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HLA: Facts and Findings

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Human Major Histocompatibility Complex also known as Human Leukocyte Antigen (HLA) system is an extended portion of human genome spanning a region of about 4000 Kb on the short arm of chromosome 6 between 6p21.31 and 6p21.32.1 [1]. This region contains a large number of polymorphic genes with variable expression and function which are arranged close together and are generally inherited as a haplotype [2]. These genes have been grouped into different clusters based on their structural and functional characteristics namely: Class I, II and III. Due to their diploid nature, an individual inherits two alleles of each HLA loci, one each from either parent. Furthermore, due to very low recombination frequency (less than 1%), a complete set of alleles on the same chromosome is usually inherited as a haplotype. Approximately 150 billion or even more genotypic combinations are possible in the HLA system. According to Klein, such a polymorphism is not only advantageous for an individual, but also enhances the survivality of the species surrounded by plethora of pathogens [3]. Additionally, racial admixture can lead to the formation of new recombinants as a result of exchange of genetic material between alleles of the same locus or due to point mutation and other genetic events [2]. All these features made the human HLA system a lucrative subject for genome based researches worldwide.

Analyses of inter-population HLA polymorphism has also gained importance in the recent past. Debnath and Chaudhuri documented highest known frequency of HLA-B14 in the Toto population of India (32.5%) when compared to that of the other world populations [4]. Another study by Debnath et al. suggested the origin of the Gurkhas from mongoloid/Tibetan stock [5]. Studies on HLA polymorphism in north and north-eastern populations of India have also been carried out by Agrawal et al., where it was shown that based on HLA alleles and haplotype similarity, the Rajbanshis have close proximity with the mongoloids [6]. Singh et al. reported highest frequency of HLA-B*37 and B*08 in the Bengalis compared to other populations of India [7].

The application of HLA system in disease association studies also revealed certain important facts. Debnath et al. reported significant positive association of HLA-A*03 gene with delusional disorder as well as paranoid schizophrenia [8], while Singh et al., further showed considerable decrease in the frequency of HLA-A*25, A*31 and HLA B*51 in schizophrenia [9,10]. Furthermore, Debnath and Chaudhuri, hypothesized HLA-G molecules as the novel regulator of immune homeostasis during early pregnancy to protect developing fetus from maternal immune attack by interacting with proinflammatory cytokines like TNF-α and different immune cells like NK cells. This regulation may be disrupted due to lowered HLA-G expression following maternal infection resulting in upregulation of detrimental inflammatory cytokines which in turn may result in neuro-developmental disorder leading to schizophrenia [11]. Lama et al. also documented significant higher frequency of HLA-DRB1*03 in asthmatic children compared to controls [12].

Future researches on HLA shall focus on exploring the intricate connection between genetic diversities and molecular attributes.

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