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Hormone-sensitive lipase: New roles for an old enzyme

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AB

Hormone-sensitive lipase (HSL) has a unique ability to hydrolyze a large panel of substrates including acylglycerols, cholesteryl esters and retinyl esters. HSL is potentially a new drug target for the treatment of obesity and type II diabetes. However, as HSL is not only expressed in white adipose tissue (WAT), but also plays significant roles in other tissues, it is of importance to better understand the different functions of this enzyme in the body.

In this thesis the aim has been to study the consequences of a targeted disruption of the HSL gene in the mouse with focus on the effects in skeletal muscle and WAT.

Expressional and functional analyses of soleus muscle of HSL null mice suggests an important role of HSL in skeletal muscle metabolism as the absence of HSL leads to increased glycogen utilization and an increased amount of lipid droplets, which presumably reflects a metabolic switch from lipid to carbohydrate metabolism.

A fibre type transformation from slow twitch oxidative fibres to an enrichment of fast twitch glycolytic fibres in soleus muscle is also suggested.

Using a proteomic approach a local inflammatory response in WAT is demonstrated in the non-obese HSL null mouse model. New methodological aspects of analysing data generated by two-dimensional polyacrylamide gel electrophoresis are also presented. Increased energy expenditure and perturbation of adipogenesis are suggested reasons behind the observed protection against diet-induced obesity in HSL null mice. Results presented in this thesis suggest an important role of HSL in lipid signalling and adipogenesis through its action as a retinyl ester hydrolyze in WAT.

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