Podocyte metabolic adaptation to lipid overload

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Objective:
Chronic kidney disease (CKD) is a serious public health burden with an estimated global prevalence of 8-16 % worldwide. Obesity-related CKD results from complex interactions between metabolic, hemodynamic factors and thickness as well as changes in the perirenal adipose tissue (PRAT). The disease is characterized by functional, histological and structural changes. One of the major features that appear in obesity related CDK is the alteration of the glomerulus causing obesity related glomerulopathy (ORG). In this pathology, podocytes (highly differentiated epithelial cells) are the major target. Podocyte injuries lead to their foot process effacement, death and/or detachment from the glomerular basement membrane, leading to proteinuria and, subsequently, to progressive loss of kidney function. Lipid overload that promotes intracellular lipid droplet (LD) accumulation and lipid metabolism impairment is now recognized as pathogenic factors in the development and the progression of obesity-induced kidney disease. Therefore, in a context of obesity, abnormal lipid accumulation might challenge podocyte homeostasis through modulation of its bioenergetics. In that context, our laboratories are studying the mitochondria adaptation and the LD dynamics during different types of lipid overload in podocyte. Indeed, the excess of free fatty acids (FFA), especially saturated FA such as palmitate (PA) leads to local oxidative stress, chronic inflammation, and insulin resistance, and eventually podocyte apoptosis.

Methods:
We developed a model of podocyte lipid overload by exposing human podocytes cells (LY cell line from Bristol University) to concentrations ranging between 50 and 700 µM of PA or oleate (OA).

Results:
We show that PA induces a 30 and 40 % decrease in podocyte metabolic activity in cells incubated for 24 h with 150 and 300 µM respectively. However, OA, an unsaturated fatty acid, does not induce any modification in metabolic activity. Interestingly, the analysis of lipid droplet formation indicated that PA is not stored in lipid droplets, in contrast to OA.

Conclusion:
The partitioning of FA in podocyte seems to differ according to the type of FA exposed and might be different than the partitioning observed for other cell types such as PTEC (proximal tubular epithelial cells). Future work will be performed to identify PA-induced podocyte modifications and analyse the crosstalk between mitochondria and lipid droplets in cells exposed to various FA.