Comparative study on the metabolic regulation patterns of skeletal muscles in rodents at different altitudes under hypoxic conditions

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Skeletal muscle, a pivotal regulator of metabolic equilibrium, facilitates body movement through the contraction and relaxation of muscle fibers and is highly dependent on mitochondrial substrate oxidation for energy production. Hypoxic environment will lead to the reduction of oxidative capacity in muscle cells and insufficient energy supply, which will affect the physiological function and survival of mammals. However, the skeletal muscle of mammals living in hypoxia environment for a long time has formed obvious evolutionary characteristics of hypoxia adaptation in terms of morphology, structure and physiological function. Here, we carried out transcriptomics and quasi-targeted metabolomics analysis on skeletal muscle tissue of Qinghai vole (*Neodon fuscus*), Brandt's vole (*Lasiopodomys brandtii*) and Kunming mice (*Mus musculus*) after hypoxia (10% O_2, 48 h) and normoxia treatment, thereby revealing the underlying molecular mechanisms. *N. fuscus*, native to high-altitude environments, tended to sustain energy supplies through enhanced fatty acid oxidation under low-oxygen conditions. Conversely, *L. brandtii* and *M. musculus*, acclimatized to middle- and low-altitude habitats, relied on aerobic oxidation and anaerobic glycolysis of glucose, respectively, for energy maintenance under hypoxic conditions. In addition to their differential metabolic preferences under hypoxic conditions, these three rodent species showed species-specific responses related to oxygen utilization, antioxidant defence mechanisms, and anti-inflammatory processes. This study provides insights into the metabolic response patterns of mammalian skeletal muscle under hypoxic conditions, thereby establishing a basis for future investigations on transcriptional–metabolic associations.