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"Temperature-dependent regulation of cytochrome c oxidase subunit expression in Leishmania"

Leishmaniasis is a chronic, persistent, often fatal intracellular protozoal infection, with visceral, mucocutaneous or cutaneous manifestations, associated with different *Leishmania* species. Leishmaniasis is transmitted by phlebotomine sandflies and at least 12 million people, residing primarily in tropical and sub-tropical regions, are infected. Current treatments against leishmaniasis are inadequate due to their toxic side effects. Further, the incidence of drug-resistant *Leishmania* strains is on the rise. Therefore, there is, an urgent need to discover new, low-toxicity drugs against *Leishmania*. A better understanding of essential gene-regulatory mechanisms employed by *Leishmania* will guide these drug-discovery efforts. During their infectious life cycle, *Leishmania* parasites must undergo metabolic adaptations to survive drastic changes in the temperature, nutrient availability, and pH that occur upon entering the mammalian host. Our previous studies have identified LmCOX4, a subunit of cytochrome *c* oxidase, required for mitochondrial ATP production, as a protein that is transiently down-regulated in response to mammalian host temperature. Discovering this novel LmCOX4 expression pattern has important implications for understanding how parasite mitochondrial function and viability is maintained throughout the infectious *Leishmania* life cycle. Importantly, our findings also suggest that LmCOX4 regulation may represent a viable drug target. The long-term goals of this project are: first, to assess the effect of temporary LmCOX4 loss upon mitochondrial function and second, to examine the impact of mitochondrial functional status on LmCOX4 expression. Current experiments are underway to examine the effect of pharmacologic disruption of mitochondrial function upon parasite viability and LmCOX4 expression.