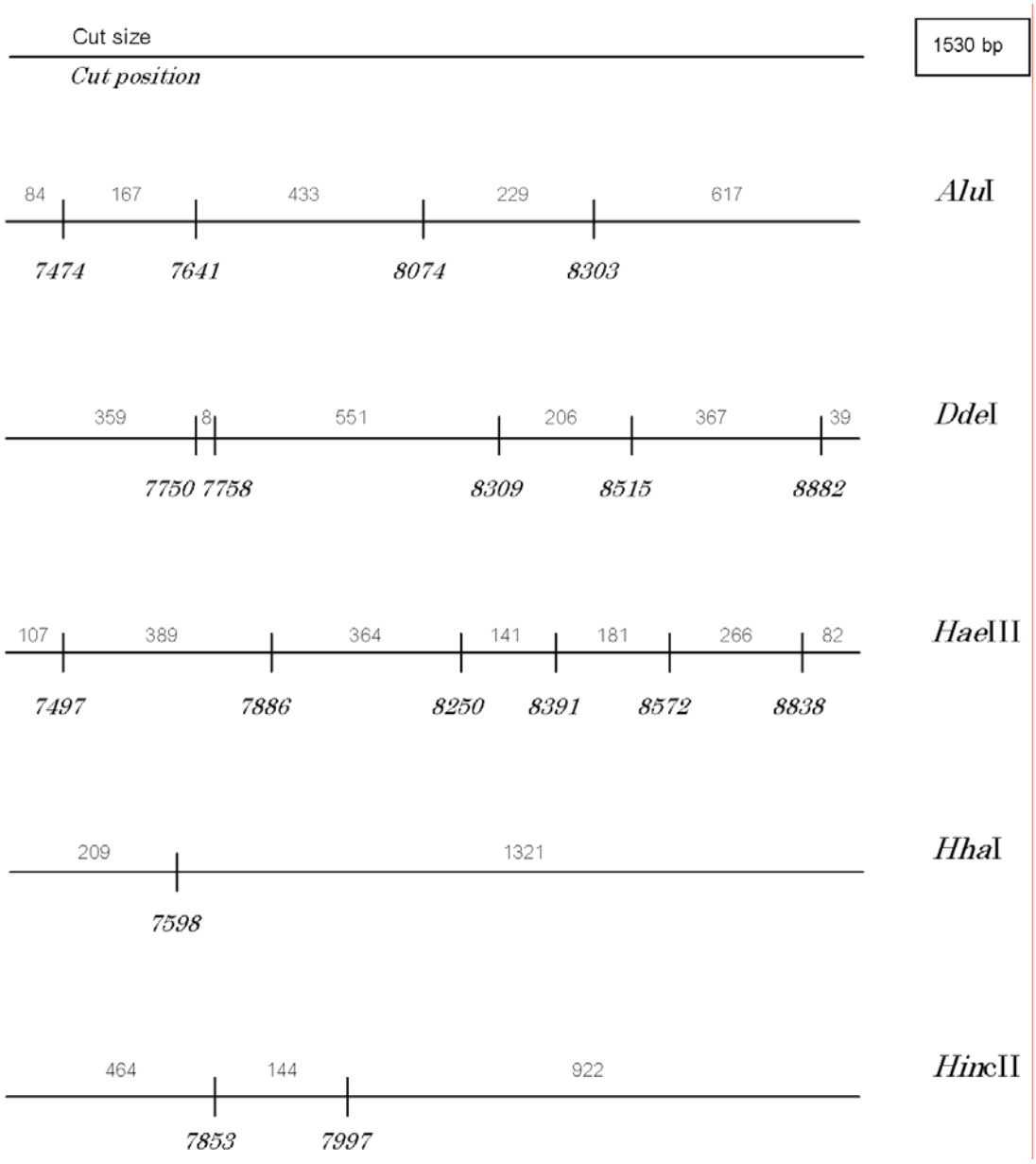


***Primer pair 3 : L5317 – H 7608 = 2292 bp* (continued)**

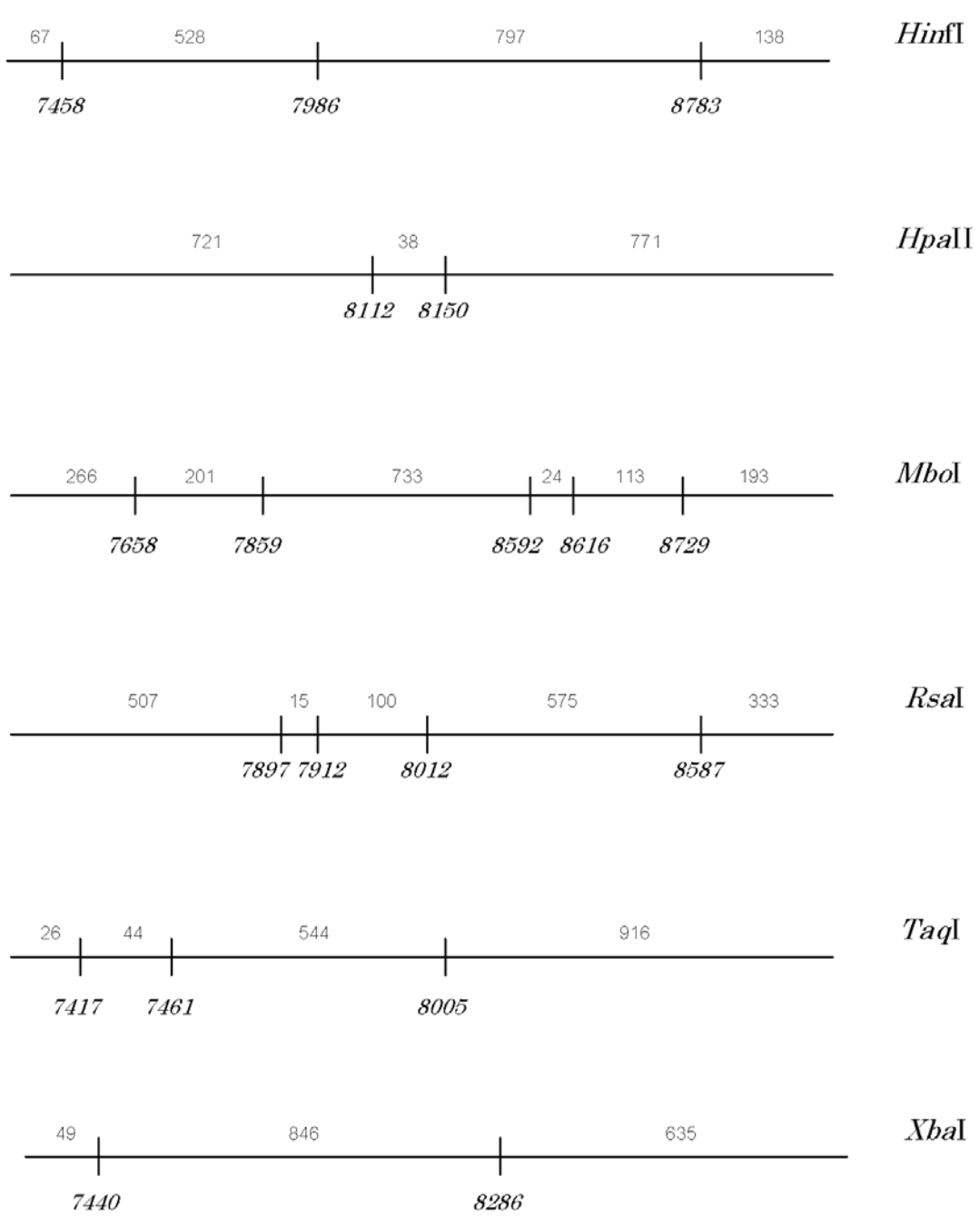


Primer pair 4 : L7392 – H8921 = 1530 bp

None of recognition site was found when using these restriction enzymes, *Ava*II, *Bam*HI, *Hae*II, *Hpa*I, *Pst*I, *Pvu*II, *Xho*II, with PCR product from this primer pair.

