

# Chromosome-level genome assembly reveals female-biased genes for sex determination and differentiation in the human blood fluke *Schistosoma japonicum*

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## Abstract

Schistosomiasis is a neglected tropical disease of humans caused by blood flukes of the genus *Schistosoma* – the only dioecious parasitic flatworms. Although aspects of sex determination, differentiation and reproduction have been studied in some *Schistosoma* species, almost nothing is understood for *Schistosoma japonicum* – the causative agent of schistosomiasis japonica. This relates mainly to a lack of high-quality genomic and transcriptomic resources for this species. As current draft genomes for *S. japonicum* are highly fragmented, we assembled here a chromosome-level reference genome (seven autosomes, the Z-chromosome and partial W-chromosome), achieving a substantially enhanced gene annotation. Utilising this genome, we discovered that the sex chromosomes of *S. japonicum* and its congener *S. mansoni* independently suppressed recombination during evolution, forming four and two ‘strata’, respectively. By exploring the W-chromosome and sex-specific transcriptomes, we identified 35 W-linked genes and 257 female-preferentially transcribed genes (FTGs) and identified a signature for sex determination and differentiation in *S. japonicum*. These FTGs cluster within autosomes or the Z-chromosome and exhibit a highly dynamic transcription profile during the pairing of female and male schistosomules (advanced juveniles), representing a critical phase for the maturation of the female worms, suggesting distinct layers of regulatory control of gene transcription at this stage of development. Collectively, these data provide a valuable resource for further functional genomic characterisation of *S. japonicum*, shed light on the evolution of sex chromosomes in this highly virulent human blood fluke and provide a pathway to identify novel targets for development of intervention tools against schistosomiasis.

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