5 Models of Rheumatoid Arthritis

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5.1 Introduction

Rheumatoid arthritis (RA) is a chronic disabling disease affecting around 1% of the population. Much progress has been made in re-
cent years towards the identification of mediators that contribute to the pathogenesis of RA, and a number of studies have pointed to a pivotal role for tumour necrosis factor-alpha (TNFα) in the disease process. Indeed, the success of biological inhibitors of TNFα (Elliott et al. 1993, 1994a, b; Moreland et al. 1997; Weinblatt et al. 1999) in the clinic is a testament to the pathological significance of this cytokine in RA. However, there is still a lack of knowledge of the underlying causes of the disease and it is for this reason, together with the need for more durable remedies, that animal models of arthritis continue to be studied. Animal models of arthritis are used in a wide variety of different studies, including preclinical testing of novel therapies, analysing mechanisms of drug action, identifying both pro- and anti-inflammatory mediators, analysing genetic susceptibility factors, and in the search for markers of disease progression.

5.2 Models of Arthritis Induced by Immunisation

5.2.1 Adjuvant Arthritis

Adjuvant arthritis was the first model of RA to be described and can be induced in rats by a single injection of Freund’s adjuvant, containing *Mycobacterium tuberculosis* (Pearson 1956). Clinical arthritis starts at around 10–45 days after injection and generally subsides after 1 month. The chief pathological features of adjuvant arthritis include oedema, infiltration into the joint of mononuclear and polymorphonuclear cells, pannus formation, periostitis, and erosion of cartilage and bone. Although an association between immunity to 65-kDa heat shock proteins and the induction of adjuvant arthritis has been suspected (van Eden et al. 1988), no single mycobacterial immunogen has been shown to be responsible for the arthritogenic response in this model (Holmdahl et al. 1992). Rather, the induction of adjuvant arthritis has been attributed to a mycobacterial cell wall component, muramyl dipeptide, which is immunostimulatory but does not evoke a specific immune response (Kohashi et al. 1982). In addition, a number of adjuvants which lack immunogenic properties have been shown to induce arthritis in susceptible strains of rats, including avridine (Chang et al. 1980), incomplete Freund’s adjuvant