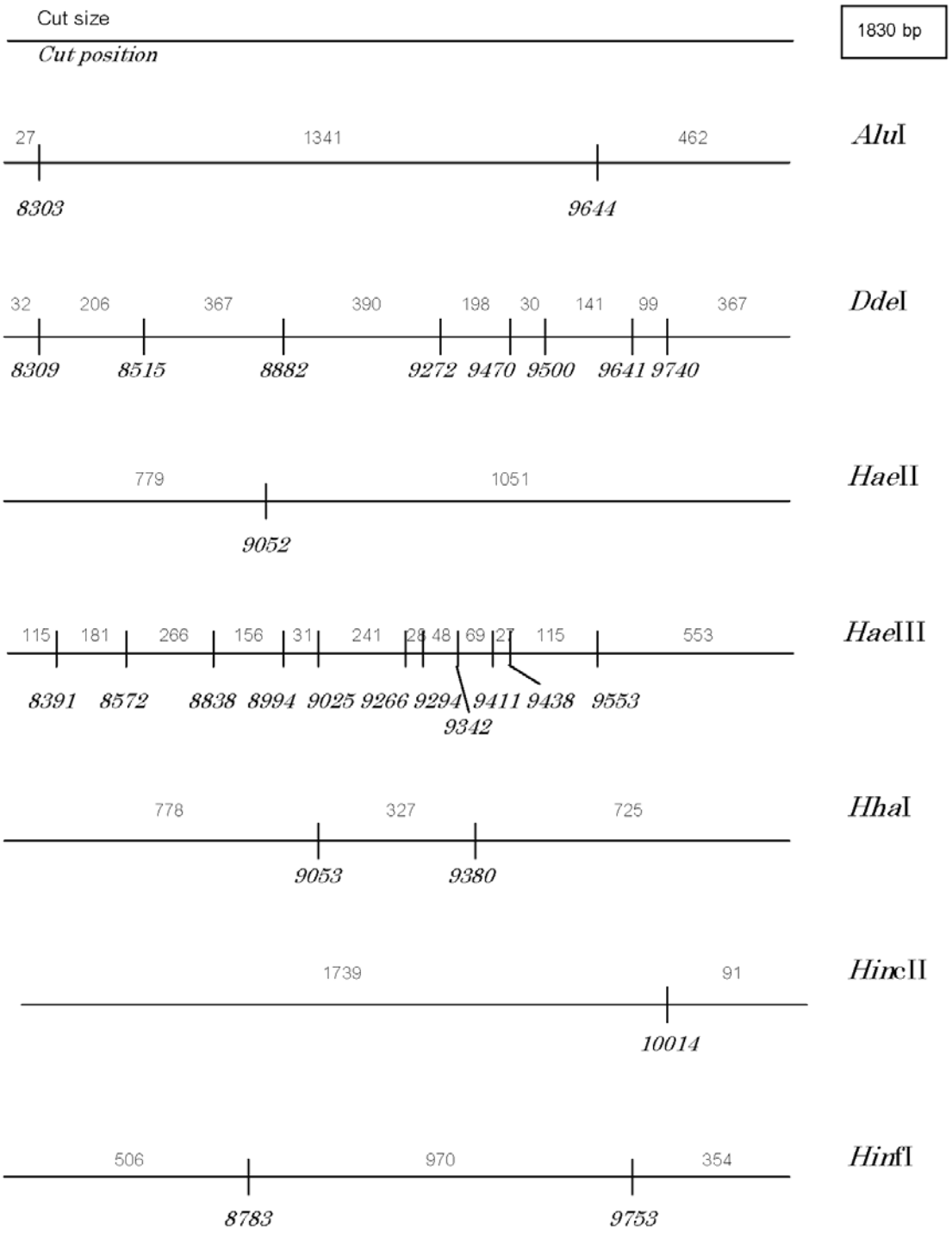


Primer pair 4 : L7392 – H8921 = 1530 bp **(continued)**

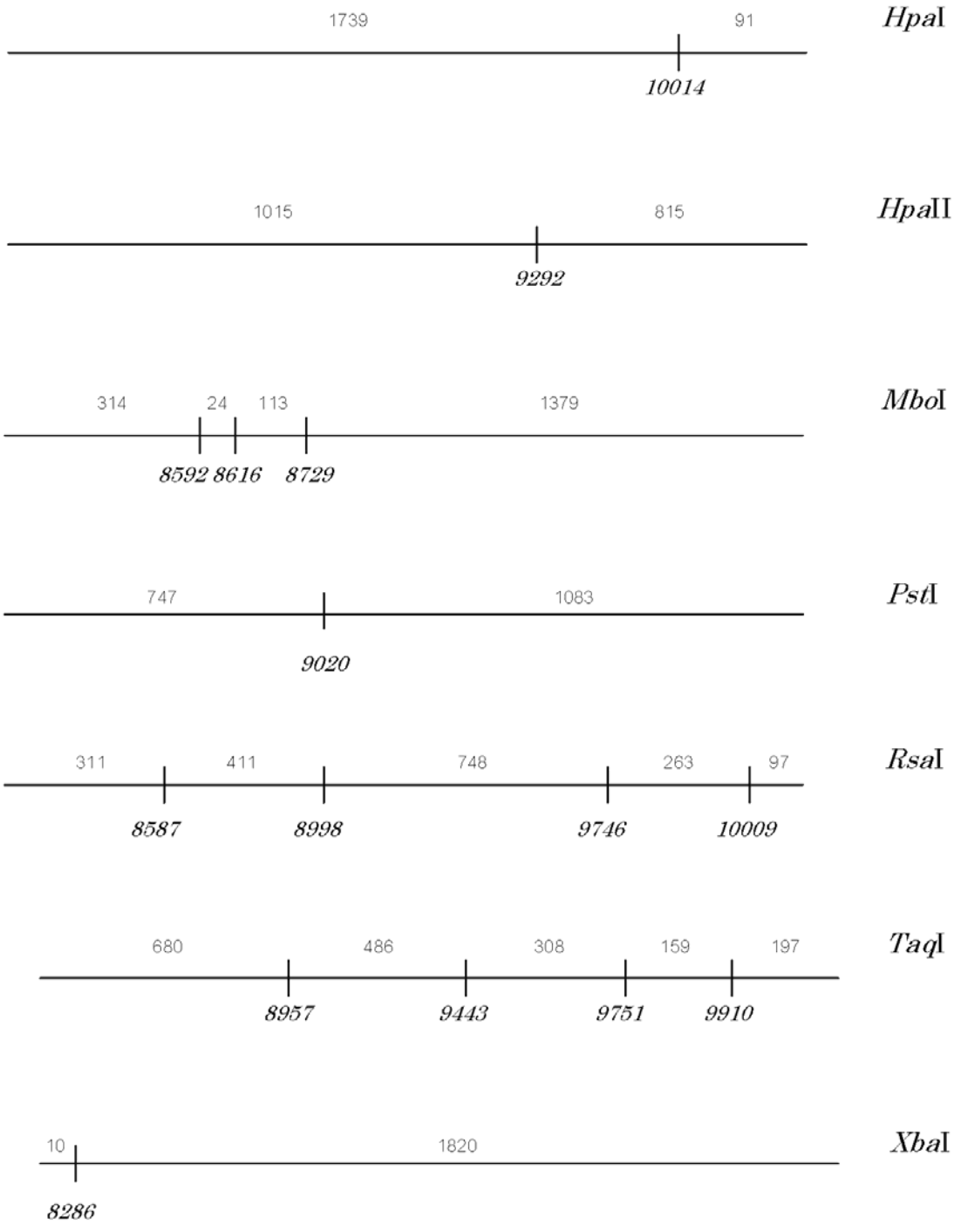


Primer pair 5 : L8278 - H10107 = 1830 bp

None of recognition site was found when using these restriction enzymes, *Ava*II, *Bam*HI, *Pvu*II, *Xho*II, with PCR product from this primer pair.

