

The *Toxoplasma gondii* mitoribosome reveals novel features of ribosome evolution and exciting differences from human mitoribosomes

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Mitochondrial ribosomes (mitoribosomes) are fundamental, and their function of synthesising mitochondrial proteins is universal, including in parasites. The apicomplexan mitochondrion is essential for parasite survival, virulence, and dissemination, and the same is thus expected for its mitoribosome. In agreement with this prediction, evidence of the essentiality of conserved mitoribosomal proteins in apicomplexan, accumulate, including from our own work. In addition to being essential, indirect observations further suggest that this mitoribosome is highly divergent from its human parallel. Divergence is expected from the prediction of rRNA fragmentation, based on different apicomplexan mitochondrial genome sequences, as well as on the sensitivity profile of some apicomplexan parasites to mitoribosome inhibitors.

Despite its essentiality and divergence, the biology of the apicomplexan mitoribosome is poorly studied. Here, using *Toxoplasma gondii* as a model organism, we employed a combination of complementary approaches to expand our understanding of the apicomplexan mitoribosome function and assembly. We discovered an rRNA fragmentation that is much more extensive than predicted according to the parasite mitochondrial genome, and revealed several novel features that enable this highly divergent ribosome to still perform its critical function.

One examples of an apicomplexan, and likely myzozoan, mitoribosome signature feature we discovered is the repurposing of several transcription factors as new mitoribosomal proteins, which we believe compensate for rRNA remodelling and we postulate that they effectively replace conserved and critical ribosomal domains.

On top of addressing the fundamental question of how divergent ribosomes function, our work has further potential to inform apicomplexan drug discovery, which we demonstrate by revisiting a previously proposed resistance mechanism of apicomplexan to a known mitoribosome inhibitor.