METABOLISM

The lipid-droplet-coating protein perilipin-5 in fast-twitch muscle fibres confers metabolic protection

Perilipin-5 might mediate systemic responses to exercise and fasting, via upregulation of expression of the myokine fibroblast growth factor 21 (FGF21), according to new research published in *Diabetes*.

Previous work demonstrated that expression of perilipin-5 is induced during fasting and is expressed in tissues that use fatty acid oxidation to generate cellular energy, as well as contributing to an increase in triglyceride storage. The team of researchers sought to investigate the role of perilipin-5 *in vivo* by overexpressing the protein in muscle fibres of mice. “As fast muscle is a large metabolically active compartment, we hypothesized that overexpression could perturb systemic metabolism,” explains Nathan Wolins, senior investigator of the study.

Indeed, transgenic mice with muscle-specific overexpression of *Plin5* (MCK-*Plin5* mice) gained less weight than their nontransgenic counterparts when fed a

high-fat diet. In addition, MCK-*Plin5* mice showed signs of browning in white adipose tissue and reduced inflammation of the liver, both of which are effects associated with FGF21 signalling.

Expression of *Fgf21* mRNA was increased an astonishing 80-fold in the gastrocnemius muscle (which has a high proportion of fast-twitch muscle fibres) of fasting chow-fed MCK-*Plin5* mice compared with control animals, but no significant differences in expression were observed in the heart, soleus and diaphragm muscles, which are predominantly comprised of slow-twitch muscle fibres. Moreover, the MCK-*Plin5* mice also showed chronic increased circulating levels of FGF21, regardless of diet. Together with the observation that *Fgf21* expression in the livers of the transgenic mice was unchanged, these findings suggest that fast-twitch muscle fibres are the primary source of FGF21 in these animals.

The researchers plan to continue their studies by investigating the mechanisms by which perilipin-5 induces FGF21 expression and regulates muscle lipid metabolism. “Understanding the metabolic responses to exercise might help design better interventions in those who are unable or unwilling to exercise,” concludes Wolins.

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Original article Harris, L.-A. S. *et al.* Perilipin 5-driven lipid droplet accumulation in skeletal muscle stimulates the expression of fibroblast growth factor 21. *Diabetes* doi:10.2337/db14-1035