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No evidence for specificity between host and parasite genotypes in experimental *Strongyloides ratti* (Nematoda) infections

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Abstract

A key requirement for several theories involving the evolution of sex and sexual selection is a specificity between host and parasite genotypes, i.e. the resistance of particular host genotypes to particular parasite genotypes and the infectivity of particular parasite genotypes for particular host genotypes. Determining the scope and nature of any such specificity is also of applied relevance, since any specificity for different parasite genotypes to infect particular host genotypes may affect the level of protection afforded by vaccination, the efficacy of selective breeding of livestock for parasite resistance and the long-term evolution of parasite populations in response to these control measures. Whereas we have some evidence for the role of specificity between host and pathogen genotypes in viral and bacterial infections, its role in macroparasitic infections is seldom considered. The first empirical test of this specificity for a vertebrate–nematode system is provided here using clonal lines of parasite and inbred and congenic strains of rat that differ either across the genome or only at the major histocompatibility complex. Although significant differences between the resistance of host genotypes to infection and between the fitness of different parasite genotypes are found, there is no evidence for an interaction between host and parasite genotypes. It is concluded that a specificity between host and parasite genotypes is unlikely in this system.

Keywords: MHC; Host–parasite coevolution; Parasitic nematodes; Genetic diversity

1. Introduction

Interest in the consequences of genetic diversity in host and parasite populations has been stimulated by our recognition of the potential of parasitism as a major force in evolution and ecology. Thus, the antagonistic interaction between hosts and parasites is central to several theories to explain the evolution of sex (Jaenike, 1978; Hamilton, 1980), patterns of sexual selection in host populations (Hamilton and Zuk, 1982) and the maintenance of genetic diversity in both host and parasite populations (Haldane, 1949; Seger, 1988) through the sustained, dynamic interaction of host and parasite genotypes. These theories are predicated on a specificity between host and parasite genotypes (Haldane, 1949); i.e. the ability of a particular parasite genotype to infect one host genotype better than other host genotypes and, conversely, the ability of a particular host genotype to resist infection by one parasite genotype better than other parasite genotypes. This specificity between host and parasite genotypes means that the fitness of a particular host genotype depends on the parasite genotypes to which it is exposed (and that of a parasite genotype depends on the host genotypes that are available). An applied consequence of any such specificity is that selective breeding programmes for increased parasite resistance may result in the selection of host genotypes resistant to a more limited range of parasite genotypes than those found naturally occurring in the field. Similarly, a specificity between host and parasite genotypes may affect the degree of protection afforded by immunization according to both the parasite antigens used in a vaccine and the genotype of the host (Morrison, 1996).

There is now a large body of empirical evidence demonstrating genetic variation in resistance of hosts to a variety of parasite species (Wakelin, 1975; Hill, 1998;

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Pemberton et al., 2004). Equally, we are beginning to build a picture of the role of genetic variation in determining the infectivity of different parasite strains (Wakelin and Goyol, 1996; Moss et al., 2002; Paterson and Viney, 2003). Some notable studies provide evidence for a specificity between host and parasite genotypes: in some invertebrate pathogens, such as microsporidian infections of crustacea (Ebert, 1994; Carius et al., 2001) and trematode infections of snails (Lively, 1987; Dybdahl and Lively, 1998; Lively and Dybdahl, 2000); in some viral infections of humans, such as HIV and influenza; and in *Theileria parva* infections of cattle (Goddeeris et al., 1990; Morrison, 1996). In general, however, the range of such studies is limited, particularly for parasitic infections of vertebrates and (at least to the author's knowledge) no studies have investigated specificity between host and parasite genotypes in nematode infections.

