BREACH OF SELF TOLERANCE IN RHEUMATOID ARTHRITIS: A ROLE FOR TH17 EFFECTOR T CELLS?

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Background and objectives While many studies on rheumatoid arthritis have focused on the active phase of the disease, the events that lead to the initial breach of self-tolerance remain ill defined. The authors have developed a model of breach of self-tolerance where a Th1 response to irrelevant antigen (OVA) results in arthropathy associated with spontaneous induction of autoreactive T and B cell responses. Here the authors investigate the role of Th17 cells, a subset of interleukin (IL)-17 producing CD4+ T important in autoimmunity, in the initial events leading to breach of self-tolerance in experimental arthritis.

Methods The authors employed TcR adoptive transfer systems together with novel arthritis model to analyse the role of Th17 cells in the events that lead to breach of self-tolerance in experimental arthritis.

Results Transfer of OVA specific Th17 cells induced similar levels of inflammation as Th1 cells, and could induce a breach of self-tolerance as demonstrated by CII specific T and B cell responses. Whereas the transferred OVA specific Th1 population retained its phenotype, the transferred Th17 population displayed significantly reduced IL-17 production. Furthermore, the CII specific T cells in both the Th1 and Th17 recipients were characterised by IFN-γ and not IL-17, production.

Conclusion The fact that the OVA-specific T cell responses in both Th1 and Th17 transfer models are characterised by IFN-γ production and not IL-17 suggests that the ensuing breach of self-tolerance is driven by IFN-γ producing cells. In support of this, the evolving CII response is also characteristic of a Th1 rather than Th17 response. These studies highlight the plasticity of transferred cell populations in vivo, and support the use of blocking and fate-mapping studies to definitively address how auto-reactive responses develop.
Breach of self tolerance in rheumatoid arthritis: a role for Th17 effector T cells?

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