The zoonotic nature of schistosomiasis in Southeast Asia, caused by *Schistosoma japonicum*, is arguably the most challenging factor facing the control and interruption of transmission in the region. Unlike other species of schistosome, *S. japonicum* infects > 40 mammalian hosts. It has been established that different definitive host species are more or less involved in transmission to human hosts in different habitat types, however, the precise impact of wild and domesticated animals acting as reservoirs of infection in maintaining transmission cycles remains unclear. The continual public health threat posed by zoonotic spillover of parasites to humans is generally well documented, and is expected to increase due to anthropogenic-induced changes, such as increased urbanisation, migration, and changes to land use practises. Zoonotic pathogen interactions within host species likely impact and alter pathogen evolution, and may have implications for established control strategies and elimination goals. It is generally thought that parasite populations able to infect multiple hosts can evolve novel Antigen Coding Genes (ACGs) specific to a particular host species, and can become increasingly virulent when infecting a different host species. In other pathogens, the diversification of ACGs has been implicated in alterations in the ability of the parasite to evade detection, and thus the ability of the host's immune system to recognise infection. This work focuses on the variation and genetic diversity of the tegumental-surface antigen tetraspanin-23 (SjTSP-23) within and between definitive host species. SjTSP-23 is regarded as a potential vaccine candidate antigen, has been demonstrated as integral to parasite survival in the definitive host, and has been shown to interact directly with the definitive host's immune system via their Large Extracellular Loop (LEL) domains.

By sequencing SjTSP-23-LEL domains from 81 FTA-archived *S. japonicum* miracidia from four definitive host species (humans, dogs, cats, and pigs), it was possible to assess the variation and frequency of parasite ACG genotypes from human and animal host populations, and identify shared antigen variants. It is expected that SjTSP-23-LEL sampled from human hosts would be more genetically diverse than those sampled from other host species, and that this increased variation will have structural, functional and antibody-binding consequences, possibly leading to challenges with downstream vaccine design and development.

Indeed, through investigating the phylogenetic relationships and distribution of SjTSP-23-LEL haplotypes among definitive hosts, it was found that although humans contain the greatest frequency of unique, divergent haplotypes, there is significant sharing of antigen variants between hosts, with antigens predicted to be more genetically variable within host populations than between them. Furthermore, the selection pressures determined to be acting on sites within the LEL domain of SjTSP-23 from all hosts were shown to induce amino acid changes and induce antigenic variation in and around predicted antibody binding-sites, suggesting that host-derived selection pressures driving amino acid changes may serve as 'escape mutations', acting to reduce SjTSP-23-LEL antigenicity as an immune evasion mechanism.