

26 A NEW MODEL OF ARTHRITIS INDUCED BY A GLUCOSE-6-PHOSPHATE ISOMERASE PEPTIDE: IMMUNOLOGICAL REQUIREMENTS AND PEPTIDE CHARACTERISATION

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Background and objectives Immune reactivity to the ubiquitous glucose-6-phosphate isomerase (GPI) protein leads to arthritis development. Immunisation with human GPI protein leads to severe arthritis on DBA/1 background, but not on C57Bl/10.Q (B10.Q).^{1 2} Recently, a peptide of the human GPI protein was identified as arthritogenic in DBA/1 mice: hGPI₃₂₅₋₃₃₉ peptide.³ The authors tested whether hGPI₃₂₅₋₃₃₉ peptide could induce arthritis in B10.Q mice and the authors characterised the immunological pathways involved and the features that render the peptide arthritogenic.

Materials and methods Arthritis was induced by immunisation of the mice with the purchased peptides (Schafer-N) diluted in DMSO and PBS and emulsified with CFA (Difco). Different knock-out and congenic mice on the B10 background were tested.

After immunisation, T cell response was characterised by measuring cytokines after *in vitro* re-stimulation of lymph node cells. The B cell response was analysed by quantitative and qualitative analysis of the antibody production. MHC binding assay tested the capacity of peptides to compete with the invariant chain peptide for binding to recombinant MHC A^q molecule.

Results The hGPI₃₂₅₋₃₃₉ peptide could induce arthritis in B10.Q mice. The disease severity was increased by the *Ncf1* mutation, a regulatory component of the NADPH oxidase complex 2 (NOX2), known to increase arthritis severity in other models.⁴⁻⁶ Arthritis development was dependent on the presence of T cells and B cells and restricted to some MHC II haplotypes. Following immunisation with hGPI₃₂₅₋₃₃₉ peptide Th1 and Th17 cells got primed. T cells and B cells cross-reacted to the murine GPI protein. Low antibody response to GPI proteins and peptides was detectable. The phenylalanine in position 331 was crucial for arthritis development and binding to MHC, a residue that differs between human and murine peptide. *Ncf1* mutated but not wt mice developed a very mild disease after immunisation with mGPI₃₂₅₋₃₃₉ peptide followed by priming of anti-mGPI₃₂₅₋₃₃₉ peptide Th1 and Th17 cells.

Conclusions The authors describe a new peptide-induced arthritis which shares important features with previously described arthritis models, as the influence of the MHC haplotype and of the binding to the MHC molecule, an intact adaptive immune system and NCF1 function. A possible target for autoimmunity *in vivo* could be identified in an endogenous protein. Differently from other arthritis models, the poor antibody response to the immunogen suggests either skewing of the antibody response to unknown targets or the development of arthritis independently from antibodies. Both hypotheses are worth further investigation.

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