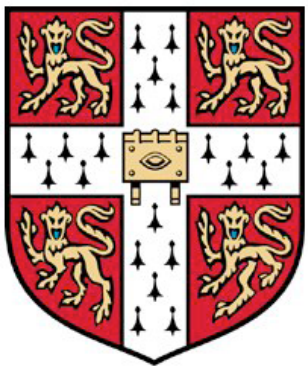
Transcriptome characterisation of the intra-mammalian stage of male and female *Schistosoma mansoni*



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Declaration

This dissertation is the result of my own work – all work done in collaboration being clearly references in the text. The work presented here was performed at the Wellcome Trust Sanger Institute (Hinxton). None of the work has been submitted, or, is being concurrently submitted for a degree or diploma or other qualification at the University of Cambridge or any other University. This thesis does not exceed the word limit established by the Biology Degree Committee.

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Summary

Schistosoma mansoni is a member of a genus of platyhelminths whose members cause the disease *schistosomiasis*. Particularly prevalent in sub-Saharan Africa, it is thought to be directly responsible for approximately 5500 deaths per year, as well as contributing significantly to morbidity, being responsible for 3.3 million lost disability-adjusted life years. Schistosomes are dioecious and male and female worms find one another and pair in the blood vessels of the host's liver. This sets in motion a unique feature of schistosome biology, the pairing-dependent sexual maturation of the female worms. Over the course of the next three weeks, the females fully develop their reproductive organs, especially ovaries and vitellarian tissue, to allow for the production of large quantities of eggs, which not only play a crucial role in the transmission of the parasites, but are also responsible for much of the pathology associated with schistosomiasis.

This thesis aims to explore the changes in gene expression which take place following pairing, and result in the sexual maturation of females. To do so, RNA-Seq data was produced from male and female worms from mixed sex as well as single sex infections at 18, 21, 28, 35, 38 and 49 days *post* infection and analysed to understand when and how gene expression changes in paired worms. Then gene expression was examined in worms that had been removed from their partner to examine the process of regression, where female worms lose much of their reproductive tissue. The last experiments describe examine gene expression in the testes and ovaries of schistosomes, to reveal differences between the gonads of worms from mixed and single sex infections and understand in more detail how these worms may regulate the growth of their reproductive organs, contributing to our knowledge of schistosome biology.

Abbreviations

BME	Basal Medium Eagle
bp	Base pairs
Cdc	Cell division cycle
CDK	Cyclin Dependant Kinase
CO_2	Carbon dioxide
d.p.i.	Days *post* infection
DEG	Differentially Expressed Gene
DMEM	Dulbecco's Modified Eagle's Medium
dsRNA	Double stranded RNA
ECM	Extracellular Matrix
EGF	Epidermal Growth Factor
FGF	Fibroblast Growth Factor
GAP	GTPase-Activating Protein
GO	Gene Ontology
kb	Kilo bases
MAP	Mitogen-Activated Protein
MAPK	Mitogen-Activated Protein Kinases
Mb	Mega bases
MS	Mixed Sex
NaCl	Sodium Chloride
PBS	Phosphate Buffered Saline
PCA	Principal Component Analysis
PCR	Polymerase Chain Reaction
qRT-PCR	quantitative Reverse Transcription-Polymerase Chain Reaction
RNA-Seq	RNA Sequencing
RNAi	RNA interference
RPM	Revolutions Per Minute
RT	Room Temperature
SMAD	(Portmanteau of SMA and MAD)
Src	Sarcoma
SS	Single Sex
TBE	Tris Borate EDTA
TGF-β	Transforming Growth Factor-β
WNT	(Portmanteau of int and Wg)

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