DISTINCT METABOLIC RESPONSES OF PODOCYTES TO PALMITATE OR OLEATE EXPOSURE

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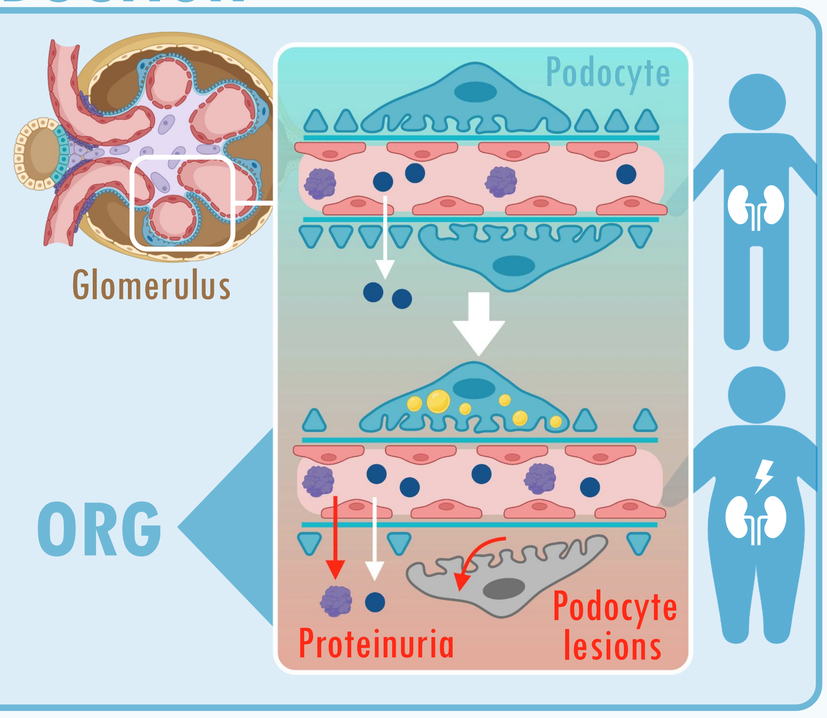
INTRODUCTION

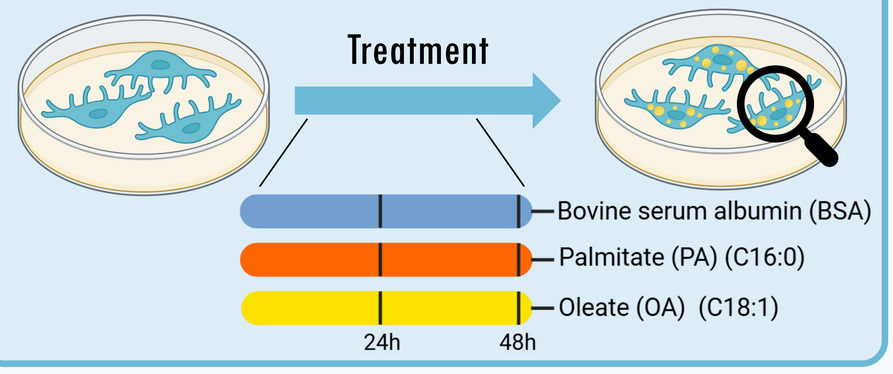
A key feature of obesity-related chronic kidney disease (CKD) is the alteration of the glomerulus, known as **obesity-related glomerulopathy (ORG).** In this condition, **podocytes**, highly specialized glomerular epithelial cells, are primary targets. Podocyte injury results in foot process effacement, 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**.