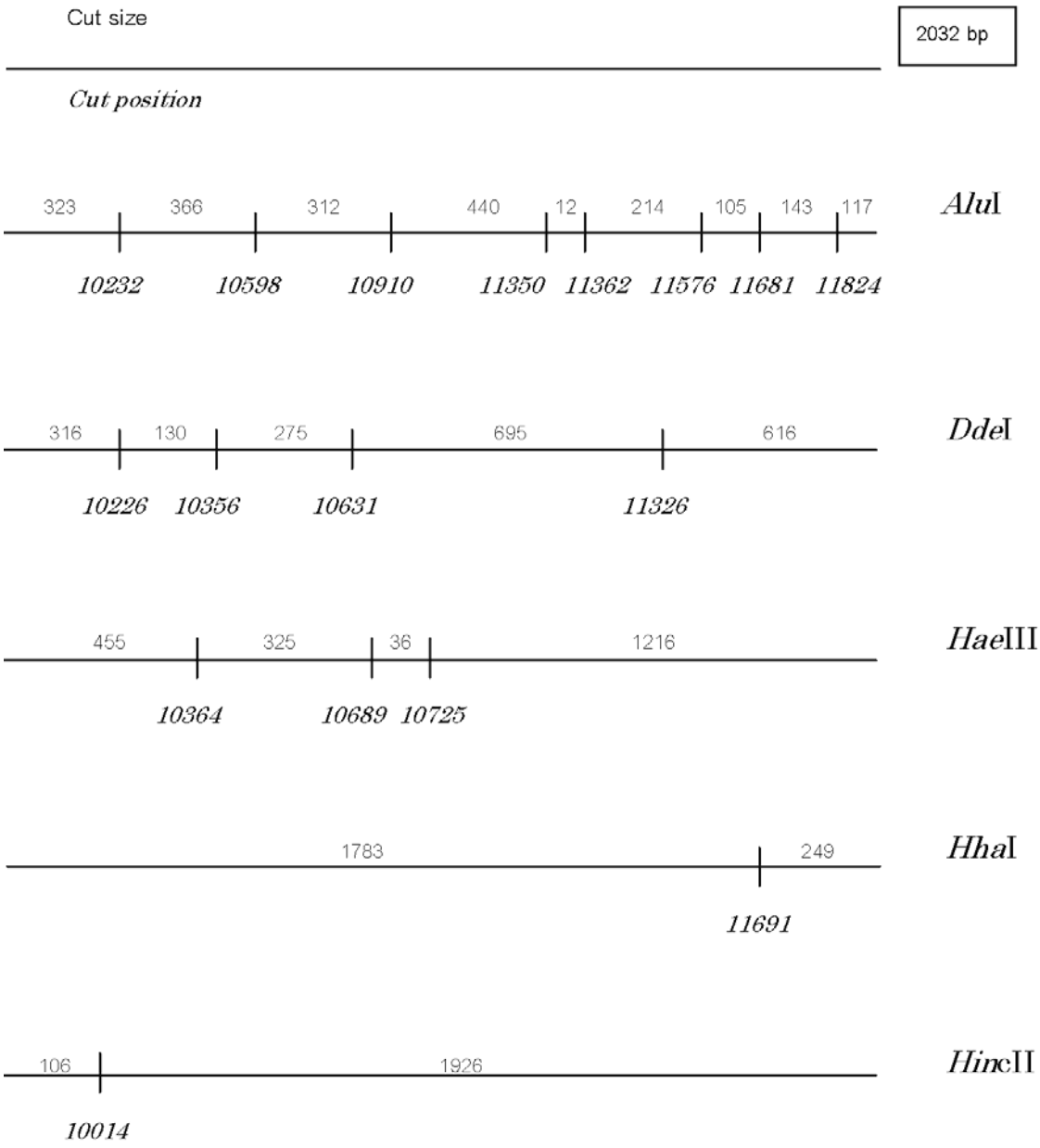


***Primer pair 5 : L8278 - H10107 = 1830 bp* (continued)**

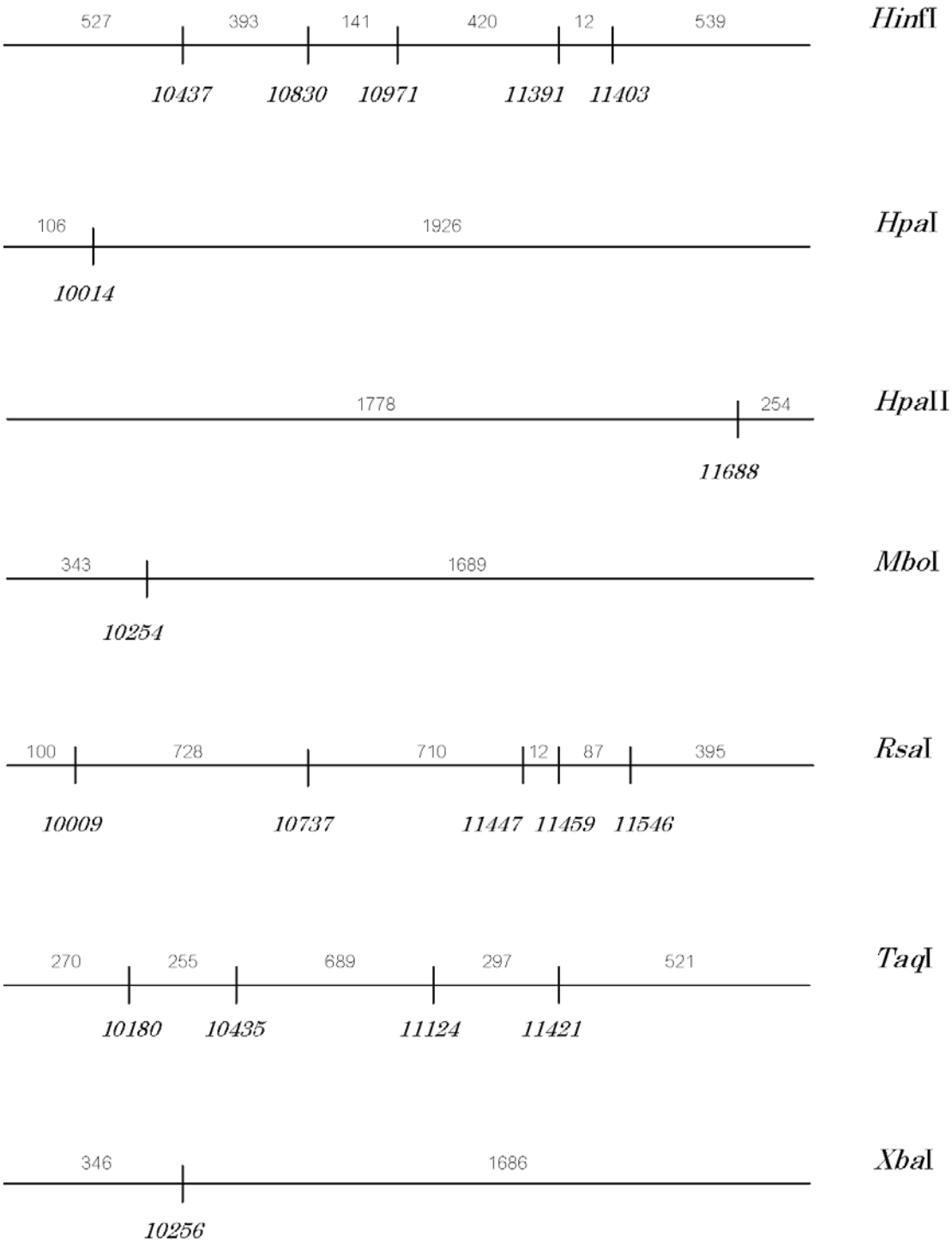


Primer pair 6 : L9911 - H11942 = 2032 bp

None of recognition site was found when using these restriction enzymes, *Ava*II, *Bam*HI, *Hae*II, *Pst*I, *Pvu*II, *Xho*II, with PCR product from this primer pair.

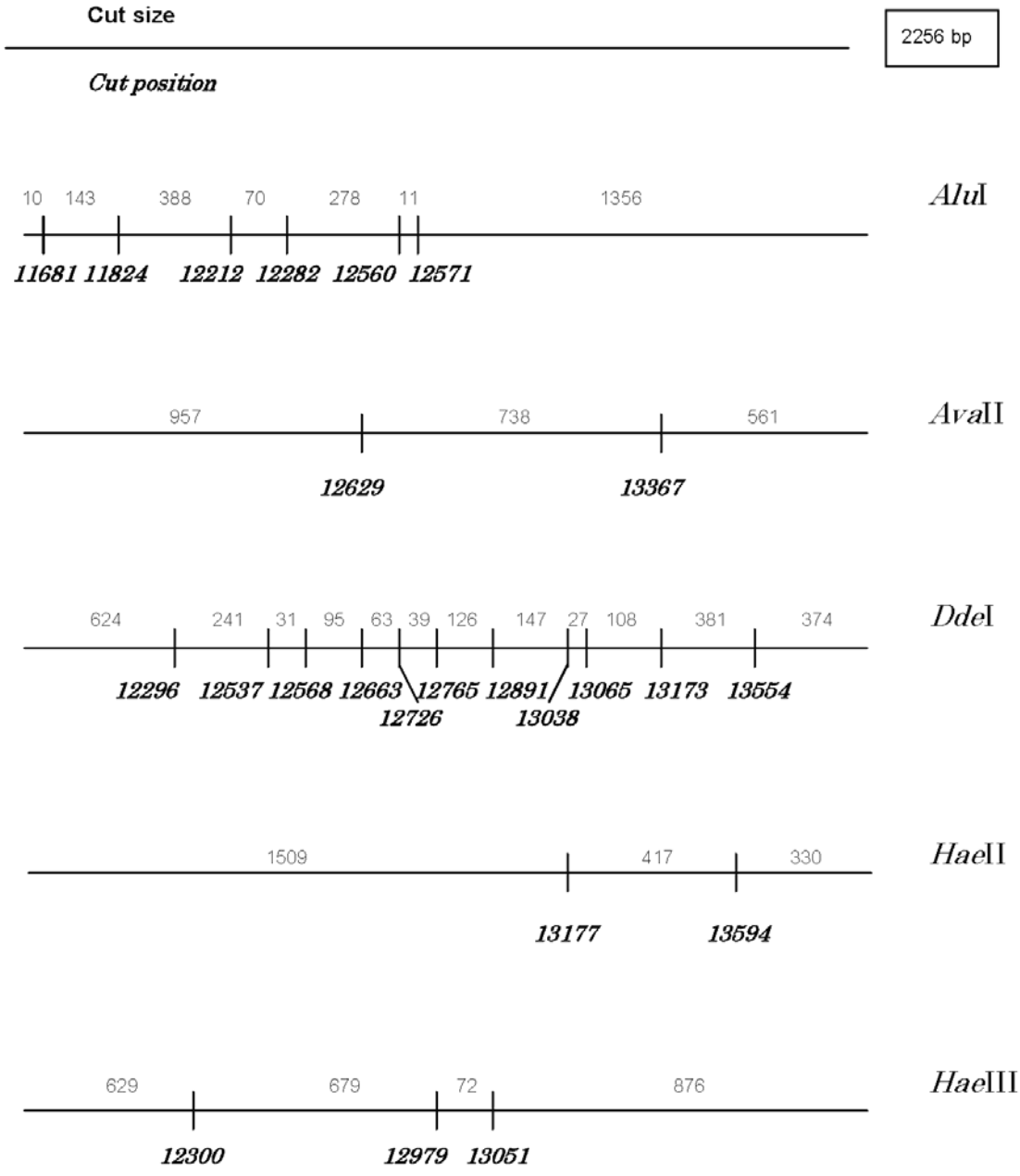


***Primer pair 6 : L9911 - H11942 = 2032 bp* (continued)**

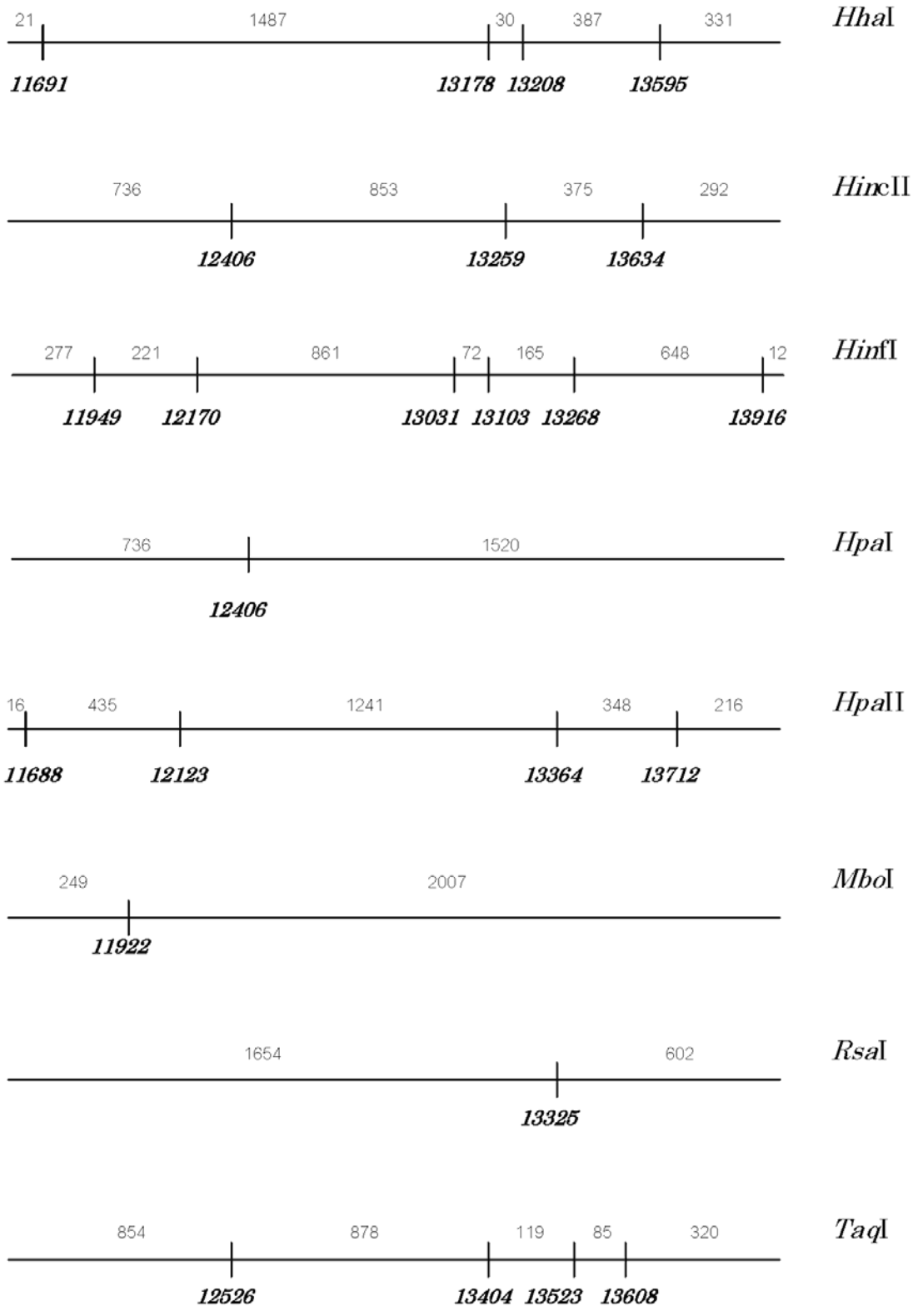


Primer pair 7 : L11673 – H13928 = 2256 bp

None of recognition site was found when using these restriction enzymes, *Bam*HI, *Pst*I, *Pvu*II, *Xba*I, *Xho*II, with PCR product from this primer pair.

