Thursday April 10, 2014
10.30am

**Pooja JHA**

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“Role of adipose tissue lipolysis and adipose triglyceride lipase (ATGL) in non-alcoholic fatty liver disease (NAFLD) progression”

Hosts: Kristina Schoonjans and Johan Auwerx

Conference Room: **Al 1153 (*)**
EPFL - Lausanne

**Abstract**

Mechanisms underlying the pathogenesis of NAFLD and its progression to steatohepatitis (NASH) are poorly understood. Increased fatty acid (FA) flux from adipose tissue to the liver and impaired FA signaling in liver may be involved. Since ATGL is a key intracellular lipase involved in hydrolysis of stored fat and lipid partitioning, we aimed to explore the role of ATGL in mouse models of NAFLD and NASH. Using methionine-choline-deficient (MCD) diet to induce NASH in ob/ob mice we showed that (i) increased ATGL and hormone-sensitive lipase (HSL) activity in adipose tissue and (ii) decreased ATGL activity in liver mediate loss of adipose tissue followed by hepatic steatosis and inflammation. We next used mice deficient in ATGL and HSL to induce steatohepatitis and endotoxemia. In both these models, we showed that ATGL plays an antiinflammatory role in liver via activation of PPARα. We found that ATGL also plays an important role in circadian regulation of hepatic lipid metabolism, in particular at zeitgeber time (ZT)12 when PPARα expression is at its peak in liver. In support of this hypothesis, we found that FA profile of PPARα ligands were attenuated in ATGL-KO mice at this time point. Our findings fuel optimism that ATGL could represent an exciting therapeutic target for metabolic and inflammatory liver diseases.

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(*) IMPORTANT NOTICE : All external participants have to pass through SV Reception/Welcome Desk to be able to access to Al 1153. Contact person to call at arrival at SV Reception Desk: Johan Auwerx 30951 / Administrative Assistant: 39522.