Abstract

Hemoglobin Constant Spring (Hb CS) is a Hb variant whose α-chain contains 172 amino acid, instead of 141, due to a single base mutation in the chain termination codon of α-2 gene. Presence of α^{CS}-gene gives rise to α-thalassemia (α-thal) due in part to the instability of α^{CS}-mRNA. However, homozygous Hb CS individuals ($\alpha^{CS}\alpha/\alpha^{CS}\alpha$) and those co-inheriting α^{CS}-gene together with α-thal 1 gene (- -/$\alpha^{CS}\alpha$; Hb H/CS) have more severe clinical symptoms than would be expected from an equivalent α-thal.

In this thesis, Scatchard plot of the binding of hemichrome to red cell membranes showed that homozygous Hb CS (3 subjects) and Hb H/CS (4 subjects) red cells contained only a specific binding site, whereas normal (7 subjects), Hb H (4 subjects) and β^{o}/β^{o}-thalassemia (3 subjects) red cells contained both specific and non-specific binding sites. The ability of rabbit glyceraldehyde-3-phosphate dehydrogenase, a known ligand of band 3, to compete with hemichrome for binding to membrane indicated that the specific binding site was band 3. Treatment of normal red cell membranes with lysate from homozygous Hb CS cells abolished the non-specific binding sites. Membrane sialic acid content of homozygous Hb CS (6 subjects) and Hb H/CS (3 subjects) red cells was reduced compared with normal (4 subjects), α-thal trait (3 subjects) and Hb H (4 subjects). Resealed ghosts prepared from normal membrane treated with CS lysate was more susceptible to neuraminidase than membrane treated with a normal lysate.

These studies suggest that the abnormal pathology of red cells with Hb CS may be associated with a cytosolic factor which mediates a transmembrane perturbation resulting in enhanced sensitivity of sialic acid to neuraminidase and hence a more rapid clearance by the body reticuloendothelial system.