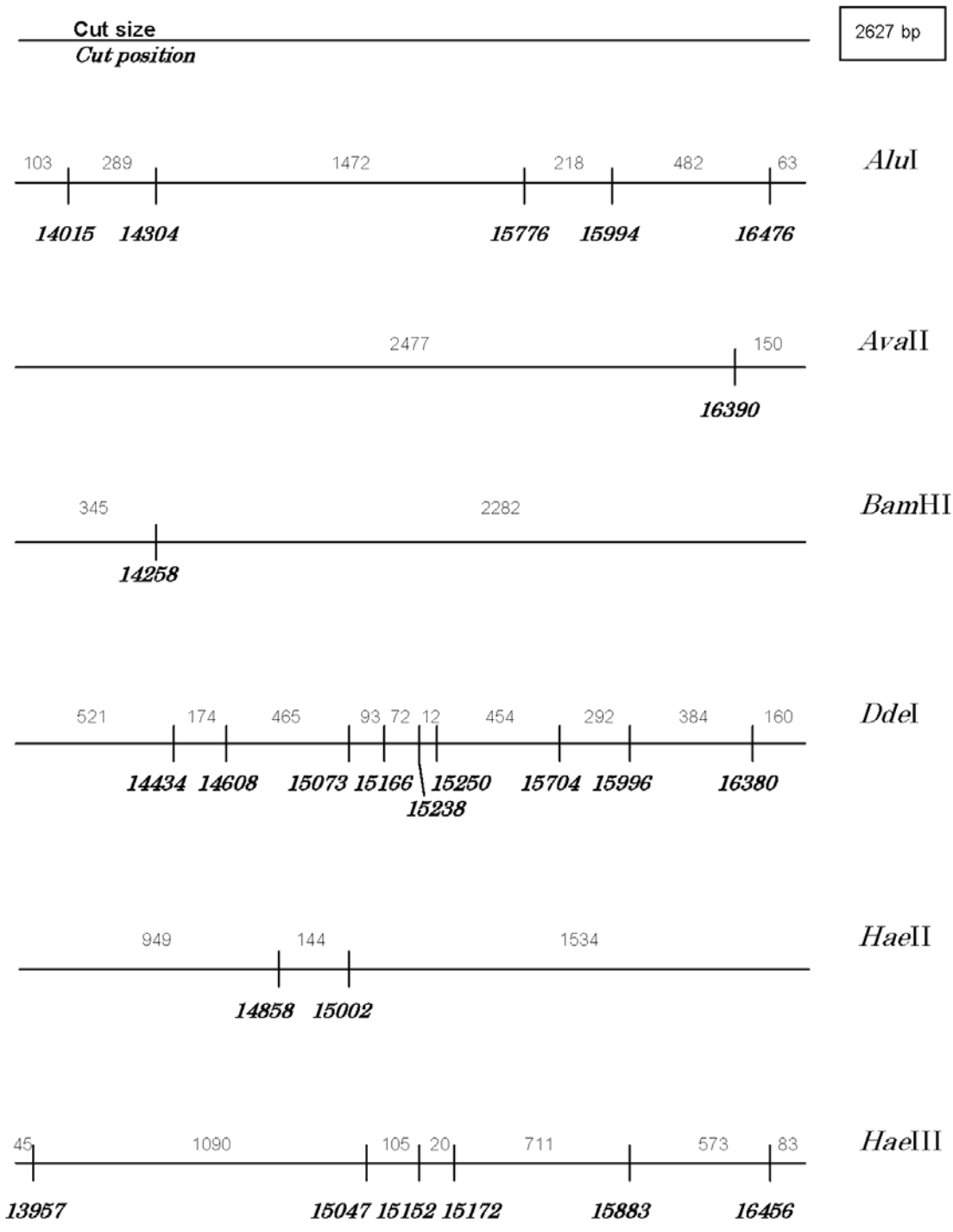


***Primer pair 7 : L11673 – H13928 = 2256 bp* (continued)**

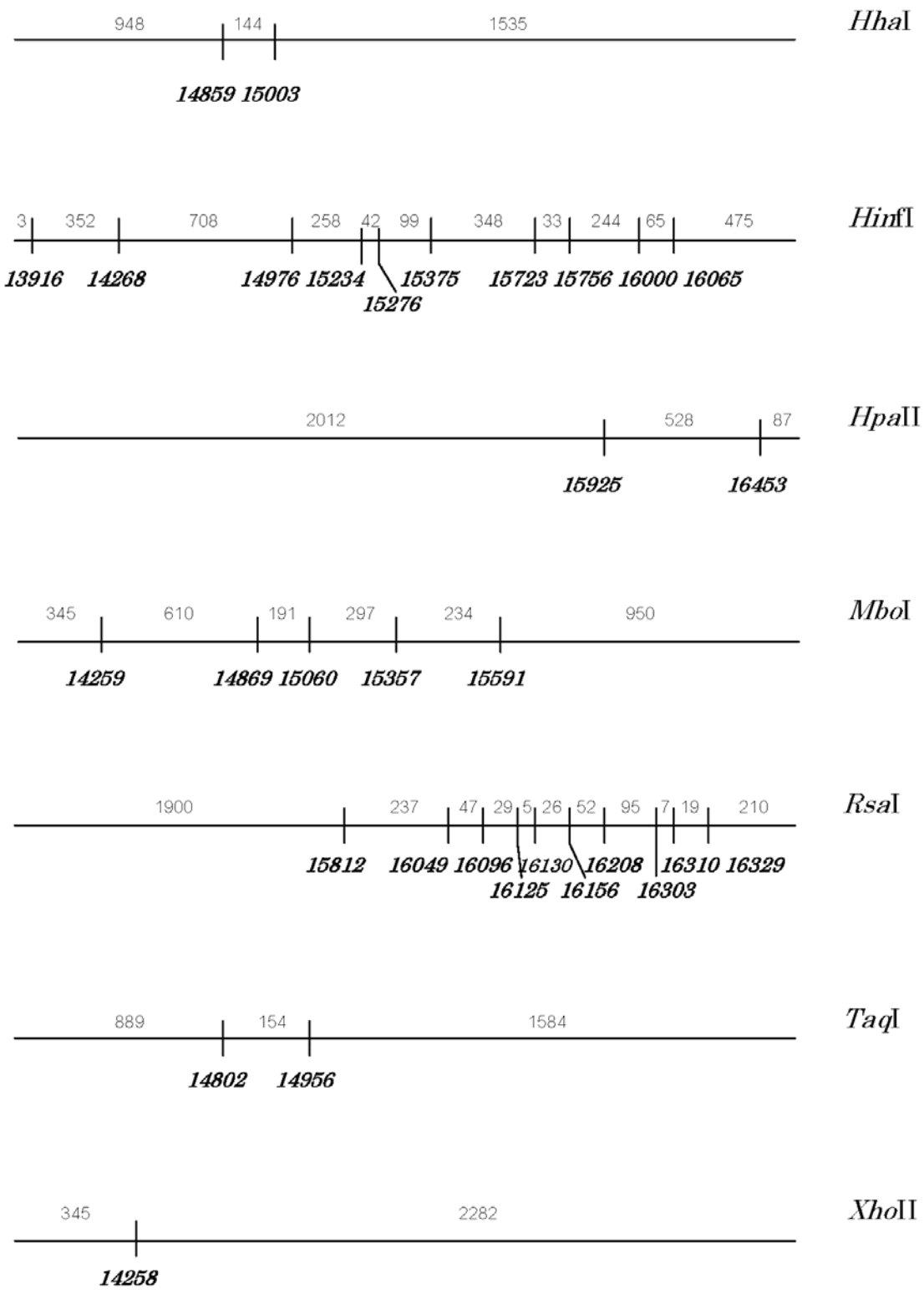


Primer pair 8 : L13914 – H16540 = 2627 bp

None of recognition site was found when using these restriction enzymes, *Hin*cII, *Hpa*I, *Pst*I, *Pvu*II, *Xba*I, with PCR product from this primer pair.