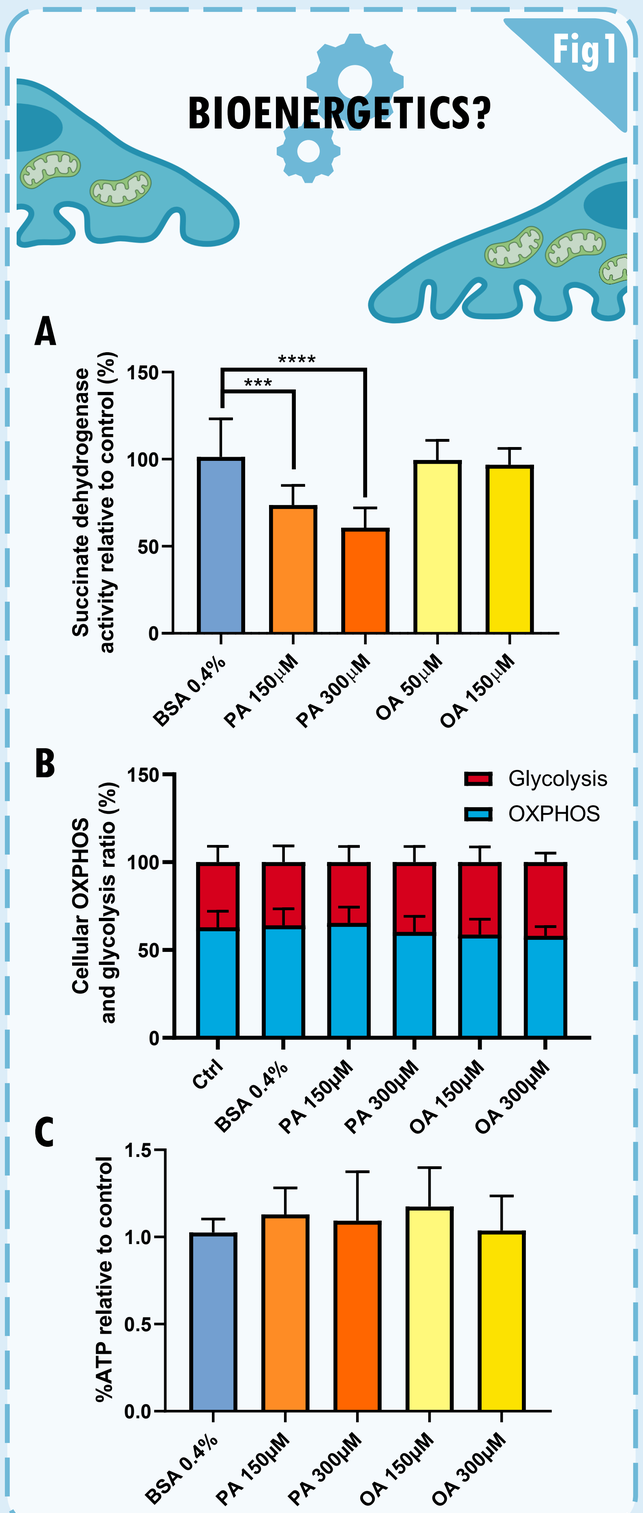
AIMS & METHODS

TO INVESTIGATE THE PODOCYTE METABOLISM ADAPTATION TO LIPID EXPOSURE

MODEL: Immortalized human podocyte "LY"



