cells (DC) and/or the transformation of synoviocytes to follicular DC may play a key role in this process. In our model a so-called amplifier gene stimulates this chemo-attraction of and/or the differentiation to DC's. The DC's present self-peptides not to disease-inducing but to regulatory auto-reactive T cells that have been recruited also to the inflamed synovium. These regulatory T cells recognise self-peptides such as DERAA peptides from the HV III region of certain HLA-DR alleles presented by DR or DQ molecules. This DC-regulatory T cell interaction is an essential checkpoint for the control of the inflammation and is controlled by HLA class II genes. In the absence of protective HLA alleles and therefore self-reactive regulatory T cells this checkpoint fails and this results in a local loss of tolerance and a (severe) chronic arthritis (RA).

This model has several important implications for the immunotherapy of RA:

- We may stop the search for a unique target antigen for disease-inducing T cells
- Immunotherapy that is exclusively targeted at T cells may have an adverse effect
- Immunotherapy strategies for RA should either be targeted at the re-establishment of a normal phenotype in synoviocytes or on restoring a functional immunoregulatory loop.

SP0051 HSP REACTIVE T CELLS AS INFLAMMATION REGULATORS

¹W Van Eden, ¹L Paul, ¹U Wendling, ¹P Van Kooten, ¹J Bos-de Ruijter, ¹R Van der Zee, ²B Prakken. ¹Department of Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, The Netherlands; ²Department of Pediatric Immunology, University Hospital for Children and Youth, Utrecht, The Netherlands

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Immunisation with heat shock proteins has protective effects in models of induced arthritis. Analysis has shown a reduced synovial inflammation in such protected animals. Adoptive transfer and immunisation with selected T cell epitopes (synthetic peptides) have indicated the protection to be mediated by T cells directed to conserved hsp epitopes. This was shown first for mycobacterial hsp60¹ and later for mycobacterial hsp70.^{2,3}

Fine specificity analysis showed that such T cells were cross-reactive with the homologous self hsp. Therefore protection by microbial hsp reactive T cells can be by cross-recognition of self hsp overexpressed in the inflamed tissue. Preimmunisation with hsp leads to a relative expansion of such self hsp cross-responsive T cells. The regulatory nature of such T cells may originate from mucosal tolerance maintained by commensal flora derived hsp or from partial activation through recognition of self hsp as a partial agonist (Altered Peptide Ligand) or in the absence of proper costimulation. Recently, we reported the selective upregulation of B7.2 on microbial hsp60 specific T cells in response to self hsp60.⁴ Through a preferred interaction with CTLA-4 on proinflammatory T cells this may constitute an effector mechanism of regulation. Also, regulatory T cells produced IL10.

REFERENCES

- 1 Anderton SM, van der Zee R, Prakken B, Noordzij A, van Eden W. Activation of T cells recognizing self 60-kD heat shock protein can protect against experimental arthritis. *J Exp Med.* 1995;**181**:943–52
- 2 Tanaka S, Kimura Y, Mitani A, Yamamoto G, Nishimura H, Spallek R, Singh M, Noguchi T, Yoshikai Y. Activation of T cells recognizing an epitope of heat-shock protein 70 can protect against rat adjuvant arthritis. *J Immunol.* 1999;**163**:5560–65

- 3 Wendling U, Paul L, van der Zee R, Prakken B, Singh M, van Eden W. A conserved mycobacterial heat shock protein (hsp) 70 sequence prevents adjuvant arthritis upon nasal administration and induces IL-10-producing T cells that cross-react with the mammalian self-hsp70 homologue. *J Immunol.* 2000;**164**:2711–17
- 4 Paul AG, van Der Zee R, Taams LS, van Eden W. A self-hsp60 peptide acts as a partial agonist inducing expression of B7-2 on mycobacterial hsp60-specific T cells: a possible mechanism for inhibitory T cell regulation of adjuvant arthritis? *Int Immunol.* 2000;**12**:1041–50

SP0052 DETECTION OF ANTIGEN-SPECIFIC T CELLS

P Bowness. MRC Human Immunology Group, IMM, John Radcliffe Hospital, Oxford, UK

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Antigen-specific T cells are thought to drive the inflammatory response in a number of rheumatic diseases including RA and the spondyloarthropathies. T cells recognise specific combinations of antigenic peptides bound to of HLA molecules, and subsequently proliferate and perform effector functions including cytokine secretion. Techniques have been developed to detect these T cells (usually *ex vivo* or *in vitro*), based upon their antigenic specificity, their function, and their clonality. Some techniques combine these attributes. Recently fluorescent-labelled multimers (usually tetramers) of synthetic HLA/peptide combinations have been used to stain T cells of defined antigen specificity. The use of HLA /peptide tetramers has greatly increased our understanding of the role of T cells in viral infections and given some insight into rheumatic diseases. Other techniques have been developed that detect cytokines produced in response to specific antigens (i.e. detecting function), or that detect populations of T cells carrying the same or related T cell receptors. Our ability to detect antigen-specific T cells has important implications for our understanding of disease pathogenesis, and for monitoring disease progress. These methodologies also offer therapeutic potential.

Polymyalgia rheumatica – Thursday 14 June, 16.00-17.30/Small Hall

SP0053 EUROPEAN DIAGNOSTIC CRITERIA FOR POLYMYALGIA RHEUMATICA

H Bird. Clinical Pharmacology Unit, University of Leeds, Leeds, UK

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A variety of separate diagnostic criteria sets exist for polymyalgia rheumatica. These include those proposed in 1979,¹ 1981² and 1989.³ All differ slightly, the optimum criteria still having to be determined.

In 1997, the Polymyalgia Rheumatica Special Interest Group was established under the auspices of the EULAR Standing Committee for International Clinical Studies. Twenty participating centres throughout Europe between them promised to make available 200 new patients each year for the comparison of criteria sets. In parallel patients, where suitable, were recruited to a study to evaluate, for the first time, response criteria for this condition. It was hoped that both studies would lead to more accurate assessment of the several drugs then being claimed to be steroid sparing agents.