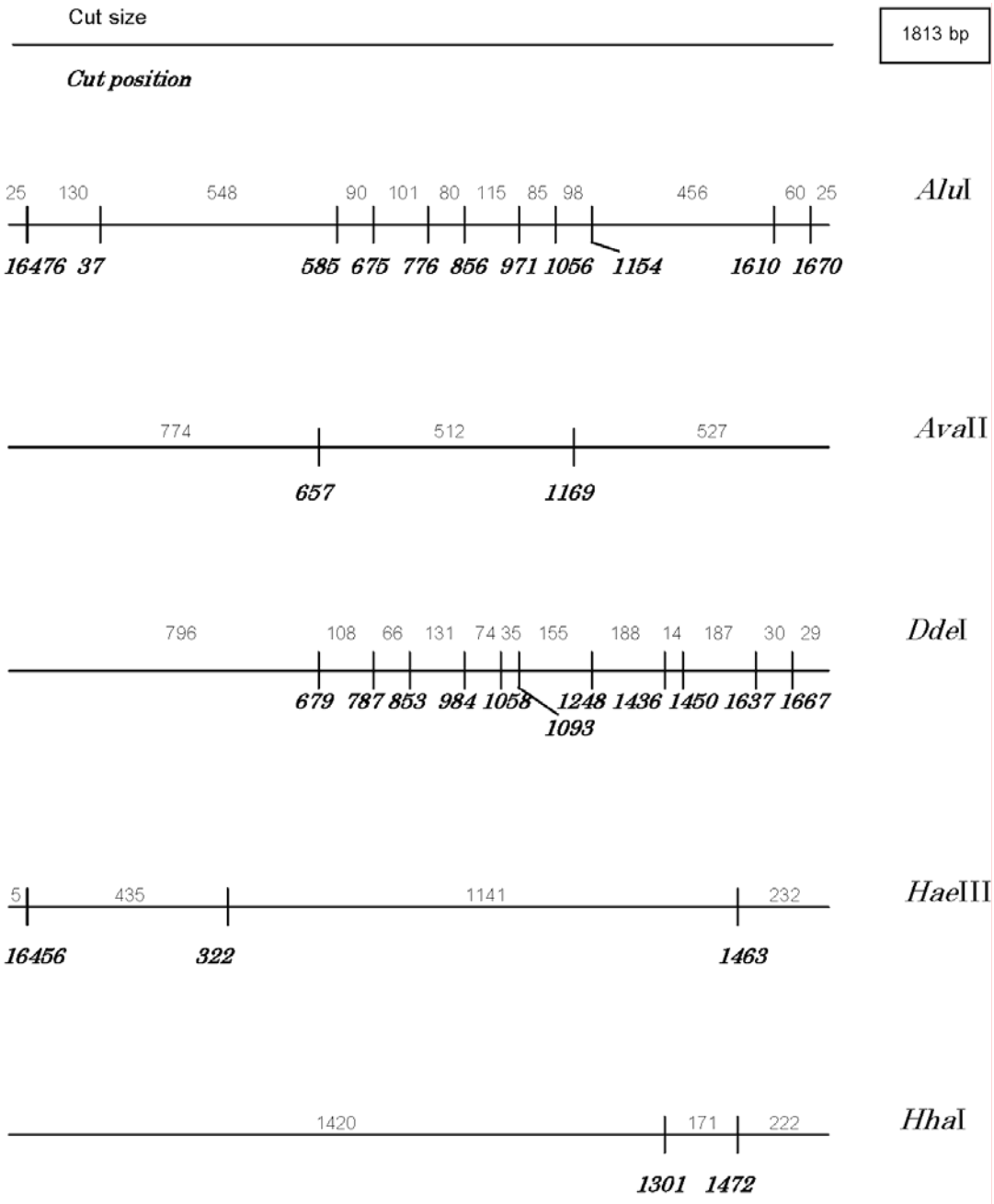


***Primer pair 8 : L13914 – H16540 = 2627 bp* (continued)**

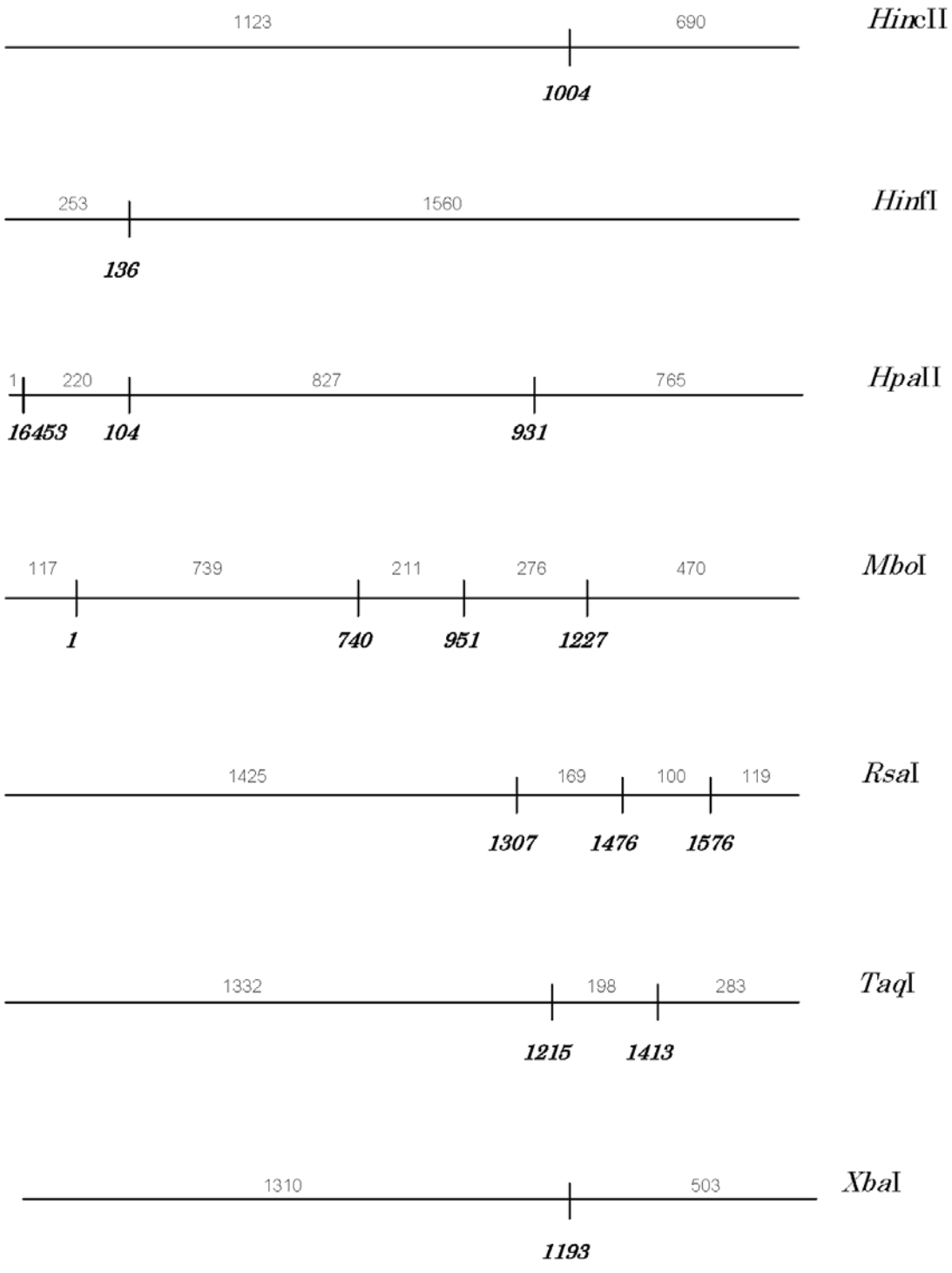


Primer pair 9 : L16453 - H1696 = 1813 bp

None of recognition site was found when using these restriction enzymes, *Bam*HI, *Hae*II, *Hpa*I, *Pst*I, *Pvu*II, *Xho*II, with PCR product from this primer pair.



***Primer pair 9 : L16453 - H1696 = 1813 bp* (continued)**



APPENDIX C

Appendix C: Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																															
	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C61	C62	C63	C64
1 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
37 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
54 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
64 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0
93 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
124 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
125 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
136 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
185 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
207 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
207 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
315 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
317 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
322 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
418 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
546 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
585 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
627 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
657 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
663 *Hae* III	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
675 *Alu* I	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1
679 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
719 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
740 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
776 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
787 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
853 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
856 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
931 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
951 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
971 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1
984 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1002 *Pvu* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1003 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1004 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
1005 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1056 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1058 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1093 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1154 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1169 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1193 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1215 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1227 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1248 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1301 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1307 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1407 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1229 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1413 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1436 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1450 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1463 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1472 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1476 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1537 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1576 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1610 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1637 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1667 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
1 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
37 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
54 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
64 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
93 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
104 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
124 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
125 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
136 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
185 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
207 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
207 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
315 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
317 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
322 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
418 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
546 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
585 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
627 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
657 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
663 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
675 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
679 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
719 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
740 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
776 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
787 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
853 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
856 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
931 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
951 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
971 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
984 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1002 *Pvu* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1003 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1004 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1005 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1056 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1058 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1093 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1154 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1169 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1193 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1215 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1227 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1248 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1301 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1307 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1407 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1229 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1413 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1436 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1450 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1463 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1472 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1476 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1537 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1576 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1610 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1637 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1667 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C60	C61	C62	C63	C64
1670 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1698 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1715 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1768 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1782 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1831 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1893 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1895 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1923 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1931 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2001 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2014 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2032 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2036 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2112 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2173 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2208 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2268 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2349 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2421 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2567 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2574 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2621 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2650 *Pvu* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2651 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2734 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2758 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2776 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2831 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2849 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2856 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2896 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2941 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2953 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2957 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2987 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2996 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3063 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3066 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3077 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3123 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3146 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3160 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3161 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3192 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3246 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3315 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3337 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3391 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3412 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3427 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3534 *Dde* I	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3537 *Alu* I	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3592 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3592 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3607 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3659 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3693 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3698 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3842 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3846 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3849 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3899 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3916 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3930 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3944 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3958 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3981 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
1670 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1698 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1715 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1768 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1782 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1831 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1893 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1895 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1923 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1931 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2001 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2014 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2032 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2036 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2112 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2173 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2208 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2268 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2349 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2421 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2567 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2574 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2621 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2650 *Pvu* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2651 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2734 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2758 *Rsa* I	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2776 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2831 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2849 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2856 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2896 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2941 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2953 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2957 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2987 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2996 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3063 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3066 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3077 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3123 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3146 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3160 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3161 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3192 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3246 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3315 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1
3337 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3391 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3412 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3427 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3534 *Dde* I	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	0	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	0	1	1	0	1	1	1	1	0	1	0	1
3537 *Alu* I	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	0	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	0	1	1	0	1	1	1	1	0	1	0	1
3592 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3592 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3607 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3659 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3693 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3698 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3842 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3846 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3849 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3899 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3916 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3930 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3944 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3958 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3981 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																																
	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C60	C61	C62	C63	C64
3987 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4092 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4122 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4125 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4142 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4157 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4180 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4225 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4260 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4310 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4332 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4341 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4344 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4356 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4360 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4411 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4420 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4428 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4464 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4481 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4529 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4530 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4533 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4536 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4556 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4563 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4685 *Alu* I	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4711 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4745 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4769 *Alu* I	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4793 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4808 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4810 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4830 *Hae* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4831 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4846 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4848 *Hae* III	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4989 *Pvu* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4965 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4990 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4994 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4886 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5003 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5054 *Rsa* I	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1
5176 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5226 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5242 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5260 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5261 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5269 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5351 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5370 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
5419 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5552 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5584 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5630 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5644 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5671 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5691 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5691 *Hpa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5697 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5699 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5711 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5742 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5766 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5779 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5789 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5811 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																																	
	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
3987 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4092 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4122 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4125 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4142 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4157 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4180 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4225 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4260 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4310 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4332 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4341 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4344 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4356 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4360 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4411 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4420 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4428 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4464 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4481 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4529 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4530 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4533 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4536 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4556 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4563 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4685 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4711 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4745 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4769 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4793 *Hae* III	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4808 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4810 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4830 *Hae* II	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4831 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4846 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4848 *Hae* III	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4989 *Pvu* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4965 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4990 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
4994 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4886 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5003 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5054 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5176 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5226 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5242 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5260 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5261 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5269 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5351 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5370 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5419 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5552 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5584 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5630 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5644 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
5671 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5691 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5691 *Hpa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5697 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5699 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5711 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5742 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5766 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5779 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5789 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5811 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

