Title

A single-cell atlas of the free-living miracidium larva of *Schistosoma mansoni*

Authors

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Abstract

The neglected tropical disease schistosomiasis affects millions of people annually, and is caused by infection with *Schistosoma*, a genus of parasitic flatworms. More than 230 million people were estimated to need treatment in 2019, and over 700 million people live in areas where they are at risk of infection. There is one currently available treatment, praziquantel, which is both safe and relatively effective. However, it has varying efficacy against different life stages, does not provide protection against re-infection, and drug resistance is of particular concern given the paucity of other treatment options. Thus, other potential drug treatments, vaccine candidates, and non-pharmaceutical interventions are all areas of active research. A key strategy to advance these goals is to develop a deeper understanding of the causative agent: *Schistosoma.*

Schistosoma mansoni has a complex lifecycle involving multiple hosts, and goes through multiple developmental transitions before reaching maturity, where it is sexually dimorphic. *S. mansoni* eggs hatch in fresh water, where the free-living miracidia emerge. These miracidia seek out snail hosts, inside which they transform into mother sporocysts, before asexually producing large numbers of daughter sporocysts that generate human-infective cercariae to continue the life-cycle. In this project we seek to build a greater understanding of the cells present in miracidia, and their transcriptional activity, through single-cell sequencing and analysis. We've established that the miracidium is composed of just 365 cells and we have sequenced enough cells to achieve >10x theoretical cover of each cell. We have identified transcriptional profiles which indicate stem, muscle, protonephridia, neural, tegumental, and parenchymal tissues, and work is in progress validating these findings with *in-situ* hybridisations. Within these tissue types, we have detected subclusters of cells. These subclusters indicate functional heterogeneity, particularly within neural tissues, and we have identified miracidia-specific cell types such as the ciliary plates for swimming. Additionally, we have identified sex-specific transcriptional activity that is particularly striking in the stem cell populations of this sexually immature developmental stage. Our focus on single-cell detail in the miracidium provides the foundation for understanding the cell types and their transcriptomes that make up *Schistosoma mansoni.* Furthermore, identifying the cellular composition of this simple and short-lived larval stage will lead to a greater understanding of its infective behaviour that leads to the propagation of the life cycle.

Track

Gene Expression, Genetic Architecture

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