

## **Diethylstilbestrol and ketoconazole alter lateral adherence of cultured bovine oviduct epithelial cells**

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The worldwide problem of increasing frequency of female reproductive disorders is considered to be partially related to the rise in endocrine disrupting chemical (EDC) production and exposure. EDCs can interfere with normal hormonal action and regulation, and the effect of the two well described EDCs diethylstilbestrol (DES; a synthetic estrogen agonist) and ketoconazole (KTZ; a steroidogenic enzyme inhibitor) are examined on bovine oviduct epithelial cells (BOECs). In this thesis work a 23-day BOEC monolayer culture in Transwell® inserts was established using the air-liquid interface (ALI) method to maintain the differentiated BOEC phenotype. BOEC-ALI cultures showed columnar epithelial cell monolayers that were confluent by cell-cell adherence at the apical side (>90%) of these cells. In this culture system four-day exposure to either DES or KTZ resulted in a substantial cell-cell adherence to a lower or even basal position in the still columnar epithelial that remained to have full confluency properties (<35 % of the cells remained apically adhered  $p < 0.001$ ). In part the removal of DES led to a recovery of the cell-cell adherence to the apical area of the columnar epithelium (>50 %; recovery effect not studied for KTZ). Currently the transflux of both EDCs from the basolateral compartment of the Transwell® inserts over the BOEC into the apical compartment are determined by HPLC-MS/MS after cold ethyl-acetate extraction from both fluids. This provides insights in the possibility that exposure of DES or KTZ to the BOEC will attenuate potential toxic EDC effects in the lumen of the oviduct and thus have a more potential to influence the processes of fertilization and early embryonal development.

\*This project is funded by the European Union's Horizon 2020 research and innovation program "FREIA" grant number 825100.