	Subject no.																																																														
Restriction site	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C61	C62	C63	C64
5818 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5823 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5823 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5837 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5877 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5910 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5911 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5917 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5971 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5978 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5983 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5984 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5987 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6000 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6014 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6022 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6027 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6080 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6165 *Hae* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6166 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6204 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6211 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6260 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
6262 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6296 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6377 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6383 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6437 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4901 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
6460 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6509 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6562 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6571 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6688 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6725 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6728 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6768 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6850 *Hpa* II	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6867 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6871 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6904 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6910 *Pst* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6915 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6920 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6931 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6957 *Hae* III	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6999 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7013 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7025 *AluI*	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7055 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7103 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7197 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7204 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7223 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7241 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7316 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7319 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7325 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7335 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7417 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7440 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7458 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7461 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7474 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7497 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7567 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7570 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7598 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Subject no.

Restriction site	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
5818 *Dde* I	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5823 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5823 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5837 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5877 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5910 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5911 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5917 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5971 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5978 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5983 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
5984 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5987 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6000 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6014 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6022 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6027 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6080 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6165 *Hae* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6166 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6204 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6211 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6260 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6262 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6296 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6377 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6383 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6437 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4901 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6460 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6509 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6562 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6571 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6688 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6725 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6728 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6768 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6850 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6867 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1
6871 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6904 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6910 *Pst* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6915 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6920 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6931 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
6957 *Hae* III	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	0	1	1	1	1	0	1	0	1
6999 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7013 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1
7025 *AluI*	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7055 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7103 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7197 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7204 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7223 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7241 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7316 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7319 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7325 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7335 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7417 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7440 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7458 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7461 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7474 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7497 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7567 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7570 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7598 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

	Subject no.																																																														
Restriction site	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C61	C62	C63	C64
7641 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7658 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7693 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7750 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7758 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7828 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
7852 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7853 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	0	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1
7859 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
7886 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7897 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7912 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7933 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7986 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7997 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7998 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8003 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8005 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8012 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8074 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8078 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8112 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8148 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8150 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8158 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8165 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8198 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8249 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8090 *Hae* III	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8250 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1	0	1	1	1	1	1
8269 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8286 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8303 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8309 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8391 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8391 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8439 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8459 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8515 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8569 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8572 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
8587 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8592 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8616 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8678 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8700 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8714 *Dde* I	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8729 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8783 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8838 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8858 *Hha* I	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8865 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8872 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8882 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8957 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8994 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8998 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9020 *Pst* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9025 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9052 *Hae* II	1	1	1	1	1	0	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
9053 *Hha* I	1	1	1	1	1	0	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
9070 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9114 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9147 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9156 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9253 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9266 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9272 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Subject no.

Restriction site	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
7641 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7658 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7693 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7750 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7758 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7828 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7852 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7853 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	0	1	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
7859 *Mbo* I	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7886 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7897 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7912 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7933 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7986 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7997 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7998 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8003 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8005 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8012 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8074 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8078 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8112 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8148 *Hae* III	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8150 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8158 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8165 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8198 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8249 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8090 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8250 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8269 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8286 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8303 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8309 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8391 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8391 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8439 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8459 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8515 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8569 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8572 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8587 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8592 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8616 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8678 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8700 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8714 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8729 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8783 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8838 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8858 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8865 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8872 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8882 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8957 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8994 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8998 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9020 *Pst* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9025 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9052 *Hae* II	1	1	1	1	1	1	1	0	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9053 *Hha* I	1	1	1	1	1	1	1	0	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9070 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9114 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9147 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9156 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9253 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9266 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9272 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																														
	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C61	C62	C63	C64
9287 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9292 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9294 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9307 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9342 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9380 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
9411 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9438 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9443 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9470 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9500 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9553 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9641 *Dde* I	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9644 *Alu* I	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9740 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9118 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9746 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9751 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9753 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9820 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9910 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10009 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10014 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10014 *Hpa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10028 *Alu* I	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10032 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10054 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10084 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10180 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10226 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10232 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10252 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10254 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
10256 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
10319 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10352 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10356 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10358 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10364 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10394 *Dde* I	0	1	0	0	1	0	1	0	0	0	1	0	0	0	1	0	1	0	1	1	0	0	0	1	0	1	1	1	0	0	1	1	1	1	1	0	1	0	1	1	1	0	0	0	1	0	1	0	1	1	1	0	1	1	0	1	1	0	1	0	1	1	1	1
10397 *Alu* I	0	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0	1	1	0	0	0	1	0	1	0	1	0	0	1	0	1	1	1	0	0	0	1	1	1	0	0	0	1	0	1	0	1	1	1	0	1	1	0	1	1	0	1	0	1	1	1	1
10325 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10407 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
10435 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10437 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10598 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10631 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10634 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10644 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10636 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10689 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10725 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10737 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10806 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10830 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10910 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8719 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10933 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10971 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11001 *Hae* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11002 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11074 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11092 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10517 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11124 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10535 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11152 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11326 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																																	
	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
9287 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9292 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9294 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9307 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9342 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9380 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9411 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9438 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
9443 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9470 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9500 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9553 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1
9641 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9644 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1
9740 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9118 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9746 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9751 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9753 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
9820 *Hin* fI	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	1
9910 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10009 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10014 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10014 *Hpa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10028 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10032 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10054 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10084 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10180 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10226 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10232 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10252 *Taq* I	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10254 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10256 *Xba* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10319 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10352 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10356 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10358 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10364 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10394 *Dde* I	0	1	1	1	1	1	1	0	0	1	1	1	1	0	1	1	1	0	0	0	1	0	0	1	1	1	1	1	0	0	1	0	1	1	0	0	0	1	1	1	1	1	0	0	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
10397 *Alu* I	0	0	1	1	1	1	1	0	0	1	0	1	1	0	1	1	0	0	0	0	1	0	0	0	1	1	1	1	0	0	1	0	1	0	0	0	0	1	0	0	1	1	1	0	1	1	0	0	0	1	0	1	1	1	1	0	1	1	0	1	0	1	1	0	1	0	1
10325 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
10407 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10435 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10437 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10598 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10631 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1
10634 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10644 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10636 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
10689 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10725 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10737 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10806 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10830 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10910 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
8719 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10933 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10971 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11001 *Hae* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11002 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11074 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0
11092 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10517 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11124 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10535 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11152 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11326 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																															
	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C60	C61	C62	C63	C64
11350 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11362 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11391 *Hin*fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11403 *Hin*fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11421 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11447 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11459 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11546 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11576 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11641 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11681 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11688 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11691 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11718 *Hin*fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11766 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11806 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11824 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11892 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11922 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11624 *Xba* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11949 *Hin*fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
12026 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12026 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12123 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12170 *Hin*fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12185 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12212 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12282 *Alu* I	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12296 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12300 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12345 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12406 *Hinc* II	1	1	1	1	1	0	1	1	0	0	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
12406 *Hpa* I	1	1	1	1	1	0	1	1	0	0	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
12424 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12507 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12526 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12529 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12537 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12540 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12560 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12568 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12571 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12629 *Ava* II	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12629 *Mbo* I	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12663 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12666 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12667 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12726 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12729 *Alu* I	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12763 *Alu* I	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12765 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12810 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12891 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12940 *Hha* I	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12949 *Hae* II	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12961 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12979 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13018 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13031 *Hin*fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13038 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13051 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13065 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13068 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13100 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13103 *Hin*fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13103 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13104 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13152 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Subject no.

Restriction site	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
11350 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11362 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11391 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11403 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11421 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11447 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11459 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11546 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11576 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11641 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11681 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11688 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11691 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11718 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11766 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11806 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11824 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11892 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11922 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
11624 *Xba* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11949 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12026 *Hinc* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12026 *Hpa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12123 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12170 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12185 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12212 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12282 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12296 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12300 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12345 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
12406 *Hinc* II	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12406 *Hpa* I	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12424 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12507 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12526 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12529 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12537 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12540 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12560 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12568 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12571 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12629 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12629 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12663 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12666 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12667 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12726 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12729 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12763 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12765 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12810 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12891 *Dde* I	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
12940 *Hha* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12949 *Hae* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12961 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12979 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13018 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13031 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13038 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13051 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13065 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13068 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13100 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13103 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13103 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13104 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13152 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																																
	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C60	C61	C62	C63	C64
13173 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13177 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13178 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13208 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13259 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13262 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13268 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13325 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13364 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13366 *Bam* HI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13366 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13367 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13367 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13404 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13512 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13523 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13542 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13554 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13594 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13595 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13608 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13634 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13707 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13712 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13730 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13803 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13916 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13957 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14015 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14068 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14139 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14258 *Bam* HI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14258 *Xho* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14259 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14268 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14279 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14304 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14382 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14434 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14452 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14580 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14583 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14608 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14749 *Hae* III	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14749 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14802 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14858 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14859 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14869 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14899 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14924 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14956 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14976 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15002 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15003 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15047 *Hae* III	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15060 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15073 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15090 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15112 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15152 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15166 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15172 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15216 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15234 *Hin* fI	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15235 *Mbo* I	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15238 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15247 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Subject no.

