A genetic disease in humans demonstrates the importance of hypoxia-inducible factor in skeletal muscle metabolism

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Abstract

The transcription factor, hypoxia-inducible factor (HIF) regulates the expression of a number of metabolic genes. In the recessive condition of Chuvash Polycythemia (CP), the normal degradation of HIF in euoxia is slowed by functional mutation within the von Hippel-Lindau (VHL) gene. Thus the disease of CP provides an opportunity to understand the role of the HIF-VHL pathway in metabolic regulation at a systemic level. We recruited 5 CP patients and 5 controls, matched for gender, and similar for age, height and weight (CP vs control: 28±8 vs 32±12 yrs; 1.67±0.1 vs 1.74±0.1 m; 61±6 vs 72±6 kg; mean±s.d.). We measured work rate and lactate during an exercise capacity test on a cycle ergometer, and skeletal muscle magnetic resonance spectroscopy at rest and during light exercise (3, 4 & 5 Watt). Compared with controls, CP patients showed a limited exercise capacity (CP vs control: 2.4±0.9 vs 3.4±0.8 W/kg; $p <$ 0.05), early lactate accumulation, greater phosphocreatine (PCr) depletion (Fig.1) and a greater fall in pH during exercise. We conclude that the VHL-HIF pathway significantly affects metabolic regulation at a systemic level.

Figure 1

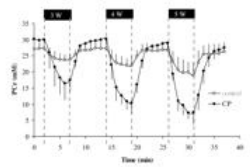

Figure 1

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