Genomic insights into host and parasite interactions during intracellular infection by *Toxoplasma gondii*

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Introduction

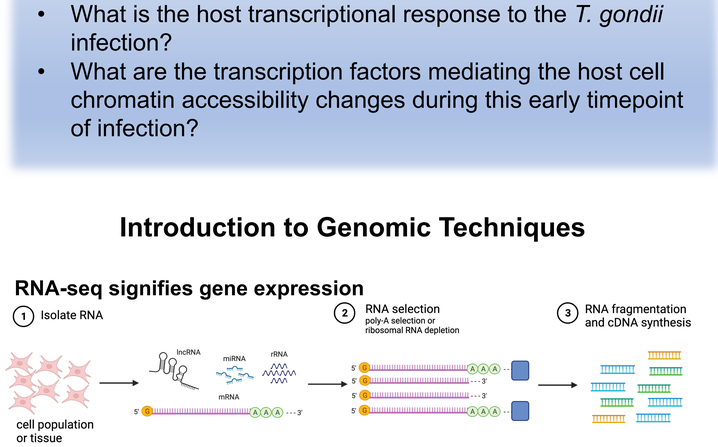
The parasite *Toxoplasma gondii* is extremely common, chronically infecting approximately one-quarter of the world's population, causing serious illness when it infects a developing fetus or someone with a compromised immune system. How this parasite manages to be so effective is not well understood. In this study, we perform transcriptional and chromatin profiling genome-wide in human fibroblasts prior to and after infection with *T. gondii.*

Questions

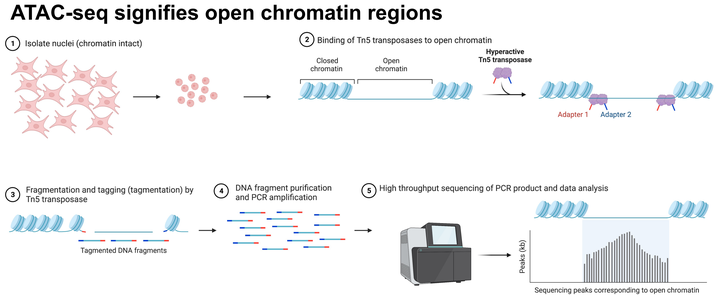
- Where are the regulatory loci in the *T. gondii* genome during an *in vitro* infection?
- What are the transcription factors of *T. gondii* orchestrating the successful infection of human cells?
- What is the host transcriptional response to the *T. gondii* infection?
- What are the transcription factors mediating the host cell chromatin accessibility changes during this early timepoint of infection?

