Epigenetics and autoimmunity at a glance

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Epigenetics is referred as stable and heritable changes in gene expression that are not accompanied by alterations in DNA sequence. Epigenetics modifications involve either methylation of cytosine in CpG dinucleotides or covatent post-translational modifications of the histones. The first evidence of epigenetic involvement in the development of autoimmunity comes from the *in vivo* studies showing that prolonged treatment with DNA methylation inhibitors induces a lupus-like disease. Interstingly, such an effect has been reproduced after adoptive transfer of DNA hypomethylated CD4+ T cells and hypomethylated B cells. The second evidence comes from the analysis of twins showing that changes in DNA methylation reflects twin discordances in lupus erythematosus systemic (SLE). The third evidence comes from the analysis of the different blood cell populations in SLE, synoviocytes in rheumatoid arthritis, or neural cells in multiple sclerosis. In SLE, we and others have established that T and B cells are characterized by a profound DNA methylation defect associated with a reduction of DNMTs and histone acetylation. As a consequence, promoter DNA demethylation permits transcriptional activation of normally repressed genes like cytokines, activated cell surface receptors, and human endogenous retrovirus. Such effect has been related to a blocage in the PKC delta/Erk pathway and/or a growth arrest at the G0/G1 interface. One of the important aspect of epigenetic regulation is the possibility of reversion, for exemple blocking the IL-6 autocrine loop in SLE B cells restores DNA methylation thus opening perspectives for the development of new therapeutics and diagnosis biomarkers.