

Thesis Title INTRATYPIC VARIATIONS AMONG HERPES
SIMPLEX VIRUS TYPE 2 ISOLATES IN
THAILAND

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ABSTRACT

Genital herpes is one of the most common sexually transmitted diseases observed worldwide. Most of the cases are affected by herpes simplex virus (HSV) type 2 (HSV-2) although type 1 (HSV-1) has been found with an increasing frequency. The signs and symptoms of genital herpes caused by both types of HSV are similar, however, HSV-2 tends to cause a much higher rate of recurrent attacks than HSV-1. Moreover, a heterogeneity within each type of HSV has been observed. Thus, an investigation of intratypic variations among HSV strains isolated from various populations may be useful in epidemiological studies and contribute some knowledge for the development of HSV vaccines. This dissertation

describes a use of monoclonal antibodies (MAbs) to investigate intratypic variations among HSV-2 strains isolated from genital herpes cases in Thailand. These MAbs were produced against HSV-2 standard strain 186 and were characterized by an indirect enzyme-linked immunosorbent assay (ELISA), plaque reduction neutralization test, immunofluorescence assay (IFA), polyacrylamide gel electrophoresis (PAGE) and immunoblotting, radiolabeling and immunoprecipitation. Antigenic variations on various HSV-2 glycoproteins were analyzed in 128 HSV-2 isolates by an indirect ELISA using MAbs to the viral gD, gG, gB and gE; all except one anti-gG were reactive against both HSV-1 and HSV-2. Isolates were considered significantly different from the standard strain 186 when their optical density (OD) values in ELISA were less than half that of the strain 186. By this criterion, HSV-2 isolates could be arranged into 30 patterns. The most common pattern differed from the standard strain 186 was the isolates that reacted with neither gE nor one of the gD epitopes. Thus, HSV-2 can readily tolerate modifications in some parts of the gD and gE molecules while remaining infectious. By the indirect ELISA, a heterogeneity was also observed among the type-specific internal components of HSV-2 as well. . Another approach to determine intratypic variations between HSV-2 isolates was a neutralization assay employing four different gD-neutralizing MAbs, two of which were complement-independent (C⁻MAbs) while the others were

complement dependent in order to enhance their neutralizing activity (C⁺MAbs). A significant difference in 50% neutralizing titers was clearly demonstrated among 65 HSV isolates when assayed with the C⁻MAbs, indicating a heterogeneity between the complement-independent neutralizing epitopes on HSV-2 gD. Whether the variations also existed in the epitopes recognized by C⁺MAbs could not be exactly indicated in this study. In conclusion, the intratypic variations of HSV-2 isolates in Thailand were revealed by comparing to a long-established laboratory strain of HSV-2 (186) using different approaches. It is likely that HSV-2 virus strains responsible for genital infections in Thailand can have widely different antigenic properties.