PSORT
Psoriasis Stratification to Optimise Relevant Therapy

HLA-C*06:02 genotype is a predictive biomarker of biologic treatment response in psoriasis

Do genetics hold the key to personalised treatment of psoriasis?

Lay Summary

Psoriasis is a common inflammatory skin disease that results from a complex interplay of factors relating to the immune system. In severe cases it is painful and debilitating, and significantly reduces patients' quality of life. In recent years, several biological therapies (biologics) have become available for the treatment of psoriasis. Although these can be remarkably effective in patients who respond to the treatment, they place a substantial economic burden on health providers due to their high cost.

In a recent article published in *The Journal of Allergy and Clinical Immunology* (JACI), Dand and colleagues hypothesised that genetics may help to predict which of the biologics are most likely to induce response in patients with moderate-to-severe psoriasis. For 1,300 patients taking either of the two first-line biologics, adalimumab and ustekinumab, the authors ascertained which version of the gene *HLA-C* they carried. *HLA-C* is one of a complex of immune genes that recognise foreign molecules in the body, and it has been firmly established that individuals in the general population that carry one specific allele (or version) known as *HLA-C*06:02* are at greatly increased risk of developing psoriasis. The researchers tested whether a patient's *HLA-C* status was associated with improved Psoriasis Area and Severity Index (PASI) score at 3, 6 and 12 months after starting adalimumab or ustekinumab treatment.

The authors found that patients who were negative for the *HLA-C*06:02* allele – that is, patients carrying other versions of the *HLA-C* gene – were significantly more likely to respond to adalimumab than to ustekinumab at all time-points. This difference in response rates between the two drugs was even more marked in patients who were both negative for *HLA-C*06:02* and positive for psoriatic arthritis, a common comorbidity. Conversely, in patients that were positive for *HLA-C*06:02,* little difference in response rates was observed - except for suggestive evidence in patients without psoriatic arthritis that ustekinumab may be more effective at the later time-points. The authors also demonstrate that the observed effects are specific to *HLA-C*06:02,* and not likely to relate to other HLA genes.

This study offers an important insight into response to biologics, and may offer a first step towards stratified or fully personalised treatment of moderate and severe psoriasis. Ascertainment of *HLA-C* status is straightforward, and as such the study results could have substantial clinical relevance for treatment selection. Ultimately, this could contribute to better outcomes for patients and more effective use of scarce healthcare resources.

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