

Differential DNA Methylation Correlates with Response to Methotrexate in Rheumatoid Arthritis

Methotrexate (MTX) is typically the first treatment prescribed in rheumatoid arthritis (RA) and whilst effective, up to 40% of patients do not respond well to MTX. Therefore, identifying factors that predict which patients are more likely to respond to which drug before starting treatment is a research priority. One factor to consider is DNA methylation. This is a modification of DNA that regulates how genes are expressed, and has been shown to play a role in disease processes in RA. In this study, we aimed to identify differences in DNA methylation between patients who responded well to MTX and patients who did not respond after 6 months of treatment. Methylation data from across the genome was generated using blood samples taken from patients before they started taking MTX and after 4 weeks of taking MTX, in order to find early changes in methylation that would predict response at 6 months. There were 12 genetic associations where changes in methylation were associated with response to MTX, and four of these associations replicated in a separate group of patients. Changes in methylation in these four regions were associated with improvement of response to MTX, and these results contribute to the personalised medicine strategy. However, further replication of these results and integration with other data is required to strengthen these findings before use as a marker in clinic.

Nair N, Plant D, Verstappen SM, Isaacs JD, Morgan AW, Hyrich KL, Barton A, Wilson AG. *Rheumatology (Oxford)*. 2019 Oct 10. pii: kez411. doi: 10.1093/rheumatology/kez411.