PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Low TNF-a and IFN-? in ankylosing spondylitis

ArticleInfo		
ArticleID	:	90
ArticleDOI	:	10.1186/ar-2001-68125
ArticleCitationID	:	68125
ArticleSequenceNumber	:	47
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2001–7–26 Received : 2001–3–23 Accepted : 2001–7–26 OnlineDate : 2001–7–26
ArticleCopyright	:	Biomed Central Ltd2001
ArticleGrants	:	

ArticleContext	:	130753311

Frances Hall,[Aff1]

Aff1 Institute of Molecular Medicine, Oxford, UK

Keywords

ankylosing spondylitis, cytokines, HLA-B27, TNF-a, IFN-?

Context

This study compares the prominence of Th1 and Th2 responses in ankylosing spondylitis (AS) patients with HLA -$B27^+$ and -$B27^-$ controls. The influence of TNF-a promoter polymorphisms on T cell TNF-a production are also investigated.

Significant findings

The median percentage of $CD4^+$ and $CD8^+$ T cells producing TNF-a and IFN-? was lower in 25 AS patients (all $B27^+$) than in 22 healthy $B27^-$ controls (P <0.01). This difference was also evident in 18 healthy $B27^+$ controls compared with $B27^-$ controls (P <0.04). The percentages of IL-4-positive cells were similar in all groups. In the 18 $B27^-$ subjects, the TNF-a promoter genotype, defined by polymorphism at TNF-a-308, was not associated with different proportions of TNF-a- producing T cells. However, in 31 subjects (16 patients and 15 controls) from the $B27^+$ group, individuals with the rare TNF-a-308 genotype 1/2 (n = 6) had higher percentages of TNF-a-producing T cells than individuals with the common genotype 1/1 (P <0.02) (n = 25). Indeed, the $B27^+$ TNF-a-308 genotype 1/2 individuals had percentages of TNF-a-secreting T cells which were comparable with those in the $B27^-$group.

The authors conclude that this suggests Th1 insufficiency in AS, rather than Th2 overactivity. A rare TNF-a promoter-308 allele (or another gene on that haplotype) modifies this phenotype in $B27^+$ individuals and may be protective.

Comments

This is a well presented study which attempts to bridge the gap between association of B27 with AS and pathophysiology. The authors have explored the cytokine production of peripheral T cells in patients with AS (all $B27^+$) and controls ($B27^+$ and $B27^-$) and have identified a 'Th1 deficiency' phenotype in patients and in $B27^+$ controls. The AS and control groups each included ~20 individuals and appropriate statistical analyses were applied. The stimulation of T cells with PMA and ionomycin is unphysiological; however, the technique probably reveals a genuine difference in T cell function in this study. This 'Th1 deficiency' can apparently be rectified, in $B27^+$ subjects, by the presence of a rare TNF-a haplotype. However, the number of individuals with the rare genotype is small and this effect should be regarded as intriguing but inconclusive at this stage. Ideally, the differences in T cell cytokine production should be confirmed following physiological challenges, such as infection with influenza or tetanus toxoid vaccination.

Methods

Stimulation of T cells with phorbol myristate acetate (PMA)/ionomycin, FACS analysis with intracellular staining, amplification-refractory mutation system PCR

Additional information

References

1. Rudwaleit M, Siegert S, Yin Z, Eick J, Thiel A, Radbruch A, Sieper J, Braun J: Low T cell production of TNF-a and IFN-? in ankylosing spondylitis: its relation to HLA-B27 and influence of the TNF-308 gene polymorphism. Ann Rheum Dis. 2001, 60: 36-42.