

B-Thalassemia in India: Genetic Adaptation in Response to the Malaria Pathogen, Ancient Population Migrations, and Ethnic Diversity

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ABSTRACT

In the 1940s, JBS Haldane hypothesized that various haemoglobinopathies including β -thalassemia had become common in regions where malaria was endemic and that natural selection had acted to increase the prevalence of traits that protect individuals from malaria in these places. Case-control studies have now confirmed that both α - and β -thalassemia provide a high degree of protection against clinical malaria. In 1956, a hematologist, JK Siddoo, published a paper reporting that β -thalassemia (also known as Mediterranean anemia since it is common among Greeks, Italians, and other Mediterranean peoples) was prevalent in Sikh populations hailing from the Punjab province of northwestern India. Her hypothesis was that invading Aryan tribes had brought the gene to India with them around 1500 BC from the southern steppes of Europe. However, although this prehistoric invasion is an oft-accepted historical theory, there is little archaeological evidence to support it. Nevertheless, there is ample evidence that nomadic Iranian (Eurasian) tribes known as “Scythians” started to invade the Indian subcontinent in succession around 50 BC, following the incursions of Alexander the Great in 325 BC. Moreover, the crumbling Indo-Greek kingdom that had persisted for almost 200 years finally fell to these invaders from the East and there is further archaeological evidence that the displaced Greeks intermarried with the conquering Scythians. Once again, there is some evidence from ancient Indian, Iranian, and Chinese historical treatises that the Sikhs of the Punjab are descended from these Scythic populations. Sequencing and comparative analysis of the beta-globin gene and DNA haplotypes/genetic markers in thalassemics from modern-day Greek and Sikh populations would be required to provide conclusive proof that this instance of gene flow actually occurred. Identical or highly conserved DNA sequences and single base substitutions would be expected since there are so many genetic mutations of the inherited β -thalassemia trait, which recurs spontaneously in many different populations world-wide. Nonetheless, the β -thalassemia trait is a classic example of genetic adaptation in humans to the most dangerous pathogen on the planet.

Keywords: α - β -Thalassemia, Gene regulation, Single base substitutions, Frameshift mutations, RNA processing mutants, Transcriptional mutants, Initiation codon mutations

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