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Bovine oviduct epithelial cell metabolism alters due to non-esterified fatty acid exposure: consequences for the micro-environment of the early embryo

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The bovine oviduct provides the early embryo with the optimal environment for its development during the first 3-4 days. However, during lipolytic conditions as seen in negative energy balance, obesity or type II diabetes the oviduct micro-environment may be flooded with high concentrations of non-esterified fatty acids (NEFAs). We investigated whether *in vitro* bovine oviduct epithelial cell (BOEC) metabolism is affected by elevated NEFAs. Hereto, a polarized cell culture system (PCC) was used to study changes in the fatty acid (FA) composition of the spent medium and in BOEC expression patterns of genes related to lipid metabolism. BOECs were seeded in a PCC system with hanging inserts following standard procedures (4 replicates). Confluency was confirmed at D9 by Transepithelial Electric Resistance, after which BOECs were NEFA-exposed (720µM NEFA-combi: 230µM PA, 280µM SA and 210µM OA) for 24h in 4 groups: 1) control (0µM NEFA + 0%EtOH), 2) solvent control (0µM NEFA + 0.45%EtOH), 3) basal NEFA (720µM NEFA + 0.45%EtOH in the basal compartment), 4) apical NEFA (720µM NEFA + 0.45%EtOH in the apical compartment). Subsequently, spent medium was photometrically assessed for total FA-concentration and subjected to gas chromatography for the measurement of individual FA-concentrations in different lipid-fractions. Furthermore, BOEC RNA was extracted and submitted to RT-qPCR, targeting genes related to FA and carbohydrate metabolism, oxidative stress and BOEC-function. Data were analyzed by one-way ANOVA. After exposure, spent medium analyses showed a 19.5% NEFA-decrease in the supplemented compartment of condition 3 (basal NEFA), with integral passage to the non-supplemented, apical compartment of PA (56.0%↑), SA (60.0%↑), OA (33.5%↑) as free FAs. However, in condition 4 (apical NEFA) 53.4% of FA-decrease was observed in the supplemented compartment, while no FA-increase was apparent at the non-supplemented side. This indicates intracellular lipid storage or consumption. Transcript abundance for oviductin (*OVGP1*), estrogen receptor (*ESR1*) and ciliogenesis marker (*FOXJ1*) was comparable in all treatments. However, condition 4 resulted in upregulated gene expression of *SOD1* (anti-oxidative), *BCL2* (anti-apoptotic) and *SHC1* (oxidative stress). Furthermore, upregulated *CPT1* and *ACSL1* (both FA-oxidation), combined with downregulated *ACACA* (FA-synthesis) and *G6PD* (glucose consumption) is indicative for altered BOEC-metabolism in response to apical NEFAs *(P<0.05)*. In conclusion, these data show that the impact of NEFAs in a polarized BOEC-model on the FA profile of the non-supplemented compartment, significantly differs depending on the exposure side. Moreover, mainly apical NEFA-exposure prompts the BOECs towards altered gene expression patterns, involving anti-oxidative, anti-apoptotic and metabolic pathways. Thus these data suggest the notion of the oviduct as gate-keeper that shields its micro-environment from detrimental metabolites, such as elevated NEFAs.