macrophage migration, promoted ROS generation and induced pro-inflammatory factors, such as IL6. This pro-inflammatory profile obtained in macrophages, after treatment with modLDL, was countered by $NO_2$-OA, promoting an increase in LRP1 expression, inhibition in ROS generation and pro-inflammatory expression. All together these results indicate that LRP1 has an active participation in the production of pro-inflammatory profiles in macrophages, which may be regulated by modLDL produced in dyslipidemia disorder.

## LI-P10-215

### MOLECULAR MECHANISMS UNDERLYING RESVERATROL EFFECT ON RENAL OSMOPROTECTION: MODULATION OF COX-2 EXPRESSION

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Resveratrol (RSV) is a polyphenol naturally present in several plants. Nowadays it is sold as an over-the-counter dietary supplement due to its antioxidant, anti-inflammatory and antitumoral effects. Paradoxically, it has been documented that RSV may also present pro-oxidizing and pro-proliferative effects. In fact, some studies suggest that RSV treatment can result in opposite effects depending on the cell type, its concentration, or the treatment time. Particularly in renal tissue, animal injury models described RSV beneficial effects, while studies with chronic intake of RSV observed nephrotoxicity. Hence, RSV effects on renal tissue are still controversial. Due to the urinary concentrating mechanism, renal medullary interstitium presents an elevated osmolality that can abruptly change depending on the hydric state of the body, reaching values up to 800-1200 mOsm/kg $H_2O$. To survive in this environment, renal cells activate protective pathways. We have demonstrated that renal epithelial cell line MDCK undergoes an adaptive process during the first 24h of hyperosmolarity, in which the transcription of the osmoprotective gene cyclooxygenase 2 (COX-2) is activated, among others. After 48h these cells are already adapted and begin to differentiate, acquiring a polarized epithelium morphology. In this work we evaluate RSV effect on adaption and differentiation mechanisms, focusing particularly on COX-2 role. To do this, MDCK cells were pretreated with different concentrations of RSV (1, 5, 10, 25 µM) and cultured in hyperosmolar medium (~512 mOsm/kg $H_2O$) for 24 and 48h. Cells were harvested to obtain cell number and viability. Cell cycle, immunofluorescence (IF), western blot and RT-PCR analysis were performed. We found that RSV significantly decreased cell number in a concentration-dependent manner at 24 and 48h. Cell cycle analysis revealed that RSV increased S-phase and Sub-G0 cell population. In addition, treated cells did not reach typical epithelium morphology. COX-2 mRNA and protein levels were surprisingly upregulated by RSV at 24 and 48h, and IF revealed an accumulation of the protein in cytoplasmic granules. To investigate the pathways leading to this upregulation, we indirectly evaluated TonEBP, NF-κB and ERK1/2 pathways, which are activated by hyperosmolarity; and SIRT1 implication, a target of RSV. TonEBP target genes mRNA did not show any significant change under RSV treatment, while NF-κB target gene mRNA presented an increase similar to that of COX-2 mRNA. Moreover, NF-κB IF revealed an increase in its nuclear localization. Regarding ERK1/2, treatment with ERK1/2 selective inhibitor (U0126) completely blocked COX-2 protein expression. These results suggest that in renal cells RSV pretreatment decreased cell number and impeded typical cell morphology acquisition; but it increased COX-2 expression, possibly through NF-κB and ERK1/2 activation.

## LI-P11-224

### EFFECTS TO STEARIC ACID DIET ON THE DEVELOPMENT, FERTILITY AND BODY FAT DISTRIBUTION IN CAENORHABDITIS ELEGANS MODEL

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Excessive intake of saturated fats and refined carbohydrates causes overnutrition, leading to a variety of diseases such as obesity and other metabolic disorders. The diet supplementation with natural bioactive compounds with ability to reduce fat accumulation is a strategy proposed to help fight these diseases. *C. elegans* has been demonstrated to constitute a powerful model for exploring the genetic basis of fatty acid synthesis and the regulation of fat storage. In this study we proposed *C. elegans* as a tool to study the metabolic disorders of excessive intake of saturated fats and the effects of natural bioactive compounds. For this, we examined: a) the effect of stearic acid (SA) diet on growth, development, fertility and body fat of worms, b) the effect of chlorogenic acid (CGA) on worms exposed to SA diet. The worms were exposed to low, moderate and high SA levels during the development cycle (egg to adult), in the growth stage (adult), and multigenerational (adults progenitors to adults progeny). In all cases, egg laid, body area, body fat storage (Oil Red O staining) and body fat content (Nile Red staining) were measured. The results showed no effects of SA on worms exposed in the adult stage for 72 hours. However, moderate and high SA showed a significant reduction in body area, egg laid, fat content and body fat storage in worms of development and multigenerational assays. All these effects were normalized with the CGA added in the multigenerational assay. The results evidence that SA diet produced a lipid reallocation between somatic and germ cells that impacts in the development and reproduction. In addition, CGA showed a protective effect on high-lipid damage to nematodes.

## LI-P12-253