

## Palmitate induces Ros generation and activates inflammation pathway

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Obesity is a social and economical problem. The prevalence of obesity has risen to epidemic proportions and continues to be one of the major worldwide health problem. Concurrent with the global obesity epidemic, there is an increasing number of people of all ages developing chronic kidney disease associated with obesity(1). Although obesity is often associated with diabetes and hypertension, which are two of the most common risk factors for the development of end-stage renal disease (ESRD), obesity in itself can be an independent risk factor for both chronic kidney disease (CKD) and ESRD. The signaling pathways leading to renal pathology in obesity are not well understood. Here we investigate the hypothesis that physio-pathological concentration of palmitate induces reactive oxygen species production in conditioned human podocytes cell line through the activation of mitochondrial mechanisms, induces endoplasmic reticulum (ER) stress and increases HMGB1 expression and inflammation. The conditionally immortalized human podocytes cell line were differentiated and then treated with/without palmitate conjugated with BSA in a control and physio-pathological condition(2) and cell morphology, under experimental conditions, were evaluated. Physio-pathological palmitate concentrations stimulate ROS generation in human podocyte and induces endoplasmic reticulum (ER) stress in podocytes. Moreover palmitate-induced ROS caused the activation of pro-inflammatory pathways (p65/NfκB and MCP-1), up-regulation of TGF-β well identified as a central mediator in renal fibrosis and induces a significantly increase of gene expression of HMGB1. Normalization of mitochondrial ROS production prevented each of these effects of palmitate. These results showed that palmitate at physio-pathological concentrations is able to induce ROS production, ER stress, inflammation, fibrosis and dysregulation of HMGB1 in human podocytes.

### References

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### Key words

Obesity, podocytes, ROS, palmitate.