Epigenetics of rheumatoid arthritis: 2018 status

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Rheumatoid arthritis (RA) is an autoimmune disease that is involved multiple molecular layer changes including genetic, epigenetic abnormal. Twins study have estimated the heritability of RA is about 60% while only 40% of them were identified by previous GWAS study including HLA-DRB1, HLA-DQA1 and more than 100 non-HLA susceptibility variants. Furthermore, more than 80% GWAS hits are regulatory variants rather than coding variants. Although more genetic variants were identified as larger sample size of the cohort were applied, the increasing of the explained heritability already come to saturation. Therefore, identifying missing heritability from epigenetics become a promising direction to identify more etiology and pathology of rheumatoid arthritis. In the past decades, genome-wide DNA methylation analysis have been conducted in multiple cells in rheumatoid arthritis including CD4+ and CD8+ T-cells, peripheral blood mononuclear cell (PBMC) and fibroblast-like synovial cells (FLS) in multiple human populations.

Genome-wide DNA methylation analysis to identify novel etiology of rheumatoid arthritis

*C6ORF10*

Pharmacoepigenomics (PeGx) of rheumatoid arthritis

Smoke-related DNA methylation changes in the etiology of rheumatoid arthritis

**The etiology of rheumatoid arthritis involves DNA methylation**

• Studies on brain and blood from patients with schizophrenia show differences in DNA methylation. This

includes differences in monozygotic twins discordant for schizophrenia.

• We argue that methylation plays a critical role during neurodevelopment. Any aberration may contribute to

the development of psychosis.

• Antipsychotic drugs that are often used to treat psychosis may function via their effect on DNA methylation.

**Methylation changes in rheumatoid arthritis affect xx pathways**

• Alterations in DNA methylation may mediate the efficacy as well as side effects of antipsychotic drugs

accomplished by a variety of unrelated pathways.

• The dopamine pathway and genes involved in glutamatergic neurotransmission are hypothesized to play a

major role in psychosis related disorders.

**DNA methylation based pharmacoepigenomics of rheumatoid arthritis**

• The dopaminergic pathway may serve as a prominent framework for the treatment of psychosis.

• Nondopaminergic pathways such as GABAergic, glutamatergic and cholinergic pathways likely also play a

significant role.

• Other pathways, some still unknown, may be important in selected patients including families.

**DNA methylation diversity of rheumatoid arthritis in different human population**

• Other pathways, some still unknown, may be important in selected patients including families.

**Future perspective**

• There is a need to fully understand the involvement of DNA methylation in rheumatoid arthritis disorders.

• DNA methylation detection in more relevant rheumatoid arthritis synovial cell such as adipocyte, macrophage,

• Multi-omics features based remission prediction model: update 2019

[1-52]

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