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Effects of heat perturbation to rhinoceros' cellular metabolism

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Abstract

Climate change is associated with increasing global mean temperatures and extreme heat events. These drastic changes in temperature can have significant deleterious physiological effects, particularly on large strict homeothermic mammals such as the threatened Southern White Rhino (SWR - *Ceratotherium simum simum*). Developing alternative strategies to understand how climatic events impact species that are logistically challenging to study are crucial. Dermal fibroblasts have proven to be effective in vitro models for studying species resilience to climate since they can reflect an organism's thermosensitivity. These cells can provide an integrative and mechanistic explanation on how cellular function can inform organismal responses to environmental changes. We investigated the effects of heat on mitochondrial function and cellular biology by exposing SWR primary dermal fibroblasts (n = 10 biological replicates) to 24 hours of heat (41°C) or 37°C as a control in culture. Then, we evaluated mitochondrial function using mitochondrial stress test, glycolytic rate test and immunofluorescence (IF) to track nucleus size and mitochondrial distribution in the cytoplasm. Metabolic function was assessed using Agilent Seahorse analyzer and IF images were analyzed on CellProfiler™ software. Our results indicate that compared to the control (37°C), heat exposure decreases mitochondrial respiration (basal: $t = 3.7$, $df = 9$, $p < 0.01$; maximum: $t = 3.0$, $df = 9$, $p < 0.02$), ATP production ($t = 5.8$, $df = 9$, $p < 0.001$), and coupling effciency ($t = 7.6$, $df = 9$, $p < 0.001$). No changes were observed in spare respiratory capacity ($t = 0.7$, $df = 9$, $p = 0.5$), proton leak ($t = 0.7$, $df = 9$, $p = 0.5$) and glycolysis (basal: $t = 0.3$, $df = 4$, $p = 0.4$; compensatory: $t = 0.6$, $df = 4$, $p = 0.6$). Furthermore, heat exposure increases nucleus size and mitochondrial distribution area (Nucleus area: $t = 6.8$, d.f. $= 9$, $P < 0.001$, Mitochondrial coverage area: $t = 5.3$, d.f. $= 9$, $p < 0.001$) and decreases fluorescence intensity of the mitochondrial dye and solidity area covered by mitochondria (Fluorescence: $t = 2.3$, d.f. $= 9$, $p = 0.04$, Mitochondrial area solidity: $t = 5.6$, d.f. $= 9$, $p < 0.001$). These findings show that acute heatwaves trigger a series of complex and interconnected responses in SWR fibroblasts resulting in mitochondrial disfunction, possibly mitophagy and/or mitochondria disintegration, and larger dispersion through the cytoplasm. The thermosensitive phenotype exhibited by SWR fibroblasts provides insights into the likely consequences of global warming on the performance of this species, as cellular and mitochondrial functioning plays a fundamental role in an organism's ability to adjust and thrive under environmental change.

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