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► **To cite this version:**

Wesley H Brooks, Marina I Arleevskaya, Yves Renaudineau. Editorial: Epigenetic aspects of autoimmune diseases. *Frontiers in Cell and Developmental Biology*, 2022, 10, pp.991693. 10.3389/fcell.2022.991693 . hal-04009872

HAL Id: hal-04009872

<https://ut3-toulouseinp.hal.science/hal-04009872v1>

Submitted on 1 Mar 2023

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SPECIALTY SECTION
This article was submitted to
Epigenomics and Epigenetics,
a section of the journal
Frontiers in Cell and Developmental
Biology

RECEIVED 11 July 2022
ACCEPTED 19 July 2022
PUBLISHED 11 August 2022

CITATION
Brooks WH, Arleevskaya MI and
Renaudineau Y (2022), Editorial:
Epigenetic aspects of
autoimmune diseases.
Front. Cell Dev. Biol. 10:991693.
doi: 10.3389/fcell.2022.991693

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Editorial: Epigenetic aspects of autoimmune diseases

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KEYWORDS

epigenetics, lupus (SLE), multiple sclerosis, rheumatoid arthritis, sjogren's syndrome

Editorial on the Research Topic

Epigenetic aspects of autoimmune diseases

Genetics, environmental factors, and epigenetics all contribute to autoimmune disease onset and progression (Gulati and Brunner, 2018). Most of the earlier research on autoimmune diseases focused on genetics and environmental factors. Research into genetics, in attempting to identify specific risk alleles has had limited success, for example, identifying HLA-DRB1, a complex of genes coding for cell surface proteins, has emerged as a risk allele for autoimmune diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) (Niu et al., 2015). However, genetic findings have not been sufficient to explain the majority of RA and SLE cases, autoimmune diseases in general, or the typical delay in initial onset, occurring later in life (early to mid-adulthood), in most autoimmune diseases. Even with identification of a risk allele, it is not clear if it is a cause of the disease or just a subsidiary factor. Likewise, environmental factors (e.g., viruses, toxins, bacteria, etc.) also present confusion as to their role since a variety of environmental factors and combinations can be involved in triggering onset of an autoimmune disease (Arleevskaya et al., 2016; Arleevskaya et al., 2020). For example, Epstein-Barr virus (EBV) is suspected of a role in autoimmune diseases, especially multiple sclerosis (MS) (Bjornevik et al., 2022). However, almost all adults have had exposure to EBV but only a small percentage develop MS and onset can be many years after initial infection with EBV. It may be that another environmental factor and/or a genetic risk allele needs to be involved, such as an especially heavy cellular viral load of EBV that may occur by viral binding and entry using HLA-DR cell surface proteins as opposed to other HLA types (Agostini et al., 2018).

Research into the involvement of epigenetics in autoimmune diseases has been steadily increasing in the past two decades. Epigenetics is the control of gene expression or suppression without changing the underlying DNA sequence of the gene (Renaudineau et al., 2011). Epigenetics can involve methylation of DNA, which typically suppresses the underlying gene, or demethylation of the DNA as a step towards expression (Fali et al., 2014). Coordinated with the DNA methylation state are

modifications to histone residues based on the “histone code” that further suppresses or opens the gene by altering how tightly the DNA is held by nucleosomes. In addition, non-coding RNA transcripts (i.e., they do not code for a protein) can add to epigenetic control, such as the X Inactivation Specific Transcript (XIST) RNA involved in silencing of the extra X chromosomes in female cells (Bost et al., 2022). Such RNAs can add structural support to heterochromatin and/or recruit the enzymes that modify the DNA and histones.

In this Research Topic, we have gathered articles discussing epigenetics in a variety of autoimmune diseases. Due to autoimmune tautology (i.e., common characteristics among different autoimmune diseases) as described previously by Anaya, we believe autoimmune researchers focused on one disease can learn from the insights and findings of researchers working on other autoimmune diseases (Anaya, 2012; Anaya, 2017; Arvaniti et al., 2019). Li and colleagues present an overview of DNA methylation by discussing its involvement in development of immune cells and in autoimmune diseases. They also provide discussion of aberrant DNA methylation modifications discovered in important disease-related cell types. With regards to specific diseases, Kabeerdoss and colleagues discuss DNA methylation in Takayasu Arteritis, an autoimmune vasculitis of the aorta. In addition, Charras and colleagues discuss a correlation between DNA methylation patterns in CD8⁺ T-cells and clinically active psoriasis in Psoriatic Arthritis, and Vecellio and colleagues present insights into DNA methylation patterns in monozygotic twins discordant for in psoriatic diseases.

RNA methylation and numerous other RNA modifications are important epigenetic biomarkers of interest in relation to normal cellular functions and diseases. Such modifications are especially important in T cell maturation and can impact RNA localization, translation, and alternate splicing among other functions (Chao et al., 2021). Wang and colleagues present a discussion of the m6A RNA methylation with regards to autoimmune diseases and the immune system. Lv and

colleagues discuss current understanding of RNA methylation in systemic lupus erythematosus, and Yao and colleagues present expression profiles of mRNAs and long non-coding RNAs in Graves' disease.

Author contributions

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Funding

Guest co-editors were supported in part by the NIH NIAID, grant R21 A1149450-01 (Brooks) and the Russian Science Foundation, grant No17-15-01099 (Arleevskaya, Renaudineau).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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