Psoriasis and interleukin-1

A translation

EDITOR'S NOTE—Scientists and clinicians sometimes appear to speak different languages, particularly when obliged to write a brief abstract of their research. We print first, the abstract as submitted by Dr Michael Cork for presentation at a recent joint meeting in July of the Canadian and British dermatology associations. Then, as a contribution to better understanding, we print Dr Cork's 'translation' which should help clinicians to appreciate the implications of the research findings.

An allelic association between type one psoriasis and a polymorphism in the interleukin-1 receptor antagonist gene

In monogenic diseases large changes in allelic frequencies of one gene or a recent mutation in a gene are often seen. In contrast, in polygenic diseases such as psoriasis small changes in allelic frequencies of several genes can be found. Dysregulation of interleukin-1 (IL-1) and related genes appears to be central to the aetiology of psoriasis. We and others have previously shown decreased IL-1 receptor antagonist (IL-1ra) protein expression within psoriatic lesions. These results would implicate the IL-1ra as a candidate gene in psoriasis.

We have demonstrated a five allele polymorphism in intron 2 of the IL-1ra gene which is due to a variable number of 86bp tandem repeats. The repeat sequence contains three potential protein binding sites which may be of regulatory significance. Using the polymerase chain reaction we have determined allelic frequencies for this polymorphism in a control population (allele 2 = 22.9%) and compared this with patients with psoriasis. We have found a 50% increase in allele 2 in type 1 psoriasis (allele 2 = 35.5%). We have also found a similar increase in allele 2 in several other inflammatory skin diseases but not in rheumatoid arthritis or juvenile chronic arthritis.

This is the first non MHC gene to be associated with psoriasis. Studies are in progress to investigate the functional significance of this polymorphism.

'Translation'

The psoriatic lesion is characterised by excessive proliferation of epidermal cells, abnormal differentiation and inflammation. There is a strong family history in patients with early-onset psoriasis (below age 40). The only genes that have been associated with psoriasis so far are within the major histocompatibility complex but we show here that other genes are probably involved as well.

Cytokines are polypeptides that regulate the proliferation, differentiation and function of cells. In psoriasis, the biological response to one of these cytokines, interleukin-1 (IL-1) is increased, because not only are there more receptors for it in psoriatic skin, but there is also less of its specific inhibitor, the IL-1 receptor antagonist (IL-1ra). We have found that the gene encoding IL-1ra has five variants (alleles) at a specific locus (ie there is polymorphism at intron 2 of the IL-1ra gene). One of these alleles, allele 2, is significantly increased in patients with early onset psoriasis and presumably contributes to the familial nature of the disease.

It is of interest that we have found similar changes in patients with other chronic inflammatory diseases such as systemic lupus erythematosus (SLE). In SLE the presence of allele 2 of the IL-1 receptor antagonist polymorphism is related to disease severity. Patients with severe disease have a high frequency of allele 2 while those with mild disease have a lower frequency. IL-1ra seems to be a new genetic marker for the severity of inflammatory skin diseases.

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