In vertebrates, the major histocompatibility complex (MHC) is, a priori, a likely source of specificity between host and parasite genotypes. First, the molecular function of genes within the MHC is to present foreign antigen to the immune system (Benacerraf, 1981). They do this by binding short peptides within their antigen presenting site (APS). Although each MHC molecule is able to bind a wide range of peptides, they are restricted in that each bound peptide must have specific 'anchor' residues to enable strong binding (Bjorkman et al., 1987; Bjorkman and Parham, 1990). Second, loci within the MHC are extremely polymorphic, with much of this polymorphism encoded within the APS, which generates functional variation between MHC alleles in the anchor residues required for effective peptide binding (Hedrick, 1994). Third, population and quantitative trait loci (QTL) mapping studies repeatedly highlight associations between MHC variation and resistance/susceptibility to a range of parasitic diseases (Else and Wakelin, 1988; Hill, 1998; Paterson et al., 1998; Wegner et al., 2003). However, few studies have so far attempted to look for associations between MHC variation and resistance to particular parasite genotypes (Penn et al., 2002) rather than resistance to a parasite species.

This study tests for genetic specificity between parasitic nematodes and their vertebrate hosts. Parasitic nematodes are widespread infectious agents, with a high prevalence of infection in most natural vertebrate populations (Shaw and Dobson, 1996), and nematode infections are generally accompanied by morbidity effects such as stunting of growth and loss of condition (Hudson and Dobson, 1995; Stephensen, 1999). These morbidity effects have particular economic importance for cattle and sheep due to the losses in productivity that they can cause. *Strongyloides ratti* is used here as a model of infection (Viney, 1999). This nematode is a natural parasite of rats and has the feature that clonal lines can be generated from a single individual and maintained thereafter either sexually or asexually [where asexual reproduction occurs without genetic recombination or inbreeding (Viney, 1994)]. This system is used to assay the fitness of defined parasite genotypes in host genotypes that differ either across their entire genomes or only at the MHC.

2. Materials and methods

2.1. Study system

Strongyloides ratti is a parasitic nematode that naturally infects rats (Dawkins, 1989). Infection is by skin penetration, followed by migration through muscle, lungs, nasopharyngeal region and finally the small intestine, where the adult parasites mature and reproduce. Parasitic stages are female only and produce eggs by mitotic parthenogenesis (Viney, 1994), which are passed in the faeces and can then develop by one of two developmental routes (Viney, 1996; Harvey et al., 2000). In homogonic development, eggs develop directly into infective third stage larvae (iL3s). In heterogonic development, eggs develop into free-living males and females, which mate and produce eggs that develop into iL3s. All parasite lines used were generated from a single iL3 and thus are known as isofemale lines (Tindall and Wilson, 1988; Viney, 1996) and were maintained by serial passage in Wistar rats. The lines ED5, ED43 and ED132 were maintained homogonically, and ED248 and ED321, heterogonically. Thus, for lines maintained homogonically, no genetic recombination occurs and all parasites are identical to each other and to the original wild isolate. For heterogonic lines, genetic recombination will occur in the free-living adults with the consequence that any loci heterozygous in the original wild female will segregate in the laboratory line. Further details on the lines used can be found in Paterson and Viney (2003).

2.2. Experiment 1

Hosts that differ across their entire genome were used to test for an interaction between host and parasite genotypes in the dynamics of experimental infection. Commercially supplied female rats (Harlan, UK), approximately 100 g, were used. These were of inbred strains PVG, Lewis and LOU/C. Groups of rats were infected by s.c. injection of iL3s and faeces collected twice weekly following patency on day 5 p.i. Faeces were cultured and viable eggs counted as described previously (Paterson and Viney, 2003) to assay the reproductive output of these infections through time. PVG and Lewis rats were tested against *S. ratti* lines ED43 and ED321 in a factorial design consisting of four groups of six rats each infected with 1,000 iL3s. Infections were monitored until day 27 p.i. PVG and LOU/C rats were then tested against *S. ratti* lines ED5 and ED132 in a factorial design consisting of four groups of six rats each infected with 100 iL3s. Two blocks were used in this design; infections were monitored until day 32 p.i. in the first block and until day 45 p.i. in the second block.