

Guest lecture

"Regulation of metabolism by PPARs and Angiopoietin like proteins"

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11.30 AM in D:IAS conference room Ø18-509-1



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Abstract: In recent years, insights into the mechanisms underlying the biological effects of fatty acids have improved considerably and have provided the foundation for the emerging concept of fatty acid sensing. Fatty acid sensing can be interpreted as the property of fatty acids to influence biological processes by serving as signalling molecules. An important mechanism of fatty acid sensing is via stimulation of DNA transcription via activation of peroxisome proliferators-activated receptors. One of the genes that is consistently and very significantly upregulated by fatty acids via PPARs in numerous organs encodes Angiopoietin like protein 4 (ANGPTL4). ANGPTL4 is a potent inhibitor of lipoprotein lipase, thereby

blocking plasma clearance of triglycerides and raising plasma triglycerides. Studies over the past couple of years have shown that ANGPTL4 regulates LPL activity during a variety of physiological conditions, including fasting, cold, and exercise. For example, increased expression of ANGPTL4 (originally called fasting-induced adipose factor) leads to a rapid reduction in adipose tissue LPL activity during fasting. The collective data point to a scenario where ANGPTL4 is the central component of a feedback mechanism that regulates plasma triglyceride hydrolysis and subsequent tissue fatty acid uptake in response to changes in lipid availability and cellular fuel demand. Based on our most recent data, it appears that ANGPTL4 mainly has a local role, at least in adipocytes, by stimulating LPL degradation after LPL processing in the ER. Overall, these data demonstrate the crucial role of ANGPTL4 in the transcriptional and metabolic response to fatty acids and the regulation of fat uptake into cells. The importance of ANGPTL4 in regulation of plasma triglycerides in humans is supported by extensive human genetic studies.

Host: Professor Susanne Mandrup, Department of Biochemistry and Molecular Biology, SDU.