Title: Wild animal derived cells as a tool to study inter-species compatibility and adaptations

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Abstract

The research community relies on a small number of model organisms to study large themes in evolution and medicine. However, incorporating non-traditional models offers new inspirations for scientific breakthroughs. The aim of my doctoral work is to demonstrate the utility of wild animal derived cell lines for ecophysiological and biomedical studies.

Using skin fibroblasts harvested from mountain hares and brown hares, we applied various methods, including transcriptomics, metabolomics, imaging and respirometry, to uncover species-specific physiological features. Furthermore, we generated hybrid cell lines (cybrids) to study mito-nuclear compatibility that may reinforce species separation and cause mitochondrial associated disorders.

The results show that brown hare fibroblasts are faster in wound closure and proliferation, while mountain hare cells exhibit increased glycerol 3-phosphate (G3P) shuttle activity, consisting of cytosolic (GPD1) mitochondrial (GPD2) enzymes. Alterations in G3P shuttle is implicated in multiple human diseases including cancer. GPD2 knockdown led to increase of proliferation and migration in mountain hare' cells, while caused no such changes in brown hare. Additionally, we uncovered that mitochondria of cold-adapted mountain hare potentially function at lower temperatures than in temperate-adapted brown hare, for the first time demonstrating differences in basal mitochondrial temperature between species. This could impact, for instance, mtDNA replication activity. Cybrid model revealed that mito-nuclear incompatibilities emerge under specific genetic backgrounds, and cybrid approach could be adopted for screening human mitochondrial donors.

In conclusion, this work demonstrates that cells retain species-specific molecular features, allowing to draw parallels between cells and whole animal physiology and so reducing the need for animal experimentation.