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Male-preferred glycolysis and female-preferred fatty acid utilization for ATP production in skeletal muscles bestowed by Pfkfb3 and Pdk4

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論 文 名　：Male-preferred glycolysis and female-preferred fatty acid utilization for ATP production in skeletal muscles bestowed by *Pfkfb3* and *Pdk4*
（*Pfkfb3*と *Pdk4*遺伝子による骨格筋の ATP 産生におけるオスが好む解糖系とメスが好む脂肪酸の利用）

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論 文 内 容 の 要 旨

Skeletal muscles are comprised of several types of fibers characterized in part by their preferential energy production. Skeletal muscles exhibit sexually dimorphic features. As for the biochemical features, glycolysis and fatty acid β-oxidation are predominately active in the muscles of males and females, respectively. However, the mechanisms underlying of the preferential utilization of these fuels remains elusive. The aim of this study is to investigate the possible mechanism causing the sexual dimorphism in the energy metabolism of muscle fiber type IIB.

Mice were gonadectomized and thereafter treated with sex steroids. Type IIB fibers of quadriceps muscles were used for transcriptome analysis. Eventually, I obtained transcriptomes from the fibers of untreated, gonadectomized, and sex steroid-treated mice of both sexes. 68 and 60 genes were obtained as male-enriched and female-enriched genes, respectively. Gene ontology analyses revealed that the male-enriched genes are related to broad range of metabolic processes, while the female-enriched genes are related to extracellular matrix.

Furthermore, analyses of the transcriptomes resulted in finding of two genes, *Pfkfb3* (*phosphofructokinase-2*) and *Pdk4* (*pyruvate dehydrogenase kinase 4*), that may function as switches between the sexually dimorphic metabolic pathways, male-preferred glycolysis and female-preferred fatty acid β-oxidation. Interestingly, *Pfkfb3* and *Pdk4* exhibit male-enriched and estradiol-enhanced expression, respectively. Additionally, the contribution of these genes to sexually dimorphic metabolism is demonstrated by knockdown studies with cultured type IIB muscle fibers. Taking into consideration that skeletal muscles as a whole are the largest energy-consuming organs, our results provide insights into energy metabolism in the two sexes, during the estrus cycle in women/female, and under pathological conditions involving skeletal muscles.