RESULTS



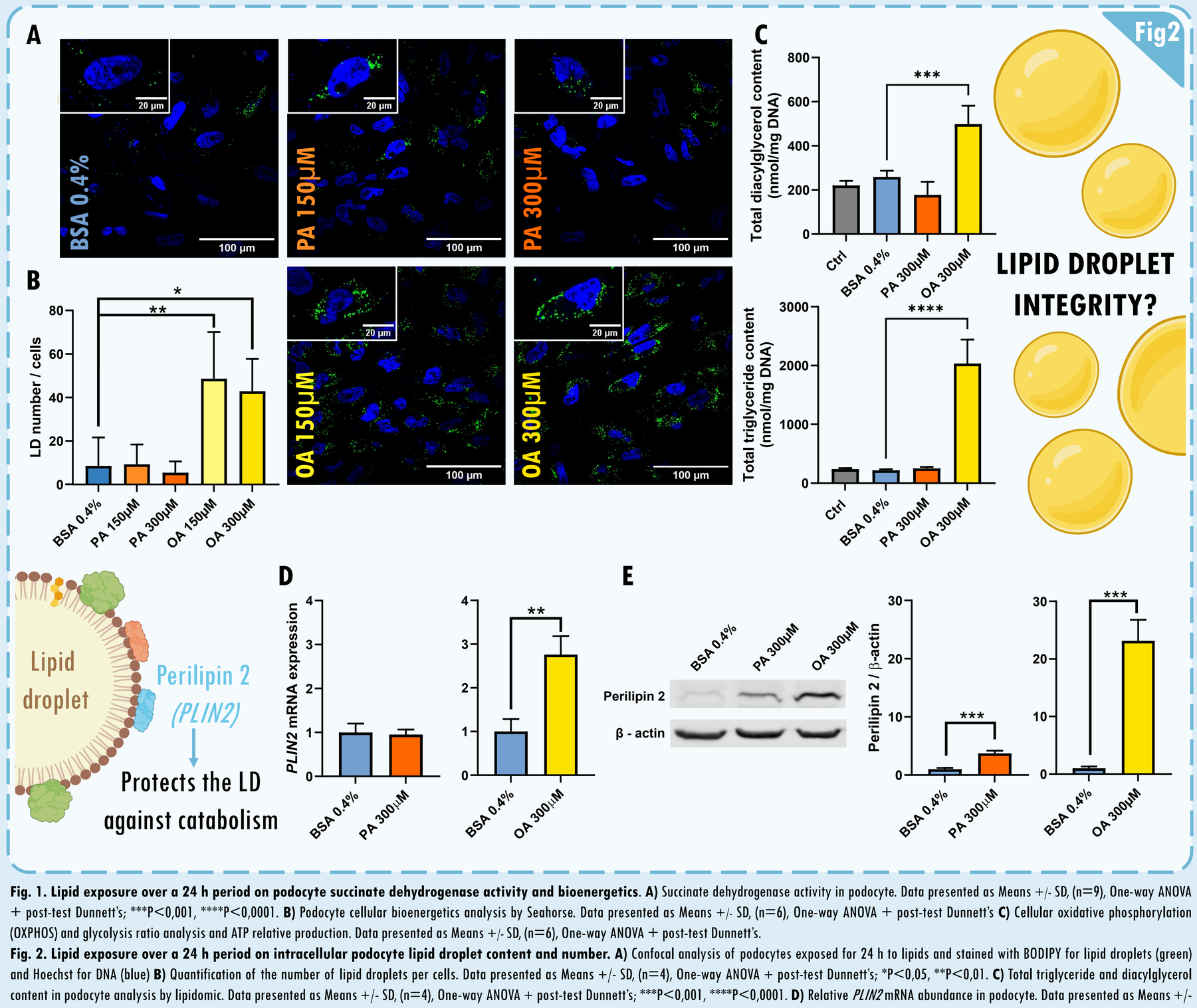


Fig. 1. Lipid exposure over a 24 h period on podocyte succinate dehydrogenase activity and bioenergetics. A) Succinate dehydrogenase activity in podocyte. Data presented as Means +/- SD, (n=9), One-way ANOVA + post-test Dunnett's; ***P<0,001, ****P<0,0001. **B)** Podocyte cellular bioenergetics analysis by Seahorse. Data presented as Means +/- SD, (n=6), One-way ANOVA + post-test Dunnett's **C)** Cellular oxidative phosphorylation (OXPHOS) and glycolysis ratio analysis and ATP relative production. Data presented as Means +/- SD, (n=6), One-way ANOVA + post-test Dunnett's.

Fig. 2. Lipid exposure over a 24 h period on intracellular podocyte lipid droplet content and number. A) Confocal analysis of podocytes exposed for 24 h to lipids and stained with BODIPY for lipid droplets (green) and Hoechst for DNA (blue) **B)** Quantification of the number of lipid droplets per cells. Data presented as Means +/- SD, (n=4), One-way ANOVA + post-test Dunnett's; *P<0,05, **P<0,01. **C)** Total triglyceride and diacylglycerol content in podocyte analysis by lipidomic. Data presented as Means +/- SD, (n=4), One-way ANOVA + post-test Dunnett's; ***P<0,001, ****P<0,0001. **D)** Relative *PLIN2* mRNA abundance in podocyte. Data presented as Means +/- SD, (n=3), unpaired parametric Student's t test; **P<0,01. **E)** Western blot analysis of perilipin 2 abundance in podocyte. Data presented as Means +/- SD, (n=3), unpaired parametric Student's t test; ***P<0,001.

CONCLUSION

Podocytes treated with PA, a saturated fatty acid (FA), showed altered metabolic activity, whereas OA, an unsaturated FA, 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).

PROSPECTS

Further investigations will be carried out to better define PA metabolic alterations, including:

- palmitoylation of proteins
- *de novo* ceramide synthesis
- cytoskeleton disorganization
- membrane rigidification

INFORMATIONS

Aurore Hecq holds a PhD fellowship from the UMons and UNamur.

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