20 Immunogenetics of micromammal-macroparasite interactions

Nathalie Charbonnel, Joelle Goüy de Bellocq and Serge Morand

1 Introductory remarks

During the last 20 years, the concepts of population biology and evolutionary ecology have been applied to the studies of immune defences, in an attempt to explain the variation of immune responses observed across individuals and species. Among these approaches, immunogenetics focuses on immunity genes and on the variability of outcomes generated by genotype-genotype interactions between and within host and parasite species.

The recent explosion of genetic data emerging from sequencing and genomics has highlighted the importance of immunity because a considerable fraction of the genome appears to be dedicated to defence against parasites. In most mammals, 5% of genes are involved in this role (Trowsdale and Parham 2004). Such advances allow investigation of the mechanisms associated with immune-related coding and non-coding mRNA transcripts, and definition of the genetic basis of susceptibility to complex diseases. Identifying the genes underlying adaptation, how these genes change in response to natural selection, and what selective pressures drive their evolution are now at the core of evolutionary biology and immunogenetics, and will be discussed here.

2 Relevance of immunogenetics for small mammals and macroparasites interactions

The profound influence of the host genetic background on resistance against infections has been established in numerous animal studies, which mainly focused on human infections such as malaria, HIV and hepatitis (see review in Cooke and Hill 2001). The emphasis of these studies is understandable given the potential implication arising from the importance of
the evolutionary mechanisms of pathogen resistance for medicine (Sorci et al. 1997). Because of their medical or veterinary importance, the genetic bases of resistance to helminths and ectoparasites have also been investigated, although to a lesser extent.

2.1 Evidence for the genetic variability of susceptibility and infectivity

2.1.1 Helminth infections

It is now well recognized that resistance to helminth infections in mammals is under genetic control, and that helminths themselves show genetic variation in their infectivity characteristics, i.e. intensity of infection or level of susceptibility to host responses (see review in Wakelin et al. 2002). Epidemiological and genetic studies in human and cattle populations have demonstrated that susceptibility to helminths frequently limited to some families, and that it differs between ethnic groups or breeds, suggesting the possible involvement of genetic factors (Quinnell 2003). On the other hand, epidemiological studies of a number of parasite species have shown that the intensity of infection (worm burden) is a host heritable character. This was first found by Wakelin (1975) in mice parasitized by *Trichuris muris*, where selection experiments enhanced host resistance after six generations from 70 % to 100 % (reviewed in Behnke et al. 2003). Heritability of worm burden varying from 0.21 to 0.44 has now been reported for many gastrointestinal helminths (Behnke et al. 2003; Quinnell 2003). The values of the heritabilities of helminth burden can provide a measure for the cumulative effect of all genes involved in helminth resistance, but cannot provide any information about the specific genes involved. Most of our current understanding of the regulation of the protective mechanisms mediating resistance to intestinal nematodes has come from laboratory studies that used rat and mouse models. These studies used well-defined inbred strains and genetic manipulation (transgenes, gene targeting; see review in Abel and Desein 1997) revealing the effects of host genes on anti-parasitic resistance. They concentrated on a limited number of intestinal nematode species such as *Acaris* spp., *Nippostrongylus brasiliensis*, *Trichinella spiralis*, *Heligmosomoides polygyrus* and *Trichuris muris* (Grencis 1997), tissue-dwelling helminths (*Brugia malayi*) and various *Schistosoma*. Although genetic control of the worm burden is likely to be polygenic, recent studies have focussed on genes of major effect, and whether the same genes of major effect are involved in controlling different helminth species.