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Regulation of hepatic fatty acid synthase properties by O-GlcNAcylation *in vivo* and *ex vivo*

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During meal intake, two metabolic pathways are activated in the liver, the glycolysis and the lipogenesis to drive the production of fatty acids. The Hexosamine Biosynthesis Pathway (HBP), the end product is UDP-GlcNAc the substrate of OGT (O-GlcNAc Transferase) to O-GlcNAcylate proteins is also activated. O-GlcNAcylation is a dynamic post translational modification (PTM) that controlled a plethora of protein properties. Disturbance in the O-GlcNAcylation dynamism is implicated in several pathologies. Numerous studies link metabolic disorders emergence to O-GlcNAcylation mechanisms deregulation. Knowing that there is a close relationship between glucose, O-GlcNAcylation levels and activation of the glucido-lipid metabolism, a link between the activation of the glycolytic and the lipogenic enzymes and O-GlcNAcylation should exist. More precisely we focused on Fatty Acid Synthase (FAS) which produces fatty acids. In this study, O-GlcNAcylation levels and FAS expression were analyzed in liver of C57BL6 mice fed a Chow Diet (CD) or High Carbohydrate Diet (HCD) in liver of mice harboring an inhibition of OGA and in primary hepatocytes of mice cultured in different O-GlcNAcylation levels. Co-immunoprecipitation experiments showed that OGT and FAS interacted physically but this interaction did not lead to FAS O-GlcNAcylation. However, a correlation between FAS expression and O-GlcNAcylation level was shown and an increase of O-GlcNAcylation levels paralleled the protection of FAS against this degradation. Moreover FAS activity was increased in fasted HCD mice compared to fasted CD mice. Taken together, our results suggest that O-GlcNAcylation may represent indirectly a new regulation of FAS protein content and activity in liver under both physiological and physiopathological conditions.

Biography

Steffi Baldini is PhD student in the field of Biology and Biotechnologies since September 2013 at the Lille 1 University (France). During her PhD, she develops a project around the regulation of hepatic Fatty Acid Synthase expression by O-GlcNAcylation.

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