

# 論文の欧文要旨

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## (Title)

The effect of aldehyde dehydrogenase 2 deficiency on the adaptation of skeletal muscle

## (Abstract)

Since skeletal muscle is highly plastic, it is important to understand muscle metabolism in different circumstances. Aldehyde dehydrogenase 2 (ALDH2) catabolizes toxic aldehydes to acetic acid. It has been recently reported that ALDH2 deficiency affects negatively skeletal muscle by increasing reactive oxygen species in skeletal muscle cells and damaging mitochondrial networking. However, it has been never researched whether ALDH2 deficiency negatively affects muscle metabolism during muscle atrophy. Thus, the purpose of the study is to investigate the effect of ALDH2 deficiency on the adaptation of skeletal muscle in muscle atrophy and hypertrophy. Firstly, the gene and protein expression of ALDH2 during denervation (DEN) and synergist ablation (SA) have been analyzed. DEN increased the *Aldh2* gene and ALDH2 protein levels. Furthermore, the gene expression of *Aldh2* was decreased after SA, but not ALDH2 protein levels. After that, it has been examined whether ALDH2 deficiency changes muscle mass and mitochondrial function during DEN using ALDH2 Knockout (KO) mice. ALDH2 deficiency exacerbated DEN-induced muscle atrophy in plantaris muscle. The KO mice had smaller muscle sizes of gastrocnemius and plantaris with and without DEN. Moreover, ALDH2 deficiency showed a decreased tendency of mitochondrial respiration after DEN and increased ROS production. Then, I investigated whether ALDH2 deficiency affects muscle hypertrophy and muscle protein synthesis after SA using KO mice. As a result, ALDH2 deficiency increased p-p70S6K and puromycin but did not change muscle mass. In summary, ALDH2 deficiency enhanced denervation-induced muscle atrophy and decreased mitochondrial function. During muscle hypertrophy,

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ALDH2 deficiency increased muscle protein synthesis, but its effect was insufficient to change muscle structures. In conclusion, ALDH2 deficiency affects muscle metabolism mostly in muscle atrophy than muscle hypertrophy. I suggest that ALDH2 deficiency adversely affects muscle health during muscle atrophy.