Restriction site	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
13173 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13177 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13178 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13208 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13259 *Hinc* II	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13262 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13268 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13325 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13364 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13366 *Bam* HI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13366 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13367 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13367 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13404 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13512 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13523 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13542 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13554 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13594 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13595 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13608 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13634 *Hinc* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13707 *Hae* III	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13712 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13730 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13803 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13916 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
13957 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14015 *Alu* I	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14068 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14139 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14258 *Bam* HI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14258 *Xho* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14259 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14268 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14279 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14304 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14382 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14434 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14452 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14580 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14583 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14608 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14749 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14749 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14802 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14858 *Hae* II	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14859 *Hha* I	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	0	0	1	1	1	1	1
14869 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14899 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0
14924 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
14956 *Taq* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
14976 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15002 *Hae* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15003 *Hha* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15047 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15060 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15073 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15090 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15112 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15152 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15166 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15172 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15216 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15234 *Hin* fI	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	0	1	1	1	1	0	1	0	1
15235 *Mbo* I	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	1	0
15238 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15247 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																															
	rCRS	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17	C18	C19	C20	C21	C22	C23	C24	C25	C26	C27	C28	C29	C30	C31	C32	C33	C34	C35	C36	C37	C38	C39	C40	C41	C42	C43	C44	C45	C46	C47	C48	C49	C50	C51	C52	C53	C54	C55	C56	C57	C58	C59	C61	C62	C63	C64
15250 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15276 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15357 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15375 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15439 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15494 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15520 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15591 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15595 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15606 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15704 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15723 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15727 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15756 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15776 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15812 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15882 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15883 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15897 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15907 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15925 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15994 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15996 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16000 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16049 *Rsa* I	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16065 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16089 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16143 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16145 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16156 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16176 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16208 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1
16217 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16226 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16239 *Pvu* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16240 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16242 *Pst* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16246 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16254 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16285 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16296 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16275 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16303 *Rsa* I	1	0	1	1	1	0	1	1	0	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
16318 *Hae* III	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16329 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16336 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16380 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1
15590 *Xho* II	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16389 *Bam* HI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16389 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16389 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16389 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16390 *Ava* II	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1
16398 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16398 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
16436 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16453 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16456 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16476 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16494 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16528 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16517 *Hae* III	0	1	1	1	1	1	0	1	1	1	1	1	0	1	0	1	1	1	1	0	1	1	0	1	1	0	1	1	1	1	1	1	0	1	1	0	0	0	1	1	1	1	1	1	0	1	1	0	0	0	0	1	1	0	1	1	1	1	0	0	0	0	0	0
9 bp deletion	0	1	0	1	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0	1	1	0	1	0	1	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0

Appendix C (continued): Polymorphic restriction sites found in 100 normal controls and 30 LHON individuals.

Restriction site	Subject no.																																																																	
	C65	C66	C67	C68	C69	C70	C71	C72	C73	C74	C75	C76	C77	C79	C80	C81	C84	C85	C86	C87	C88	C89	C90	C91	C92	C93	C94	C95	C96	C97	C98	C99	C100	C101	C102	C104	C105	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17	F18	F19	F20	F21	F22	F23	F24	F25	F26	F27	F28	F29	F30
15250 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15276 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15357 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15375 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15439 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15494 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15520 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15591 *Mbo* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15595 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15606 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15704 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15723 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15727 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15756 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15776 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15812 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15882 *Ava* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15883 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15897 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15907 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15925 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15994 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
15996 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16000 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16049 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16065 *Hin* fI	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16089 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16143 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16145 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16156 *Rsa* I	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16176 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16208 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1
16217 *Taq* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16226 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16239 *Pvu* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16240 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16242 *Pst* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16246 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16254 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16285 *Alu* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16296 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16275 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16303 *Rsa* I	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1
16318 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16329 *Rsa* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16336 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16380 *Dde* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1
15590 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0
16389 *Bam* HI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16389 *Hin* fI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	0	0
16389 *Xho* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16389 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16390 *Ava* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1
16398 *Hae* III	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16398 *Mbo* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16436 *Rsa* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16453 *Hpa* II	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16456 *Hae* III	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16476 *Alu* I	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
16494 *Hpa* II	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16528 *Dde* I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16517 *Hae* III	1	1	1	0	1	1	0	1	1	0	1	0	0	1	0	0	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	0	1	1	1	1	0	1	1	1	1	0	1	0	1	1	1	1	0	1	1	0	0	0	1	1	1	1	0	0	1	0	1	1	1	0
9 bp deletion	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	0	1	0	0	1	0	1	1	0	0	0	1	0	0	1	1	0	0	1	0	0	0	0	1	0	0	1	0	0	0	0	1	0	1	0

APPENDIX D

Appendix D: The clinical manifestation and genetic findings of the G11778A patients and their maternal relatives in this study.

Family ID	Research Code	Sex	% G11778A mutation load	Other LHON Mutations	Affected status	Age of Onset	Final VA RE log MAR	Final VA LE log MAR	Definite haplo group
F1	SR-03-159	M	100 (Homoplasmy)	None	Affected	14			M
F1	SR-94-012	M	100 (Homoplasmy)	None	Affected	19	1.00	2.00	M
F1	SR-98-044	M	100 (Homoplasmy)	None	Affected	7	0.30	0.70	M
F2	SR-96-008	M	100 (Homoplasmy)	None	Affected	18	2.00	2.00	B*
F2	SR-97-021	F	30 (Heteroplasmy)	None	Unaffected				B*
F3	SR-96-010	M	100 (Homoplasmy)	None	Affected	20	2.00	2.00	
F3	SR-97-005	F	45 (Heteroplasmy)	None	Unaffected				
F3	SR-97-006	M	84 (Heteroplasmy)	None	Unaffected				
F3	SR-97-007	M	74 (Heteroplasmy)	None	Unaffected				
F4	SR-96-013	M	100 (Homoplasmy)	None	Affected	30	2.00	2.00	M
F5	SR-96-015	M	100 (Homoplasmy)	None	Affected	19	2.00	2.00	M
F5	SR-97-016	F	68 (Heteroplasmy)	None	Unaffected				M
F5	SR-97-017	F	54 (Heteroplasmy)	None	Unaffected				M
F6	SR-97-025	M	44 (Heteroplasmy)	None	Affected	18	2.00	2.00	M
F6	SR-97-028	F	45 (Heteroplasmy)	None	Unaffected				M
F6	SR-97-030	M	45 (Heteroplasmy)	None	Unaffected				M
F7	SR-97-032	M	100 (Homoplasmy)	None	Affected	44	0.80		B
F8	SR-97-038	M	100 (Homoplasmy)	None	Affected	24	2.00	2.00	M
F9	SR-03-073	F	34 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-074	M	76 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-076	F	31 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-078	F	46 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-081	M	48 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-083	F	70 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-084	F	57 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-085	F	55 (Heteroplasmy)	None	Unaffected				M
F9	SR-03-087	M	70 (Heteroplasmy)	None	Unaffected				M
F9	SR-97-040	M	100 (Homoplasmy)	None	Affected	12	2.00	3.00	M
F9	SR-97-047	F	100 (Homoplasmy)	None	Unaffected				M
F9	SR-98-014	M	100 (Homoplasmy)	None	Affected	10	1.00	2.00	M
F10	SR-98-007	F	100 (Homoplasmy)	None	Affected	53	3.00	3.00	B
F10	SR-98-028	F	100 (Homoplasmy)	None	Unaffected				B
F11	SR-98-015	M	100 (Homoplasmy)	C3497T	Affected	16	2.00	2.00	B
F11	SR-98-016	M	100 (Homoplasmy)	C3497T	Affected	8	1.51	1.30	B
F11	SR-98-018	M	100 (Homoplasmy)	C3497T	Affected	8	0.70	0.70	B

Appendix D (continued): The clinical manifestation and genetic findings of the G11778A patients and their maternal relatives in this study.

Family ID	Research Code	Sex	% G11778A mutation load		Other LHON Mutations	Affected status	Age of Onset	Final VA RE log MAR	Final VA LE log MAR	Definite haplo group
F11	SR-98-020	M	100	(Homoplasmy)	C3497T	Affected	33	2.00	2.00	B
F11	SR-98-021	M	100	(Homoplasmy)	C3497T	Unaffected				B
F11	SR-98-022	F	100	(Homoplasmy)	C3497T	Affected	30			B
F11	SR-98-023	M	100	(Homoplasmy)	C3497T	Affected	10	1.30	1.50	B
F12	SR-98-019	M	100	(Homoplasmy)	None	Affected	28	2.00	2.00	
F13	SR-00-004	F	92	(Heteroplasmy)	None	Unaffected				M
F13	SR-98-017	M	100	(Homoplasmy)	None	Affected	19	2.00	2.00	M
F13	SR-98-029	F	100	(Homoplasmy)	None	Unaffected				M
F14	SR-98-041	M	100	(Homoplasmy)	None	Unaffected				B*
F14	SR-98-042	M	100	(Homoplasmy)	None	Unaffected				B*
F14	SR-98-043	M	100	(Homoplasmy)	None	Affected	16	2.00	2.00	B*
F15	SR-02-070	M	100	(Homoplasmy)	None	Affected	19	2.00	2.00	M
F15	SR-02-071	F	100	(Homoplasmy)	None	Unaffected				M
F15	SR-02-073	F	100	(Homoplasmy)	None	Unaffected				M
F15	SR-02-074	F	100	(Homoplasmy)	None	Unaffected				M
F15	SR-99-030	M	100	(Homoplasmy)	None	Affected	20			M
F15	SR-99-061	F	100	(Homoplasmy)	None	Unaffected				M
F15	SR-99-062	M	100	(Homoplasmy)	None	Affected				M
F15	SR-99-063	M	100	(Homoplasmy)	None	Unaffected				M
F15	SR-99-064	F	100	(Homoplasmy)	None	Unaffected				M
F16	SR-99-031	M	100	(Homoplasmy)	None	Affected	21	1.00	0.70	M
F17	SR-01-092	F	100	(Homoplasmy)	None	Unaffected				M
F17	SR-99-032	M	100	(Homoplasmy)	None	Affected	12	2.00	2.00	M
F18	SR-00-027	M	100	(Homoplasmy)	None	Unaffected				M
F18	SR-00-028	M	100	(Homoplasmy)	None	Affected	19	1.20	3.00	M
F18	SR-00-029	F	100	(Homoplasmy)	None	Unaffected				M
F18	SR-00-030	F	100	(Homoplasmy)	None	Unaffected				M
F18	SR-00-031	F	100	(Homoplasmy)	None	Affected	20	2.00	2.00	M
F18	SR-00-032	F	100	(Homoplasmy)	None	Affected	40	0.80	0.80	M
F18	SR-00-033	F	100	(Homoplasmy)	None	Affected	30	0.50	3.00	M
F18	SR-00-034	F	100	(Homoplasmy)	None	Affected	45	3.00	3.00	M
F18	SR-00-035	F	100	(Homoplasmy)	None	Affected	10	1.51	1.51	M
F18	SR-00-036	M	100	(Homoplasmy)	None	Affected	39	0.80	0.50	M
F18	SR-00-038	F	100	(Homoplasmy)	None	Unaffected				M
F18	SR-99-045	M	100	(Homoplasmy)	None	Affected	20	1.00	3.00	M
F19	SR-00-026	M	100	(Homoplasmy)	G3316A	Unaffected				
F19	SR-02-052	F	18	(Heteroplasmy)	G3316A	Unaffected				
F19	SR-99-069	M	72	(Heteroplasmy)	G3316A	Affected	16	2.00	2.00	
F19	SR-99-070	F	72	(Heteroplasmy)	G3316A	Affected	13	2.00	3.00	

Appendix D (continued): The clinical manifestation and genetic findings of the G11778A patients and their maternal relatives in this study.

