PhD defence of Nele Boon

Evolutionary epidemiology of schistosomiasis in the Senegal River Basin: Linking parasite genetics with human infection and disease

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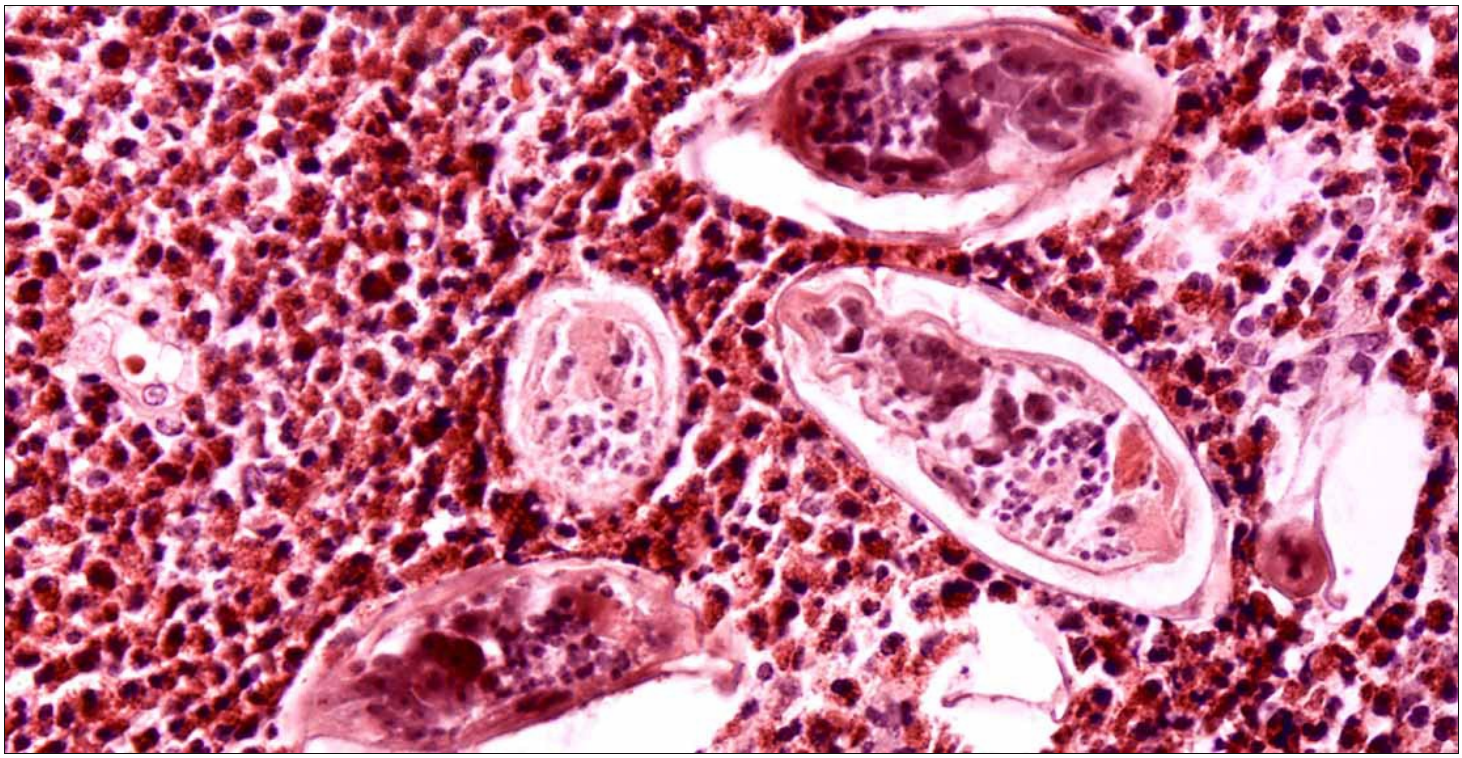
Zoological Institute (groot auditorium 02.21), KU Leuven - Leuven
Registration not required



Dit is de omschrijving

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Summary:

Schistosomiasis is a major poverty-related disease, infecting more than 200 million people in developing countries. More than 90% of them live in Sub-Saharan Africa. It is caused by infection with *Schistosoma* flatworms that reside in the vascular system of the definitive host. Freshwater snails are the intermediate hosts of schistosomes and essential for the completion of their life cycle. *Praziquantel* is currently the only recommended drug for treating all species of schistosomes. It is effective in killing adult schistosome worms, but does not kill immature schistosomes and so does not prevent reinfection. Therefore schistosomiasis continues to (re-)emerge. The main schistosomiasis-related pathology is caused by the accumulation of eggs in tissues, leading to a typical inflammatory reaction, which can develop into fibrosis of the liver or urinary bladder.

