Transcriptomic studies on host-parasite interactions in *Schistosoma mansoni* intramammalian stages

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Pembroke College

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Arporn Wangwiwatsin

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Declaration

The work presented in this thesis was carried out at the Wellcome Trust Sanger Institute (Hinxton) between October 2012 and March 2017. This dissertation is the result of my own work – contributions from collaborations are clearly referenced. No part of this dissertation has been or is being submitted for any qualification in any other university. This thesis does not exceed the word limit established by the Biology Degree Committee.

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Summary

The life cycle of the parasitic flatworm *Schistosoma mansoni* is split between snail and human hosts. In humans, it lives in the bloodstream and can survive for over 10 years, during which time, interactions with the host are essential for its survival. Starting the infection, cercariae penetrate human skin and become schistosomules which enter blood vessels. The schistosomules follow blood circulation to the lung and the liver where they develop into adults which migrate to the mesenteric venules for egg-laying. The association with certain host tissues and egg-laying site may involve interactions and adaptations. Moreover, the parasite needs to evade or modulate host immune responses and to optimise its acquisition of host metabolites. Molecular mechanisms involved in these interactions are not completely understood.

To gain deeper understanding into the interactions of *S. mansoni* and its mammalian host, I sought to understand what biological processes are required for successful intramammalian infection; specifically, what guides the tissue tropism of the parasite and what roles do the host tissues play in the infection? In the first part, parasite transcriptomes were produced from *S. mansoni* obtained from experimentally infected mice. The dataset includes novel transcriptomic profile of the lung stage, and covers developmental and egg-laying stages. In the next two parts, co-culture experiments were set up using mechanically transformed schistosomules and cells derived from human tissues. Transcriptomic profiles of the co-cultured schistosomules were investigated in the second part of this thesis; and transcriptomic profiles of the co-cultured human cells were investigated in the final part. The outputs of this thesis provide new insights into the infection biology, provide a large data resource for the research communiy, and propose avenues for further investigation and characterisation of interaction mechanisms.

Abbreviations

BLAST	Basic Local Alignment Search Tool
C1	Complement component 1
CFH	Complement factor H
CFI	Complement factor I
DAF	Decay-accelerating factor
DMEM	Dulbecco's Modified Eagle's Medium
DMT	Divalent metal transporter
ES	Excretory/secretory products
ESTs	Express Sequence Tags
FPKM	Fragments Per Kilobase of transcript per Million mapped reads
GO	Gene Ontology
GPCR	G-protein coupled receptor
ICAM1	Intercellular adhesion molecule 1
IL-2	Interleukin-2
IPA	Ingenuity Pathways Analysis
KEGG	Kyoto Encyclopedia of Genes and Genomes
LDL	Low density lipoprotein
Log_2FC	Log_2 fold change
LPS	Lipopolysaccharide
MEG	Micro-exon gene
NPC2	Niemann Pick type C2 protein
PCA	Principal component analysis
PDB	Protein Data Bank
RNA-seq	RNA-sequencing
ROS	Reactive oxygen species
SELE	Selectin E
TAL	Tegumental-allergen-like
TGF-β	Transforming growth factor-beta
TNF-α	Tumour-necrosis factor-alpha
VCAM1	Vascular cell adhesion molecule
WTSI	Wellcome Trust Sanger Institute

Table of Contents

Chapter 5

Transcriptomes of cell lines exposed to schistosomules *in vitro* 155

Chapter 6

List of Figures

List of Tables

List of Appendices