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Review

Compatibility polymorphism in snail/schistosome interactions: From field to theory to molecular mechanisms

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ABSTRACT

Coevolutionary dynamics in host–parasite interactions potentially lead to an arms race that results in compatibility polymorphism. The mechanisms underlying compatibility have remained largely unknown in the interactions between the snail *Biomphalaria glabrata* and *Schistosoma mansoni*, one of the agents of human schistosomiasis. This review presents a combination of data obtained from field and laboratory studies arguing in favor of a matching phenotype model to explain compatibility polymorphism. Investigations focused on the molecular determinants of compatibility have revealed two repertoires of polymorphic and/or diversified molecules that have been shown to interact: the parasite antigens *S. mansoni* polymorphic mucins and the *B. glabrata* fibrinogen-related proteins immune receptors. We hypothesize their interactions define the compatible/incompatible status of a specific snail/schistosome combination. This line of thought suggests concrete approaches amenable to testing in field-oriented studies attempting to control schistosomiasis by disrupting schistosome–snail compatibility.

Contents

1. Introduction

Parasites cause substantial deleterious effects to their hosts, and therefore represent a major driving force in their evolution (Howard, 1991). In parallel, parasites have to cope with host-defence mechanisms to avoid elimination. This reciprocal antagonistic co-evolution between both partners can be illustrated by an arms race in which host and parasite develop mechanisms to circumvent counter-measures developed by their opponent. In certain interactions and at a particular time of their evolution, parasite virulence and host defence can be in equilibrium in natural populations. This can lead to a phenomenon called compatibility polymorphism. Compatibility is a characteristic of a host–parasite system where the parasite species is capable of establishing infection and achieving transmission using this host species (Coustau and Theron, 2004). To achieve compatibility, the parasite has to evade host defense systems in order to complete its life cycle (Sapp and Loker, 2000; Van Der Knaap and Loker, 1990). In certain host–parasite systems, compatibility is incomplete: sometimes the host wins

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and the parasite is eliminated, and sometimes the parasite wins and succeeds in infecting the host. This phenomenon is called compatibility polymorphism. It occurs in the interaction between the metazoan parasite *Schistosoma mansoni*, the agent of human intestinal schistosomiasis (Gryseels et al., 2006) and its invertebrate intermediate host, the gastropod mollusk *Biomphalaria glabrata* (see Fig. 1 for life cycle description). Genetic studies conducted with the *S. mansoni/B. glabrata* model demonstrated that compatibility is heritable and can be selected in the laboratory, either for susceptibility/resistance of the snails or the infectivity of the parasite (Davies et al., 2001; Richards et al., 1992; Webster et al., 2004). Compatibility may reside in a concordance of genetically determined phenotypes in snail and schistosome, each of which being polymorphic with respect to the relevant trait (Basch, 1975, 1976). Understanding the underlying mechanisms that maintain such sustainable interactions represents a major challenge for both parasitologists and immunologists. Here we review results obtained recently with this host–parasite system with the aim of linking empirical data from field studies to experimental studies focusing on the molecular components of host resistance and parasite infectivity, and their interactions.

2. From field observations to a theoretical framework

Temporal and spatial variation in the degree of compatibility between snails and schistosomes is an important phenomenon of direct relevance to the epidemiology of transmission (Prugnolle et al., 2006). However, a key problem concerning these compatibility studies is that data have been exclusively obtained from one or several generations of laboratory bred snails and/or schistosome strains passed through laboratory definitive hosts. Consequently they are poorly representative of the genetic variation present in their original populations. A limited initial sampling of the diversity present in the field, laboratory host-induced selection, founder effects and bottlenecking processes during lab maintenance have been demonstrated to sharply reduce genetic diversity in laboratory strains, particularly for the parasite (Bech et al., 2010; Stohler et al., 2004).

Recently, for the first time, snail–schistosome compatibility was investigated using both field-derived miracidia and snails from the same geographic locality (Guadeloupe) and in optimized conditions: numerous naturally infected definitive hosts were used as sources of miracidia, and varying doses of miracidia per host were used for snail exposures. This protocol took into account the great extent of parasite and host genetic diversity present in the natural populations (Theron et al., 2008). Dose–response curves showed that infection rates increased with increasing doses of parasites (from 1 to 20 miracidia per host) and reached 100% infection up to a dose of 10 or 20 miracidia (Fig. 2). Snails and parasites from this same geographic source were then used to establish laboratory strains, and compatibility was tested during several successive laboratory passages. In the transition from field to lab, compatibility dropped from 100% to around 50% after the first laboratory generation (Fig. 2). This compatibility level remained relatively stable during the entire time the parasite strain was maintained (from 2005 to present), while the neutral genetic diversity of the schistosome strain declined steadily (Bech et al., 2010).

