



# Exercise Biochemistry Review

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Proceedings of IBEC 2018, Beijing, China, October 23-25

OR-026

## Exercise induces HIF-1 $\alpha$ redistribution in the small intestine

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**Objective** Intestinal epithelial cells are positioned between an anaerobic lumen and a highly metabolic lamina propria, affected by reduced blood flow and tissue hypoxia. Exercise induces blood flow redistribution, leading to hypoperfusion and gastrointestinal (GI) compromise. The hypoxia-inducible factor (HIF) 1 $\alpha$  is pivotal in the transcriptional response to oxygen flux. In this study, we hypothesized that exercise induces GI system hypoxia and accumulates HIF-1 $\alpha$ .

**Methods** (1) ROSA26 ODD-Luc/+ mouse model (ODD-Luc) was used to detect HIF-1 $\alpha$  expression in the intestine (female, 8-week, n=6/group). ODD-Luc mice were randomized into 4 groups: stayed in 21% O<sub>2</sub> as the normoxic control (C), exercise (E), injected HIF-1 $\alpha$  inhibitor PX-478 before swimming (PS), placed in the chamber containing 9% O<sub>2</sub> for 4 hours as the positive control (PC). (2) Exercise models were conducted by volume: Moderate Exercise (ME): mice voluntarily swam for 30 min; Heavy-intensity Exercise (HE): mice swam for 1.5 hours with 5% body weight loads attached to their tails; Long-time Exercise (LE): mice voluntarily swam for 3 hours or till fatigue.

**Results** (1) Exercise increased HIF-1 $\alpha$  in the abdominal area. The luciferase activities boosted after exercise, compared to the controls (ME v.s. C,  $P < 0.05$ ; HE v.s. C,  $P < 0.05$ ; LE v.s. C,  $P < 0.05$ ) but no differences among three exercise groups (ME v.s. HE,  $P > 0.99$ ; ME v.s. LE,  $P > 0.99$ ; HE v.s. LE,  $P > 0.99$ ); (2) Exercise altered HIF-1 $\alpha$  distribution in the small intestine in a time-dependent manner. The expression of HIF-1 $\alpha$  was significantly increased after exercise and gradually reduced to the rest level. The photons increased at the 0<sup>th</sup> hour after exercise compared to that of the normoxic control ( $P < 0.01$ ). The level of photons then reduced over time, while the 2<sup>nd</sup>, 4<sup>th</sup> and 6<sup>th</sup> hour post-exercise were still greater than that of the normoxic control (2<sup>nd</sup> hour v.s. C,  $P < 0.01$ ; 4<sup>th</sup> hour v.s. C,  $P < 0.01$ ; 6<sup>th</sup> hour v.s. C,  $P < 0.05$ ), and returned to normal after 24 hours (24<sup>th</sup> hour v.s. C,  $P > 0.99$ ).

**Conclusions** Exercise induced the distribution of HIF-1 $\alpha$  in the small intestine. The expression of HIF-1 $\alpha$  is shown in a time-dependent manner after exercise.