About this Research Topic

During human development a complex interplay of DNA elements and dynamic epigenetic processes i.e. chromatin modifications govern tissue-specific patterns of gene expression that may be stably maintained during life or may be changed when necessary. In cells of the immune system, epigenetic modifications have been implicated in disrupting immune tolerance and perpetuating autoreactive responses. For instance, it has been demonstrated that hypomethylation of DNA regulatory regions leads to overexpression of CD11a, CD40L and CD70 genes in Systemic Lupus Erythematosus (SLE) CD4+ T cells and miR-30a plays a crucial role in B cell hyperactivity in SLE. Moreover, demethylation of IL-6 promoter causes the over-expression of IL-6 in Peripheral Blood Mononuclear Cells (PBMCs) during Rheumatoid Arthritis (RA). Additionally, hypomethylation of CXCL12 loci in RA synovial fibroblasts, induces the overproduction of matrix metalloproteinases leading to joint destruction. Overall, several recent studies have uncovered the role of epigenetic changes in autoimmune diseases such as SLE, RA and Type I diabetes. In line with this, it has been proposed that therapeutic alteration of epigenetic patterns that corrects disease-specific epigenetic changes, such as miRNA targeting with small molecules and increasing DNA methylation, could be employed in the treatment of these immunological diseases.   
  
Recent technological advancements have allowed considerable progress in understanding the role played by epigenetic mechanisms in pathogenesis of autoimmune diseases. Since epigenetic changes are not detectable at the DNA sequence level, epigenome mapping, which explores genome-wide chromatin modification patterns, may help in discovering disease-causing genes and in developing novel diagnostic and treatment strategies. For example, it has been shown that distinct patterns of methylation are associated with specific cancer types, have prognostic value, and can help in suggesting the most favorable treatment. Genome-wide DNA methylation studies have also allowed for the identification of methylation changes in disease-causing genes in the most widely studied autoimmune diseases such as SLE, Systemic sclerosis and RA.  
  
One of the large-scale epigenome mapping methods is bisulfite sequencing that is used to obtain high-resolution methylation profiles. The broad spectrum of possible applications of this technique not only include the study of tumor development but also of autoimmune diseases. Indeed, the application of Bisulfite sequencing to Type I diabetes has uncovered disease-associated epigenetic variation that antedates disease diagnosis. Moreover, in RA synovial cells, it was shown that specific methylation, which downregulates the expression of DR‐3 protein, favors resistance to apoptosis. In T cells of SLE patients, bisulfite sequencing has helped in detection of demethylation state of regions flanking the ITGAL promoter that could lead to increased LFA‐1 expression, which alone has been shown to cause a lupus‐like disease.   
  
In this Research Topic, we welcome Original Research articles, Reviews, and Methods that apply modern technical approaches to study the role of epigenetics in the pathogenesis of autoimmune diseases and to identify new potential therapeutic strategies. We specially aim to cover:  
  
(1) Next-generation sequencing (NGS) both for genome-wide and targeted analysis to detect susceptibility loci in autoimmune diseases.  
(2) Approaches to identify genes and epigenetic markers (risk variants) associated with autoimmune diseases and corresponding drug treatments.  
(3) Reduced Representation Bisulfite Sequencing (RRBS) and Bisulfite sequencing to study the epigenetic mechanisms underlying the development of autoimmune diseases.  
(4) Single cell transcriptome analysis integrated to single-cell NGS for the analysis of epigenetic transcriptional correlations that can determine susceptibility to autoimmune diseases.  
(5) Network analysis of combined gene, lncRNA, and miRNA expression profiles for the identification of epigenetic mechanisms that play a role in the autoimmune disease pathogenesis.

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**Keywords**: Epigenetics, Genome-wide Analysis, Autoimmune Diseases, Therapeutic Strategies