Investigating a stem-linked sensory pathway controlling female maturation in *Schistosoma*

Abstract

Schistosomiasis is a neglected tropical disease affecting over 200 million people worldwide. Infection with the parasitic flatworm *Schistosoma* leads to chronic and often severe pathology, primarily caused by parasite eggs that become lodged in host tissues. In the absence of a vaccine and with only a single widely used drug available, advancing our understanding of parasite biology, development, and host interaction at the molecular level is essential for identifying new therapeutic targets. Single-cell RNA sequencing has enabled the characterization of cell types at several stages of schistosome development. Our study focuses on a distinct but uncharacterized “stem-like” cell population in juvenile schistosomes, sampled a day 17 and 21 during their intramammalian development. These cells are defined by the expression of some markers commonly associated with stem cell populations but lack many canonical stem markers, such as Ago-2. Analysis of the day 17/21 post-infection scRNA-seq atlas identified two cell-type-specific markers, a putative nuclear receptor and a transcription factor, whose expression patterns change dynamically throughout the parasite life cycle. Notably, both markers become female-specific upon reproductive maturation. During schistosomule development, the nuclear receptor is expressed in stem, muscle, and neural cell populations, suggesting involvement in a sensory regulatory pathway. Moreover, this specific nuclear receptor regulates sexual development in other metazoans. In preliminary experiments, we are investigating the function of these “stem-like” markers using RNA interference (RNAi) in schistosomule *in vitro* cultures. Knockdown of these genes resulted in developmental arrest and morphological abnormalities, indicating their functional importance during early parasite development. Together, these findings support our hypothesis and motivate further investigation into whether this “stem-like” cell population coordinates the development of a sensory pathway required for female sexual maturation in *Schistosoma*.