Al collegio docenti del Dottorato in Medicina Molecolare

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Ciclo: XXXVII

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Introduction

Among several factors recognized as causes leading to infertility, exposure to environmental pollutants and toxins are directly toxic to gametes. Endocrine Disrupting Chemicals (EDCs) are defined as exogenous agents that interfere with synthesis, secretion, binding action, or removal, of hormones that are responsible for homeostasis, reproduction, and developmental processes.

Materials and Methods

In order to investigate the impact of selected EDCs in female reproduction, granulosa cells (GC) from follicular fluid and Cumulus Cells (CC) 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. Subsequently, immortalized cell line hGL5 (human Granulosa Line 5) are used.

To investigate the effect of selected EDCs compounds on the viability of the hGL5 cells, cytotoxicity assay was performed using cell counting kit-8 (Abcam). Gene expressions of several genes coding for proteins involved in steroidogenesis such as STAR (Steroidogenic Acute Regulatory Protein), and CYP11 (Cytochrome P450 Family 11 Subfamily A Member 1) were evaluated. Expressions of key proteins involved in proliferation and survival pathways such as Nf-kB, PKC/PKD were studied by Western Blot. Also, mitochondrial activity was evaluated by MitoTracker® Red CMXRos probes which diffuse across the plasma membrane and accumulate in active mitochondria. Images were further on processed by MiNa software, to compare the mitochondrial footprint of cells in different conditions.

Results

The results obtained from the preliminary experiments served to set-up a tailored method for the isolation of human granulosa from the follicular fluid. More importantly, EDCs such as Biochanin A and Genistein increase the expression of several genes coding for receptors involved in hormone signal transduction pathways in granulosa cells, highlighting the importance on understanding the full mechanism of action of these compounds in female reproductive physiology.

Abstracts and participation in courses and congresses:

- Participated in the Congress: "How to deal with reproductive and metabolic problems in women at a fertile age" held in Siena on 30/09/2022.
- Participated at ESHRE International Conference held in Milan from 03/07/2022 to 06/07/2022 with two peer reviewed Abstracts + Posters, published in Human Reproduction journal:

1. L Governini, **A Haxhiu**, C Landi, R Ponchia, G Morgante, P Piomboni, A Luddi, Characterization of Epididymosomes and Prostasomes in Seminal Plasma of Infertile Males. (Poster P-089) *Human Reproduction*, Volume 37, Issue Supplement_1, July 2022, deac107.085. https://doi.org/10.1093/humrep/deac107.085

2. A Luddi, FP Luongo, R Ponchia, F Cecconi, F Dragoni, **A Haxhiu**, M Zazzi, I Vicenti, P Piomboni, SARS-CoV2 infection in human testis and sperm: in vivo and in vitro studies. (Poster P-073) *Human Reproduction*, Volume 37, Issue Supplement_1, July 2022, deac107.069. https://doi.org/10.1093/humrep/deac107.069

Scientific Publications in international journals with Impact Factor:

1. Ponchia, R.; Bruno, A.; Renzi, A.; Landi, C.; Shaba, E.; Luongo, F.P.; **Haxhiu, A**.; Artini, P.G.; Luddi, A.; Governini, L.; Piomboni, P. Oxidative Stress Measurement in Frozen/Thawed Human Sperm: The Protective Role of an In Vitro Treatment with Myo-Inositol. *Antioxidants*. **2022**, *11*, 10. https://doi.org/10.3390/antiox11010010
2. Shaba, E.; Vantaggiato, L.; Governini, L.; **Haxhiu, A**.; Sebastiani, G.; Fignani, D.; Grieco, G.E.; Bergantini, L.; Bini, L.; Landi, C. Multi-Omics Integrative Approach of Extracellular Vesicles: A Future Challenging Milestone. *Proteomes* **2022**, *10*, 12. https://doi.org/10.3390/proteomes10020012
3. Luddi, A.; Luongo, F.P.; Dragoni, F.; Fiaschi, L.; Vicenti, I.; Lupetti, P.; Gentile, M.; Paccagnini, E.; **Haxhiu, A**.; Ponchia, R.; Governini, L.; Zazzi, M.; Piomboni, P. Cellular and Molecular Mechanisms of In Vivo and In Vitro SARS-CoV-2 Infection: A Lesson from Human Sperm. *Cells*, **2022**, *11*, 2631. https://doi.org/10.3390/cells11172631