GENETICS

***PTPRC* mutation associated with response to anti-TNF therapy in rheumatoid arthritis**

Patients with rheumatoid arthritis (RA) who harbor a particular mutation at the protein tyrosine phosphatase receptor type C (*PTPRC*) gene locus have a better response to anti-tumor necrosis factor (TNF) therapy than individuals who lack it. This finding, from a multicenter analysis by Jing Cui and colleagues, might eventually be incorporated into a composite genetic prediction tool for identifying patients with RA who are likely to benefit from drugs that inhibit TNF activity. “In addition to tailoring therapy to the appropriate patient population, a biomarker of treatment response would provide insight into drug mechanism of action and potentially enhance design approaches for more efficient larger-scale clinical trials,” suggest the authors.

The researchers included data from nine RA cohorts ($n = 1,283$), with the inclusion criteria for patients being active

disease prior to infliximab, etanercept or adalimumab treatment ($n = 625$, 502 and 156, respectively) and available disease activity score (DAS28) data within 3–12 months of commencing therapy. The investigators tested 31 RA risk alleles for correlation with response to anti-TNF therapy and only one single nucleotide polymorphism (SNP) in *PTPRC* (also known as *CD45*) was significantly associated with response in both univariate and multivariate models ($P = 0.0004$ and $P = 0.0001$, respectively). Following anti-TNF therapy, possession of the SNP, termed rs10919563, correlated with a ‘good response’ according to EULAR response criteria (DAS28 < 3.2). Furthermore, the change in DAS28 from baseline was also associated with the presence of rs10919563.

Despite strong statistical evidence that the *PTPRC* SNP is a reliable predictor

of response to anti-TNF therapy, the researchers remain cautious about interpreting the results owing to the heterogeneity between the nine cohorts (e.g. study design, ascertainment criteria, duration of follow-up, population ancestry). “We need to replicate this finding in other collections to verify it is real, following which it will be important to fine-map and understand the functional consequences of the mutation,” explains Robert Plenge, the study’s lead investigator, who goes on to say that “unbiased genome-wide association studies are required to identify additional mutations that influence response to therapy.”

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Original article Cui, J. et al. *PTPRC* rheumatoid arthritis risk allele is also associated with response to anti-TNF therapy. *Arthritis Rheum.* doi:10.1002/art.27457