Establishing functional mitochondrial translation Readouts in *Toxoplasma gondii*

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Abstract

Toxoplasma gondii is the causative agent of toxoplasmosis, a globally prevalent infectious disease that poses significant health risks to immunocompromised individuals and pregnant women. The development of robust and reliable assays for evaluating potential drug candidates is essential for the identification of effective drug treatment.

The mitochondrion represents a promising multi-target organelle for antiparasitic drug development due to its central role in energy metabolism and other essential cellular processes. In particular, the mitochondrial ribosome (mitoribosome), which mediates mitochondrial translation, provides a functional readout of mitochondrial integrity. Impairment of mitochondrial translation can serve as a sensitive indicator of mitochondrial dysfunction and may reflect the efficacy of compounds that disrupt mitochondrial activity.

We are developing a mitochondrial translation assay based on two complementary approaches: (1) an incorporation of radiolabelled ^{35}S-methionine into newly synthesized mitochondrial proteins; and (2) an mRNA-based luciferase reporter system, to monitor translation efficiency. Crude mitochondrial fractions have been isolated from parasites and are being used to evaluate the performance and sensitivity of these assays.

In parallel, mutant parasite lines carrying deletions of specific amino acid residues within the mitoribosomal exit tunnel subunit have been generated to explore and characterize their function of differences from the mammalian exit tunnel which may serve as targets for inhibition.

This work should enable us to leverage mitochondrial translation as a novel therapeutic agent which forms an exciting new avenue to inform drug discovery.