From whole worm to single cells: using transcriptomics to understand how a gastrointestinal nematode thrives in its host.

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Heligmosomoides bakeri, a parasitic nematode of mice, is closely related to economically important parasites of livestock and hookworm parasites of humans. As a murine parasite it is more amenable to being maintained and manipulated in a controlled laboratory environment than its relatives. The worm enters its host during its third larval stage and develops through another larval stage into adults that reside in the lumen of the small intestine to mate and lay eggs. Unravelling these processes and others critical to *H. bakeri* survival will not only reveal new targets for new drugs but also refine previous predictions of parasite immunomodulatory molecules, which have therapeutic potential in humans as anti-inflammatories. We set out to describe the gene expression of *H. bakeri* during the parasitic phase of its life cycle.

First, we investigated how the whole worm expression of genes varies across infection time-points. We found that up to 68% of genes were differentially regulated between male and female worms, including genes associated with modulating the host's immune response and potential anthelmintic targets. In comparing tissue-encysted larvae with lumen-dwelling adults, we found an increased importance for anaerobic respiration and hypothesise that aerobic conditions are important for the critical developmental processes of molting and cuticle synthesis.

To understand gene expression at a finer granularity, we generated single cell RNA-seq data from young adult male and female worms. We used cell type markers from *C. elegans* to putatively identify gamete, embryo, intestine, hypodermis, neuron, and muscle cells. Putative intestinal transcription profiles suggest compartmentalisation of function along the anterior-posterior axis of the worms, with an emphasis on protein synthesis in the anterior portion. Embryonic profiles are noticeably different from *C. elegans* embryogenesis, particularly with respect to paternal contributions to the early embryo.

Overall, these datasets extend our understanding of how *H. bakeri* survives in its host and provide a public resource for further investigation into host-parasite interactions and anthelmintic discovery. They also lay the groundwork for more comprehensive comparisons with other nematodes.