

The Potential Implication of Immunogenetics in Cancer and Autoimmunity

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Immunogenetics is a rapidly evolving branch of biology that incorporates medical immunology, molecular biology, and medical genetics to elucidate the genetic basis of the immune system and immune reactions. This scientific discipline started to expand when it was established that some inflammatory disorders have a genetic background (1). The discovery of allograft responses during World War II and Burnet's theory of clonal selection in 1959 (2) also significantly contributed to our current understanding of immunogenetics as an independent field in immunology (1). Immunogenetics studies not only the genetic controls regulating the normal functioning of immunological pathways but also the genetic variations resulting in immune response abnormalities, leading to various immune defects and immune system disorders (1). In this light, immunogenetics aims to explore the genetic factors responsible for defects in plenty of immune system elements, which can thereby result in developing novel therapeutic approaches targeting these genes to improve the prognosis of the related disorders. A high level of polymorphism has been discovered in the genes involved in the immune response of human beings (3). This feature is explicable by a high diversity of infectious agents and the need for human populations to adapt to their pressuring environments by natural selection (3). These extraordinary diversities in the genetic materials responsible for regulating the immune system functions can, however, serve as hurdles, challenging researchers to efficiently elaborate on the role of the immune-related genes and their functions in healthy and unhealthy conditions.

Apart from combating pathogenic invaders, the immune system is actively engaged in fighting cancer cells (4). Different components of the innate and adaptive arms of the immune system collaborate to produce an anti-tumor environment, preventing the emergence of cancer cells and also inhibiting tumor progression in case a cell could earn cancerous features (5). Both genetic and environmental factors play considerable roles in the development of cancers. In this context, numerous genetic variations have been identified to predispose cells to become cancerous and also to facilitate their evasion from the immune response (6). On the other hand, the inadequacy of immune surveillance against

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tumors, arising from the defects in the genes encoding specific immune mediators and molecules used in cancer control, like different T cell receptors, Immunoglobulins, and cell-surface differentiation molecules that have roles in antigen presentation, are other significant factors predisposing patients to develop different types of progressive cancers. For instance, acute lymphoblastic leukemia (ALL) is highly related to the gene polymorphisms and methylations of the suppressor of cytokine signaling (SOC) family molecules playing roles in controlling immune response and cytokine signaling (7, 8). In line with this, the effects of methylation of SOC1 and SOC3 genes on ALL and genetics of aberrant immune response during tumor progression will be investigated in the current issue.

Autoimmune disorders are another major category of disorders arising from the disruption in the immune system, leading to an abnormal immune response to normal body tissues. Like cancer development, both genetic and environmental factors contribute primarily to the emergence of autoimmunity. Accordingly, plenty of variations in the genes encoding different immune mediators and elements like cytokines, antibodies, adhesion molecules, and growth factors have been shown to cause the loss of tolerance against self-antigens, excessive lymphocyte activation, disorganization of blood-system barriers, recruitment of the immune cells into different tissues and local inflammation, leading ultimately to autoimmunity-related manifestations (9). The contribution of the associated genes to these disorders could range from simple Mendelian inheritance of the causative alleles to the complex interactions between several genomic loci, enhancing the risk of these diseases (10). Accordingly, the severity and nature of the immune response are highly dependent on the type of allelic changes occurring at the gene loci responsible for encoding the related immunological molecules (9). In this regard, immunogenetics can significantly enlighten the pathogenic features of different autoimmune abnormalities and also could lead to the discovery of efficient therapeutic targets for these disorders. Inflammatory bowel diseases, including ulcerative colitis (UC) and Crohn's disease (CD), can serve as examples of autoimmune disorders

emerging when an uncontrolled immune response affects the bowel and leads to unrestricted tissue inflammation, resulting in numerous clinical manifestations (11). In this regard, the current issue will elaborate on the role of the epigenetic changes and methylation in the nucleotide-binding oligomerization domain containing (NOD2) gene in the CD and UC pathogenesis and also the role of the Janus kinase 2 (JAK2) methylation in UC.

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