GLOSSARY

HEAT-SHOCK PROTEINS Families of proteins found in both prokaryotic and eukaryotic cells and bacteria, synthesized in response to environmental stresses

TOLEROGENIC EPITOPES Sites on antigens that are recognized by an antigen receptor (i.e. an antibody or T-cell receptor) that induce tolerance

A link between TLR5 signaling and susceptibility to systemic lupus erythematosus

Signals from Toll-like receptors (TLRs) are essential for regulating inflammation and for generating innate immune responses to pathogens. A study now shows that signaling downstream of TLR5 might have a role in the development of systemic lupus erythematosus (SLE).

The *TLR5* gene, which encodes the receptor for bacterial flagellin, contains a common stop-codon polymorphism that blocks signaling downstream of this receptor. In this paper, Hawn *et al*. used transmission disequilibrium testing to investigate whether the allele containing this stop codon (allele C1174T) was associated with susceptibility to SLE.

In a cohort of 199 SLE patients and their unaffected relatives (75 siblings and 326 parents) the wild-type allele was preferentially transmitted to individuals with SLE, but the stop-codon allele was not. The allele containing the stop codon was under-represented in individuals with SLE; other TLR5 alleles were equally distributed between the two groups. These data suggest that the TLR5 stop codon is associated with resistance to SLE.

What effect does the presence of the stop codon have on the immune response to flagellin? Peripheral-blood mononuclear cells from individuals with the TLR5 stop codon produced lower levels of proinflammatory cytokines in response to flagellin stimulation than individuals carrying the wild-type allele. The authors concluded that abrogation of TLR5 signaling might therefore blunt the immune response in individuals carrying the stop-codon polymorphism, thereby protecting them from developing SLE.

Jenny Buckland

Original article Hawn TR *et al.* (2005) A stop codon polymorphism of Toll-like receptor 5 is associated with resistance to systemic lupus erythematosus. *Proc Natl Acad Sci USA* **102**: 10593–10597

Progress in immunotherapy for juvenile idiopathic arthritis

T-cell reactivity to autologous HEAT-SHOCK PROTEIN 60 (HSP60) in juvenile idiopathic arthritis (JIA) is often associated with positive patient outcome. Specific HSP60 TOLEROGENIC EPITOPES need to be identified in order for further research into HSP60-peptide immunotherapy in autoimmune diseases to be possible.

In their recent study, Kamphuis and colleagues analyzed 8 potential HSP60 epitopes in patients with JIA. The epitopes, which were obtained using a computer algorithm, originated from both self and microbial HSP60 binding to different HLA-DR molecules. T-cell responses to each of these potential tolerogenic epitopes were analyzed in a total of 57 patients with JIA, 27 healthy controls and 20 disease control patients with diabetes.

Out of the 8 potential HSP60 epitopes, 5 peptides resulted in tolerogenic T-cell immune responses in patients with JIA (50–70%). Tolerogenic responses were not seen in either of the control patient groups. Further investigation into peptide-specific cytokine production showed that peripheral-blood mononuclear cells from both the patients with JIA and the healthy controls produced interferon-γ when reacting to the peptides in question. Antigen-specific production of interleukin-10, however, was only induced in cells from patients with JIA.

The authors conclude that the set of pan-DR peptides identified can provide better insight into the inflammation control mechanism observed in oligoarticular JIA. Further studies should investigate if the newly identified epitopes are involved in other HSP60-related inflammatory diseases, such as rheumatoid arthritis and atherosclerosis.

Jasmine Farsarakis

Original article Kamphuis S *et al.* (2005) Tolerogenic immune responses to novel T-cell epitopes from heat-shock protein 60 in juvenile idiopathic arthritis. *Lancet* **366:** 50–56

Comparison of antibody assays for monitoring systemic lupus erythematosus

The recently available EliA dsDNA is an automated fluorescent immunoassay that measures anti-double-stranded DNA (anti-dsDNA) antibodies. The assay is performed in polystyrene wells coated with circular plasmid dsDNA from *Escherichia coli*. López-Hoyos *et al*. carried out a retrospective trial in a cohort of 181 patients to assess the utility of EliA dsDNA for monitoring clinical activity in systemic lupus erythematosus (SLE) in comparison with CLIFT (*Chrithidia luciliae* Immunofluorescence test).