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The Revolution of Epigenetics in the Field of Autoimmunity

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Abstract Autoimmunity is believed to develop when genetically predisposed individuals encounter epigenetic modifications in response to environmental factors. Recent advances in the understanding of epigenetic mechanisms, their contribution to the immune function, and to the development of autoimmunity are presented in this special issue of *Clinical Reviews in Allergy and Immunology*. Potential new therapeutic strategies and biomarkers are also addressed.

Keywords Autoimmunity · Epigenetics · Immunology

The field of epigenetics has emerged to explain how cells with the same DNA can differentiate into alternative cell types and how a phenotype can be passed from one cell to its daughter cells. It is now well established that epigenetics mechanisms are important to control the pattern of gene expression during development, the cell cycle, and in response to biological or environmental changes. It is also essential to note that epigenetic regulation is a reversible driving force that changes rapidly during the cell cycle, in response to a stimulus, and environmental factors. Thus, it is not surprising that several reports have linked epigenetic dysregulation with both idiopathic autoimmune diseases (AID) and with chemical/drug-induced AID [1].

The definition of epigenetics is now referred as stable and heritable changes in gene expression that are not accompanied by alterations in DNA sequence. Epigenetic includes the study of DNA methylation, histone modifications, and the interaction of microRNAs with the genome. The current state-of-the-art of epigenetics in AID has revealed different profiles according to the disease. S. Zhao and colleagues have specified how alterations in genomic DNA methylation and histone modifications may be implicated in the pathogenesis of systemic lupus erythematosus (SLE). M. Trenkmann and colleagues clearly reveal that histone acetylation pattern is affected in rheumatoid arthritis (RA). In multiple sclerosis (MS), the abnormal expression of retroviral elements from the epigenetically silenced endogenous retrovirus HERV-W has been associated with the evolution and prognosis of the disease as reported by H. Perron and A. Lang.

Unlike genetic alterations which are permanent and affect all cells, epigenetic modifications are cell type specific: CD4+ T cells and B cells in SLE [1, 2], lymphocytes and synovial fibroblasts in RA, lymphocytes and skin fibroblasts in patients with systemic sclerosis (SSc), and brain cells in MS. Identification of the cellular process that are epigenetically deregulated will contribute to our knowledge of the diseases as described for B cells.

Epigenetic states can become disrupted by environmental influences or during ageing, suggesting an attracted explanation for age-related AID. Indeed, as reported by E. Ballestar, monozygotic twins are epigenetically indistin-

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guishable early in life but, with age, exhibit substantial differences in particular when they have led different lifestyles and had spent less of their lives together [3]. Since epigenetics changes increase with age, A. Grolleau-Julius and colleagues reviewed their contribution to autoimmune disorders in the elderly. The role of X-chromosome inactivation in predisposition of women to autoimmunity and neoplasia is also questioned by W.H. Brooks.

Whilst our current knowledge of epigenetic process is limited, the epigenome will undoubtedly serve as a tool for diagnosis, prognostic biomarkers, and serve as a therapeutic target in the future. In fact, the epigenetic therapies are being evaluated as reported by M. Szyf. Finally, J. Dieker and S. Muller discuss how epigenetic histone modifications are associated with disease progression and autoantibody (Abs) production and how these Abs may be used as biomarkers.

To conclude, in this issue of Clinical Reviews in Allergy and Immunology, the authors provide the most recent data and ideas regarding the impact of epigenetic process in the field of autoimmunity. Together, the arguments presented here indicate that epigenetic change precedes AID and confers risk for AID suggesting a strong argument for causality in genetically predisposed individuals. Albert Einstein once declared that "God does not throw dice." The subject of epigenetics obviously would argue otherwise and we predict will become an increasingly difficult subject in the field of autoimmunity. Finally, in addition to this special issue on epigenetics, there have been several recent publications which have focused not only on epigenetics and autoimmunity but epigenetics as a developmental origin of a variety of human diseases [4–14]. We hope that you will enjoy these reviews and thank the authors for their contributions.

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