Distinct metabolic responses of podocytes to palmitate and oleate exposure

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A key feature of obesity-related chronic kidney disease (CKD) is the alteration of the glomerulus, known as obesity-related glomerulopathy (ORG). In this condition, podocytes, highly specialized glomerular epithelial cells, are primary targets. Podocyte injury results in foot process effacement, detachment, and death, causing proteinuria and progressive kidney function loss. Lipid overload, with intracellular lipid droplet (LD) accumulation and impaired lipid metabolism, is now recognized as a driver of obesity-induced kidney disease. In obesity, abnormal lipid buildup disrupts podocyte homeostasis by altering its bioenergetics. Our groups study mitochondrial adaptation and LD dynamics under various lipid overloads in podocytes. Notably, excess saturated free fatty acids like palmitate (PA) induce oxidative stress, chronic inflammation, insulin resistance, and podocyte apoptosis.

Here, we developed a model of lipid exposure by treating human podocytes cells (LY cell line from Bristol University) with 150 or 300µM of PA, oleate (OA), or albumin as a control for 24H. First, PA-treated cells showed altered metabolic activity, whereas OA, an unsaturated fatty acid, had no effect. Interestingly, lipid droplet analysis indicated that PA is not stored in lipid droplets, in contrast to OA. Fatty acid partitioning in podocytes seems to vary depending on the type of FA and may differ compared to other cell types such as PTEC (proximal tubular epithelial cells). Preliminary data regarding lipidomic analysis reveal an accumulation of triglycerides (TG) and diacylglycerols (DG) under OA treatment, with no significant increase in total TG or DG observed in the other conditions, and further analyses are ongoing.