

Old Dogmas, New Tricks: Rethinking Mitochondrial Biology in the Age of Multi-Omics, Artificial Intelligence, and De-extinction

Abstract: For much of the twentieth century, mitochondria were portrayed as cellular powerhouses with small, highly conserved genomes, limited coding capacity, and relatively simple regulation. Advances in genomics, multi-omics, and artificial intelligence are challenging this model, revealing mitochondria as dynamic systems involved in metabolism, signaling, adaptation, and mitonuclear communication. Drawing from our work on organisms ranging from the newly described cavefish genus *Demogorgonichthys* to imperiled fishes, I will highlight molecular and computational approaches that are changing how we study mitochondrial genomes. Our research investigates mitochondrial-derived peptides (MDPs) encoded by previously overlooked open reading frames and 6mA DNA methylation as a potential component of mitochondrial epigenetic regulation. I will also introduce NeoEdit, an open-source platform designed to visualize and investigate canonical mitochondrial genes alongside noncanonical ORFs translated under alternative genetic codes, as well as long-range PCR approaches for recovering complete mitogenomes. Finally, I will discuss MitoBank, a mitochondrial biobank designed to preserve mitochondrial genetic diversity for conservation research. Together, these approaches are moving mitochondrial biology beyond its traditional roles in bioenergetics and phylogenetics toward a richer understanding of mitochondrial coding, regulation, evolution, and function.