Al collegio docenti del Dottorato in Medicina Molecolare

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Attività scientifica svolta nel 2° anno di Dottorato, Anno Accademico 2022-2023

Introduction

The risk assessment of chemicals is usually studied on singular compounds, although humans are exposed to a wide range of mixtures consisting of chemicals found in plastics, hygiene products etc. There is a limited amount of data on the combined effect of Endocrine Disrupting Chemicals. Our aim was to test a wide range of compounds, individually or as mixtures, and the potential effect on mechanisms related to female reproduction.

Methods

The effect of Probenecid, Melamine, Perfluorooctanoic acid, Biochanin A, Daidzein and a mixture of phthalates were investigated. Granulosa cells (GCs) from follicular fluid and Cumulus Cells (CCs) from cumulus-oocyte complex were collected as waste material during the *in vitro* procedure of assisted reproductive techniques (ART) at the Centre for Couple Sterility, University Hospital in Siena. Immortalized cell lines HGL-5, 12-Z and RL95-2 were commercially obtained. A novel 3D model was established from Endometrial Epithelial Cells from healthy patients (South-Estonian Hospital, Voru, Estonia). The cytotoxicity was measured with the Resazurin Test (Sigma) and CellTiter 3D (Promega). The total RNA was extracted from the samples and proceeded with the transcriptomic analysis. Gene expressions of several genes coding for proteins involved in steroidogenesis was investigated by qRT-PCR. RNA extracted from 3D Organoids was used for library preparation and sequenced on Next-Seq 1000/2000 (Illumina, USA). Mitochondrial morphology, lipid droplets amount and steroid hormones secretion were measured.

Results

Endometrial 3D Organoids from epithelial cells resulted an optimal in-vitro model to test the effect of EDCs. Neither of the concentrations chosen for the treatment was toxic to the cells. Data from transcriptomic and proteomic analysis suggest that these compounds alter survival and proliferation pathways, as well as hormone signal transduction pathways. Furthermore, estrogen and progesterone secretion was altered by some of the compounds.

Abstracts and participation in courses and congresses:
-Participated at ESHRE International Conference held in Copenhagen from 25/06/2023 to 28/06/2023 with one peer reviewed Abstract+ Posters, published in Human Reproduction journal:

1. C Scarica, P Petrocelli, E Pontemezzo, A Haxhiu, S Perez Casasus, A Luddi, P-178 The interaction between spermatozoa and cumulus cells: a more physiological approach to the selection of good quality spermatozoa for assisted reproduction, *Human Reproduction*, Volume 38, Issue Supplement_1, June 2023, dead093.538, https://doi.org/10.1093/humrep/dead093.538

Scientific Publications in international journals with Impact Factor:

1. Luongo FP, Passaponti S, **Haxhiu A**, Raeispour M, Belmonte G, Governini L, Casarini L, Piomboni P, Luddi A. Bitter Taste Receptors and Endocrine Disruptors: Cellular and Molecular Insights from an In Vitro Model of Human Granulosa Cells. Int J Mol Sci. **2022** Dec 8;23(24):15540. doi: 10.3390/ijms232415540. PMID: 36555195; PMCID: PMC9779643.
2. Luongo, F.P.; Perez Casasus, S.; **Haxhiu, A**.; Barbarulo, F.; Scarcella, M.; Governini, L.; Piomboni, P.; Scarica, C.; Luddi, A. Exposure to Cumulus Cell Secretome Improves Sperm Function: New Perspectives for Sperm Selection In Vitro. *Cells* **2023**, *12*, 2349. https://doi.org/10.3390/cells12192349

Traineeship:

- Traineeship in Competence Center of Health Technologies in Tartu, Estonia, from 11/05/23 to 13/11/23.