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Exposure to elevated non-esterified fatty acids alters bovine oviductal epithelial cell gene expression in a cell polarity dependent manner

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Elevated non-esterified fatty acids (NEFA) hamper *in vitro* bovine oviductal epithelial cell (BOEC) physiology, however the importance of exposure side and cell polarity on severity of the effects, and the underlying mechanisms remain unknown. Hereto, we observed the impact of NEFA on BOEC gene expression, since altering the pre-implantation embryo's micro-environment may affect overall fertility during maternal metabolic disorders.

BOECs were seeded in a polarized cell culture system with hanging inserts following standard procedures (n=4). Confluency was confirmed at D9 by TER, after which BOECs were NEFA-exposed for 24h in 4 groups: 1) control (0µM NEFA + 0%EtOH), 2) solvent control (0µM NEFA + 0.45%EtOH), 3) apical NEFA (720µM NEFA + 0.45%EtOH in the upper, apical compartment), 4) basal NEFA (720µM NEFA + 0.45%EtOH in the lower, basal compartment). Subsequently, BOECs were trypsinized, RNA was extracted using Trizol, and submitted to RT-qPCR. Data were analyzed by one way ANOVA and expressed as relative mRNA abundance. Additionally, fatty acid (FA) content was photometrically measured in the spent medium.

Oviductin (*OVGP1*), estrogen receptor (*ESR1*) and ciliogenesis marker (*FOXJ1*) were evenly expressed in all groups. In the apical NEFA group, results showed upregulated *SOD1* (anti-oxidative), *BCL2* (anti-apoptotic) and *SHC1* (ROS metabolism). Energy metabolism appeared to be shifted with downregulated glucose (*G6PD)* and upregulated FA oxidation (high *CPT1* + *ACSL1,* and low *ACACA* expression*)(P<0.05)*. Medium analyses showed 53.40% consumption of apical FA, while only 19.45% of the FAs were taken up when supplied in the basal compartment.

We conclude that only apical NEFA exposure may lead to an altered BOEC-metabolism with preferential use of FA rather than glucose as energy source, and also with upregulated anti-oxidative and anti-apoptotic pathways. The increased FA-uptake and stimulation of BOEC defensive mechanisms may protect the early embryo from NEFA-toxicity.