There is a large difference between compatibility levels observed under wild vs. laboratory conditions. First, all wild snails become infected if exposed to enough wild miracidia. We hypothesize this is because the probability of a match (infection) increases with the dose of miracidia simply because a larger fraction of the phenotypic diversity present in the parasite population is included. All *B. glabrata* are potentially susceptible to *S. mansoni*, and will develop a patent infection if given enough genetically diverse miracidia. Reciprocally, we speculate that all *S. mansoni* miracidia

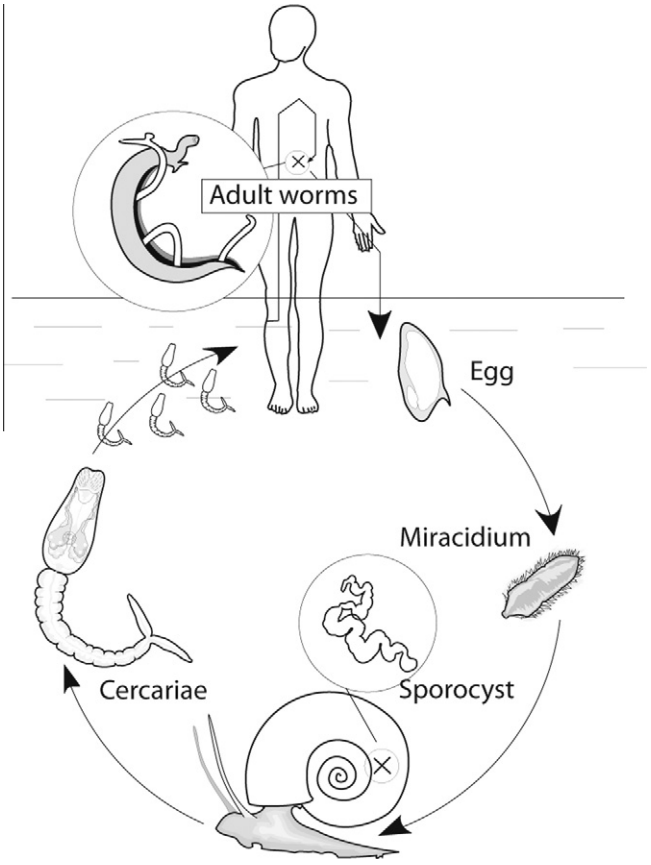

Fig. 1. *Schistosoma mansoni* life cycle. The genus *Schistosoma* currently contains 22 species, three of which, *S. haematobium*, *S. japonicum*, and *S. mansoni* are the principal agents of human schistosomiasis, the world's second most important parasitic disease after malaria. It infects 210 million people and is estimated to kill over 200,000 persons each year (Chitsulo et al., 2004). Schistosome parasites (Digenea) have a complex life cycle that involves two hosts (see life cycle). Adult worms mate in the venous system of a vertebrate host. They produce eggs that are expelled with the feces or urine. If deposited in an aquatic environment, the eggs hatch to release a miracidium that will infect specific species of freshwater snails. Inside the snail tissues, the miracidium transforms into a primary sporocyst (Sp1) that multiplies asexually to produce secondary sporocysts (Sp2), which then produce cercariae. Cercariae leave the snail and actively infect the vertebrate definitive host.

are potentially infective, if they are exposed to the right individual snail with a matching genotype, although this experiment is difficult to undertake because the same miracidium cannot be exposed to multiple snails. The low natural snail prevalence of snails with patent schistosome infection that is usually observed in transmission foci (Anderson and May, 1979; Sire et al., 1999) is then potentially due to the low probability that a schistosome phenotype encounters its corresponding compatible host phenotype rather than the existence of high level of resistance within host populations. The drop in compatibility after laboratory passage may result from a relatively more severe genetic bottleneck in the parasite (Bech et al., 2010; Stohler et al., 2004; Theron et al., 2008) than the host (Campos et al., 2002; Mulvey and Vrijenhoek, 1981). The parasite strain exhibits a reduced set of phenotypes that match only with a fraction of the phenotypes present in the host strain (Theron and Coustau, 2005). Even with high doses of miracidia per snail (Theron et al., 2008), there are some lab reared snails that will never become infected with this laboratory strain of parasite (Fig. 2). They would however, potentially remain susceptible to another schistosome strain that has retained a different set of matching phenotypes.