Introduction to Genomic Techniques

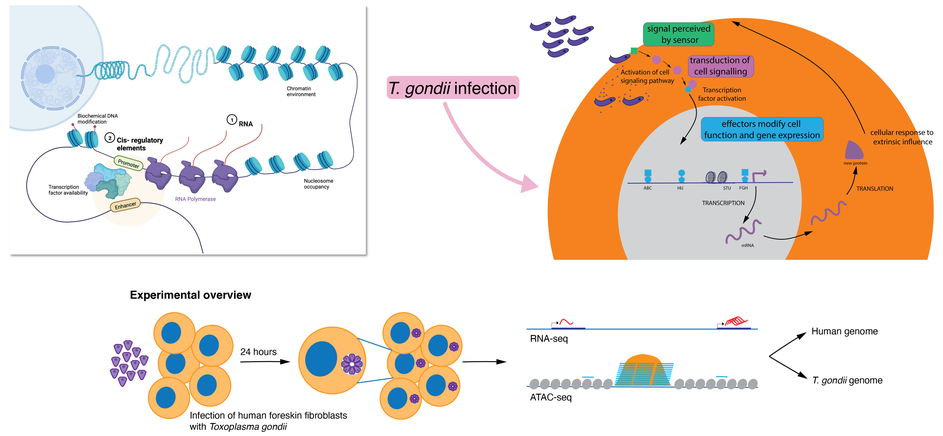
RNA-seq signifies gene expression



ATAC-seq signifies open chromatin regions

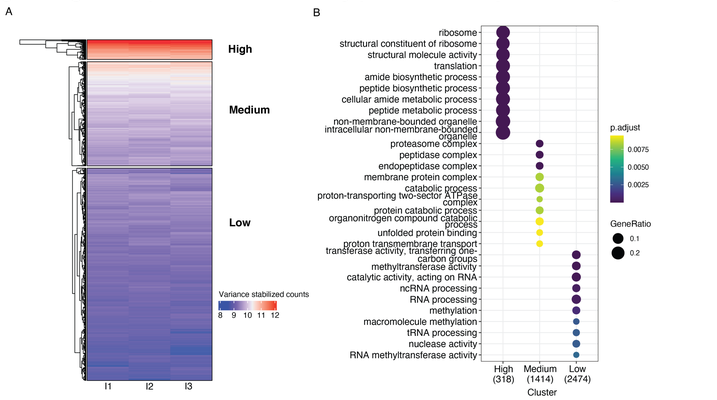


Experimental Design

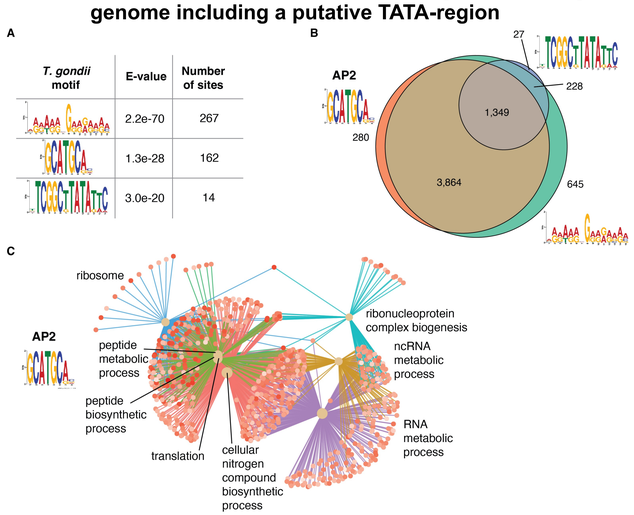


Toxoplasma gondii

T. gondii gene expression reveals key processes required during infection

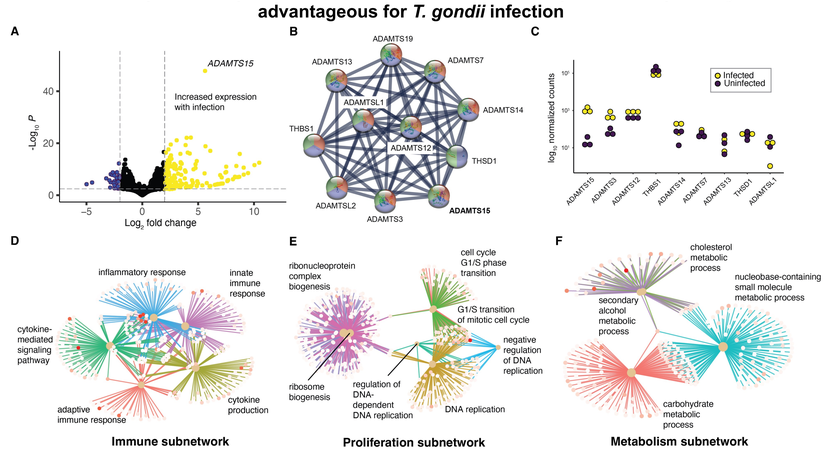


Inference of two novel transcription factor binding motifs in *T. gondii* genome including a putative TATA-region



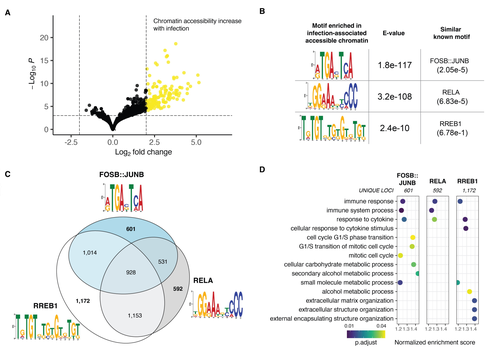
Host response to infection

Transcriptional response includes immune activation responses and pathways advantageous for *T. gondii* infection



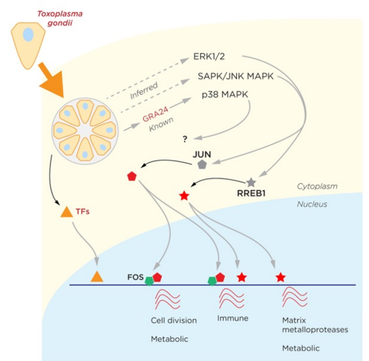
FOSB:JUNB, RELA, and RREB1 mediating host cell chromatin accessibility changes

De *novo* motif enrichment analysis revealed enrichment at loci opening chromatin during infection for the AP-1 (JUN-FOS), RELA (an NFκB family member) and RREB1 TFs. All three TF binding motifs were associated with genes mediating immune response while AP-1 (FOSB::JUNB) motifs were also enriched at genes involved with cell division and metabolic processes, and the motifs for RREB1, which mediates RAS-MAPK signaling, are associated with the genes mediating metabolic and extracellular matrix functions.



Conclusions

- Discovery of two potential transcription factors regulating the tachyzoite infectious process
- Host response during infection include immune activation and induction of metabolic reprogramming and mitotic gene responses
- NFκB response appeared to be predominantly involved in host cell immune responses
- JUN:FOS (AP-1) and RREB1 are likely to have additional properties of cell division, metabolic processes, and extracellular matrix gene regulation
- Cell signaling pathways influencing JUN and RREB1 TFs may be caused by exported *T. gondii* proteins so the host gene expression may be affected through conserved TF regulatory mechanisms



A model derived from genomic assay data for the host cellular response to *T. gondii* infection.

Acknowledgements

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