Investigation of the genetic background of inflammatory rheumatological diseases

**Objective:** Study I.: To characterize experimentally induced spondylarthropathy in arthritis-susceptible inbred mice and in their F1 and F2 hybrid generations of susceptible and resistant mouse strains.

Study II.: To determine the frequency of HLA-DR1 and -DR4 phenotypes in a Northeastern Hungarian population of patients with RA in comparison to healthy control subjects.

**Methods:** Study I.: Spondylarthropathy was induced in susceptible BALB/c and C3H/HeJCr (C3H) strains of mice, and in their F1 and F2 generations derived from intercrosses with arthritis- and/or spondylitis-resistant DBA/2 and DBA/1 parent strains, by systemic immunization with cartilage proteoglycan (PG) aggrecan. The incidence and severity of PG-induced spondylitis (PGIS) were scored histologically, and these scores for spine involvement were correlated with serum antibody and cytokine levels and with in vitro T cell responses to cartilage PG.

Study II.: We performed HLA-DRB1 genotyping (DRB1*01-DRB1*16) in 83 RA patients and 55 healthy controls using polymerase chain reaction with sequence specific primers (PCR-SSP).

**Results:** Study I.: 60–70% of susceptible mouse strains and their F2 hybrids developed spondylitis either with or without arthritis. The DBA/1 strain appeared to carry genes protecting this strain and its F1 and F2 hybrids from spondylitis, whereas the DBA/2 strain, although resistant to PGIS, harbored genes permitting PGIS in its hybrid generations.

Study II.: The frequency of HLA-DR4 alleles was significantly increased in the patients compared to controls (31.3% vs. 10.9%; p<0.05). HLA-DR1 showed a tendency to be more frequent in the patients than in the controls (32.5% vs. 18%).

**Conclusion:** Study I.: PGIS, a murine model of autoimmune spondylitis, shows similarities to ankylosing spondylitis. This model allows for the elucidation of genetic components involved in the etiology of PGIS, independent of those controlling the susceptibility to PGIA.

Study II.: Results regarding frequencies of HLA-DR1 and HLA-DR4 are generally in accordance with the findings observed in other Caucasian populations.