## **ASHBi SEMINAR**

Unraveling mitochondrial influence on mammalian11pluripotency via enforced mitophagy

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## Abstract

Mitochondrial abundance and genomic sequence are crucial for cellular function, with disruptions often associated with disease. However, methods to modulate these parameters remain limited. In this study, we used enforced mitophagy to eliminate mitochondria from pluripotent stem cells (PSCs). Remarkably, PSCs survived for several days in culture without mitochondria. We then leveraged enforced mitophagy to generate interspecies PSC fusions (composite PSCs) that harbored either human or non-human hominid (NHH) mitochondrial DNA (mtDNA). Comparative analyses indicate that human and NHH mtDNA are largely interchangeable in supporting pluripotency in composite PSCs. However, they induce subtle, species-specific transcriptional and metabolic variations. Additionally, we developed a transgenic enforced mitophagy approach to study how mitochondrial abundance influences mammalian development. We found that reducing mitochondria led to delayed development in pre-implantation mouse embryos. Our study opens new avenues for investigating mitochondrial roles in development, disease, and interspecies biology.

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