Family ID	Research Code	Sex	% G11778A mutation load		Other LHON Mutations	Affected status	Age of Onset	Final VA RE log MAR	Final VA LE log MAR	Definite haplo group
F19	SR-99-071	M	78	(Heteroplasmy)	G3316A	Affected	20	3.00	2.00	
F19	SR-99-072	F	80	(Heteroplasmy)	G3316A	Affected	10	1.30	1.30	
F19	SR-99-073	F	87	(Heteroplasmy)	G3316A	Unaffected				
F20	SR-00-007	M	100	(Homoplasmy)	None	Affected				M
F21	SR-00-010	F	100	(Homoplasmy)	None	Affected	12	0.00	3.00	M
F22	SR-00-042	M	74	(Heteroplasmy)	None	Affected	42	0.50	0.50	B*
F23	SR-01-005	M	100	(Homoplasmy)	None	Affected	6	0.60	0.70	M
F24	SR-01-017	M	100	(Homoplasmy)	None	Affected	36	2.00	2.00	
F24	SR-03-060	M	76	(Heteroplasmy)	None	Unaffected				
F24	SR-03-100	M	59	(Heteroplasmy)	None	Unaffected				
F24	SR-03-102	M	94	(Heteroplasmy)	None	Unaffected				
F24	SR-03-103	F	37	(Heteroplasmy)	None	Unaffected				
F24	SR-03-104	M	100	(Homoplasmy)	None	Unaffected				
F24	SR-03-105	F	3	(Heteroplasmy)	None	Unaffected				
F24	SR-03-106	F	4	(Heteroplasmy)	None	Unaffected				
F24	SR-03-108	F	44	(Heteroplasmy)	None	Unaffected				
F24	SR-03-110	M	100	(Homoplasmy)	None	Unaffected				
F24	SR-03-111	F	99	(Homoplasmy)	None	Unaffected				
F24	SR-03-112	F	1	(Heteroplasmy)	None	Unaffected				
F25	SR-01-019	M	90	(Heteroplasmy)	None	Affected	30	2.00	2.00	M
F26	SR-02-029	M	100	(Homoplasmy)	None	Affected	16			M
F27	SR-02-037	M	100	(Homoplasmy)	None	Affected				
F28	SR-02-041	M	100	(Homoplasmy)	None	Affected	16	2.00	2.00	M
F28	SR-02-044	M	95	(Homoplasmy)	None	Unaffected				M
F28	SR-02-061	F	98	(Homoplasmy)	None	Unaffected				M
F28	SR-03-059	F	100	(Homoplasmy)	None	Affected	20	2.00	1.80	M
F28	SR-03-115	M	93	(Heteroplasmy)	None	Affected	20	0.70	0.20	M
F28	SR-03-116	F	97	(Homoplasmy)	None	Unaffected				M
F28	SR-03-117	F	100	(Homoplasmy)	None	Unaffected				M
F28	SR-03-118	M	100	(Homoplasmy)	None	Affected	8	3.00	3.00	M
F28	SR-03-119	F	42	(Heteroplasmy)	None	Unaffected				M
F28	SR-03-120	F	70	(Heteroplasmy)	None	Unaffected				M
F28	SR-03-121	F	100	(Homoplasmy)	None	Unaffected				M
F28	SR-03-122	M	100	(Homoplasmy)	None	Affected	31	0.70	3.00	M
F28	SR-03-124	M	100	(Homoplasmy)	None	Affected	33	2.00	2.00	M
F28	SR-03-126	F	7	(Heteroplasmy)	None	Unaffected				M
F28	SR-03-127	F	100	(Homoplasmy)	None	Affected	35	0.70	0.70	M
F28	SR-03-129	F	100	(Homoplasmy)	None	Unaffected				M
F28	SR-03-131	F	100	(Homoplasmy)	None	Affected	45			M

Appendix D (continued): The clinical manifestation and genetic findings of the G11778A patients and their maternal relatives in this study.

Family ID	Research Code	Sex	% G11778A mutation load		Other LHON Mutations	Affected status	Age of Onset	Final VA RE log MAR	Final VA LE log MAR	Definite haplo group
F28	SR-03-132	M	100	(Homoplasmy)	None	Unaffected				M
F28	SR-03-133	F	85	(Heteroplasmy)	None	Affected				M
F28	SR-03-134	F	46	(Heteroplasmy)	None	Unaffected				M
F28	SR-03-135	M	100	(Homoplasmy)	None	Unaffected				M
F28	SR-03-136	F	31	(Heteroplasmy)	None	Unaffected				M
F28	SR-03-137	M	100	(Homoplasmy)	None	Unaffected				M
F28	SR-03-138	F	26	(Heteroplasmy)	None	Unaffected				M
F28	SR-03-139	M	28	(Heteroplasmy)	None	Unaffected				M
F29	SR-02-059	M	100	(Homoplasmy)	None	Affected	13			B*
F30	SR-03-007	M	100	(Homoplasmy)	None	Affected	18	2.00	2.00	M
F30	SR-03-008	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-009	M	100	(Homoplasmy)	None	Affected	15	0.00	0.30	M
F30	SR-03-010	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-011	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-013	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-014	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-015	F	100	(Homoplasmy)	None	Affected		1.60	1.60	M
F30	SR-03-017	M	100	(Homoplasmy)	None	Affected	22	1.00	1.30	M
F30	SR-03-018	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-019	M	100	(Homoplasmy)	None	Affected	44	1.51	1.80	M
F30	SR-03-022	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-023	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-024	F	100	(Homoplasmy)	None	Affected	38	2.00	2.00	M
F30	SR-03-025	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-026	F	100	(Homoplasmy)	None	Affected		2.00	2.00	M
F30	SR-03-027	F	100	(Homoplasmy)	None	Affected		1.80	2.00	M
F30	SR-03-028	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-032	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-033	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-034	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-037	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-038	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-039	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-040	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-041	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-045	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-046	F	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-047	M	100	(Homoplasmy)	None	Unaffected				M
F30	SR-03-048	F	100	(Homoplasmy)	None	Unaffected				M

APPENDIX E

Reagents

1. Reagents for DNA extraction from peripheral blood leukocytes

1.1 Red Cell Lysis Buffer (RCLB)

10 mM Tris-HCl, pH 7.6

5 mM $MgCl_2$

10 mM NaCl

Dissolved in distilled water and then autoclaved.

1.2 Lysis Buffer

50 mM Tris-HCl, pH 9.0

100 mM EDTA, pH 8.0

2% SDS

Dissolved in distilled water and then autoclaved.

1.3 20 mg/ml Proteinase K

1.4 Saturated Phenol

1.5 Isoamyl:chloroform (1:24)

1.6 Absolute ethanol

1.7 70% ethanol

1.8 Sterile distilled water

2. Reagents for DNA amplification

2.1 10x amplification buffer

500 mM KCl

100 mM Tris-HCl, pH 9.0

0.1% Gelatin (w/v)

1% Triton X-100

Dissolved in distilled water and then autoclaved.

2.2 25 mM $MgCl_2$

2.3 10 mM dNTP (dATP, dCTP, dGTP, dTTP)

2.4 10 pmol Primer

2.5 2.5 Unit *Taq* DNA polymerase

3. Reagents for DNA precipitation from PCR product

3.1 3 M NaOAc, pH 5.2

3.2 Absolute ethanol

3.3 70% ethanol

3.4 Sterile distilled water

4. Reagents for agarose gel electrophoresis

4.1 50x Tris-Acetate-EDTA (TAE) buffer

121.1 g Trisma base (M.W.=121.1)

28.55 ml Glacial acetic acid

50 mM EDTA, pH 8.0

Dissolved in distilled water to final volume of 500 ml. This stock solution was diluted 50 times before use.

4.2 2% agarose gel

Dissolved 2 g agarose in 100 ml of 1x TAE

4.3 3% agarose gel

Dissolved 3 g agarose in 100 ml of 1x TAE

4.4 4% agarose gel

Dissolved 4 g agarose in 100 ml of 1x TAE

4.5 Ethidium bromide

Dissolved 1 g ethidium bromide in 100 ml of distilled water

4.6 Gel loading buffer

0.25% bromophenol blue

30% glycerol (w/v) in water

Dissolved in distilled water.

4.7 100 bp ladder

5. Reagents for polyacrylamide gel electrophoresis

5.1 30% acrylamide (32:1)

145.45 g acrylamide

4.55 g bis-acrylamide

Dissolved in distilled water to final volume of 500 ml.

5.2 10x Tris-Boric acid-EDTA (TBE) buffer

54 g Tris-base (M.W.=121.1)

27.5 g Boric acid

20 mM EDTA, pH 8.0

Dissolved in distilled water to final volume of 500 ml and then autoclaved.

5.3 12% polyacrylamide gel (final volume of 15 ml)

6 ml of 30% acrylamide (32:1)

3 ml of 5x TBE

105 μl of 10% Ammoniumpersulfate (APS)

22.5 μl TEMED

6 ml distilled water

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