This doctoral thesis builds on the integration of parasite genetics and evolutionary biology with the epidemiology of schistosomiasis, the so called **"**evolutionary epidemiology", in the Senegal River Basin (SRB) in Northern Senegal. In the late eighties, the construction of dams on the Senegal River induced ecological changes that resulted in a huge outbreak of *Schistosoma mansoni*, causing intestinal schistosomiasis. Few years after this outbreak, also the prevalence of *S. haematobium,* causing urinary schistosomiasis, and the prevalence of *S. bovis,* infecting livestock, increased greatly. Today, *S. mansoni* and *S. haematobium* are co-endemic in the SRB and around Lac de Guiers, resulting in mixed-infections in humans.

In the first part of this thesis, we studied the molecular epidemiology of *Schistosoma haematobium* across the SRB. Transmission dynamics of *S. haematobium* in the SRB may be influenced by the hybridisation between *S. haematobium* and *S. bovis.* Hybridisation events of *Schistosoma* species are reported with increasing frequency, but the consequences of these hybridisation events have yet to be fully explored. The introgression of new genes in parasites may affect their virulence, transmission and drug susceptibility. **Chapter 2** describes the heterogeneous distribution of hybrids across villages in the lower and middle valley of the Senegal River. The majority of hybrids in the SRB showed a *S. haematobium* nuclear (ITS rDNA) and a *S. bovis* mitochondrial profile (*cox*1). Remarkably, the occurrence of *S. haematobium* x *S. bovis* hybrids was significantly associated with the prevalence of *S. mansoni,* but not with *S. haematobium.* In **Chapter 3** we found that egg morphology appears of limited value to detect parasites with a hybrid ancestry. In contrast to experimental studies, all eggs resembled the typical *S. haematobium* egg type. Based on the results of 17 microsatellite markers (**Chapter 4**), the hybrid parasites with a *S. haematobium* nuclear ITS rDNA profile and a *S. bovis* mtDNA profile did not cluster apart from the 'pure' *S. haematobium* parasites. This indicates that hybrids are in "panmixis" with pure *S. haematobium* worms, but not with *S. bovis*: they form a random mating schistosome population, without mating restrictions in the next generation. No first generation hybrids were found. This indicates that, in nature, a strong species boundary between *S. haematobium* and *S. bovis* persists. In *S. haematobium* populations, transmission appeared restricted between villages across the SRB, in comparison to transmission between individual hosts. These findings on *S. haematobium* contrast with the high transmission potential of *S. mansoni* populations across the SRB, as previously published by our group. This difference between both species may be related to the presence and the genetic constitution of the intermediate snail host populations, or to their different colonisation history.

In the second part of the thesis we took a closer look at the evolutionary epidemiology of *Schistosoma mansoni,* at the scale of the individual host. We hypothesized that, in addition to host-related factors, parasite genetic variation may explain a significant part of the variation in disease phenotype. In **Chapter 5**, a highly significant association was found between allelic variation at the parasite locus *L46951* and host infection intensity as well as bladder morbidity. It was hypothesized that this locus may be linked with parasite fecundity. We performed *in vivo* experiments (**Chapter 6**) to prove the causality of this association on a genetically diverse field strain of *S. mansoni*. Although we did not obtain sufficient biological replica, the experimental set-up was promising. Preliminary results suggested that each parasite genotype induces a specific disease phenotype in its vertebrate host.

A better understanding of the interactions and hybridisation between schistosome species in the SRB is crucial to improve control strategies. Elucidating the functional mechanism that leads to the association between parasite genetic variation and human disease may guide the development of new drugs and vaccines.