UNIVERSITÀ DI SIENA 1240

DIPARTIMENTO DI MEDICINA MOLECOLARE E DELLO SVILUPPO

Università degli Studi di Siena
Dottorato di Ricerca in Medicina Molecolare

Scheda Relazione Annuale Dottorando

Al Collegio Docenti del Dottorato
in Medicina Molecolare

Siena, 07 Ottobre 2024

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Ciclo XXXVIII

Attività scientifica svolta nel 2° anno di Dottorato, A.A. **2023/2024**

- *Introduction*

Human primordial germ cells (hPGCs) play a critical role in early development, serving as precursors to gametes and contributing to genetic transmission. Their specification is influenced by a variety of factors, including signaling pathways, transcription factors, epigenetic modifications and environmental factors like endocrine-disrupting chemicals (EDCs). Given the pivotal role of hPGCs in early development and the potential disruption of endocrine signaling by EDCs, it is essential to investigate their effects on these cells. Ethical constraints limit direct studies on hPGCs in human embryos, making in vitro-generated human primordial germ cell-like cells (hPGCLCs) a valuable model for exploring how EDCs, such as perfluorinated compounds and phthalates, impact early germ cell development. During the second year of my PhD program, my project focused on investigating the impacts of these chemicals on hPGCLCs development and differentiation.

- *Materials and Methods*

The effects of MEHP, a phthalate, and PFOS, a perfluorinated compound, on human induced pluripotent stem cells (hiPSCs) were investigated using a well-established culture method. These cells were cultured and after 4-days of cell growth, changing the medium daily and adding the compounds at different concentrations, the cells were induced to form hPGCLC. After a 5-day incubation to promote embryoid body (EB) formation, EBs were dissociated into single cells. The dissociated cells were then subjected to FACS to determine the percentage of cells that had differentiated into hPGCLCs.

- *Results*

The results obtained with MEHP were inconsistent and inconclusive, displaying variability across different experiments. In contrast, exposure to PFOS significantly reduced the percentage of hPGCLCs obtained from the cultures. These findings suggest that while MEHP may not exert a clear impact on hPGCLC differentiation, PFOS could have a detrimental effect on the development of these cells, highlighting the potential risks posed by this EDC.

Scientific Publications on International Journals:

I. Luongo FP*, **Pérez Casasús 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 (19), 2349; doi.org/10.3390/cells12192349

II. **Pérez Casasús S***, Luongo FP*, Haxhiu A, Orini M, Scupoli G, Governini L, Piomboni P, Buratini J, Del Canto M, Luddi A. *Paternal Age Amplifies Cryopreservation-Induced Stress in Human Spermatozoa.* Cells 2024, 13 (7), 625; https://doi.org/10.3390/cells13070625

Abstracts and Participation to Congresses:

- ESHRE 40th Annual Meeting, Amsterdam, The Netherlands, 07-10 July 2024:
  Pérez Casasús S, Luongo FP, Haxhiu A, Governini L, Scupoli G, Orini M, Del Canto M, Buratini J, Morgante G, Piomboni P, Luddi A. *Advanced Paternal Age (APA) amplifies cryopreservationinduced stress in human spermatozoa.* (Poster P-354) Human Reproduction, Volume 39, Issue Supplement_1, July 2024, deae108.712, https://doi.org/10.1093/humrep/deae108.712

"Attività Didattica Dottorato Medicina Molecolare" a.a. 2023-2024

- 23 February 2024, 9:00-11:00; University of Florence (Florence, Italy)
  Prof. M. Linari: *Dual filaments regulation of muscle contraction*.
  Prof. P. Bianco: *The molecular motor of muscle studied in vitro mechanics.*
- 23 February 2024, 11:00-13:00; University of Florence (Florence, Italy)
  Prof.ssa C. Ferrantini - Prof.ssa N. Piroddi: *Mechanical dysfunction in genetic-based cardiomyopathies: perspectives for the use of novel small molecules and biomimetic polymers.*
- 23 February 2024, 14:30-16:30; University of Florence (Florence, Italy)
  Prof.ssa Betti Giusti: *High-throughput sequencing: technologies and application in molecular medicine.*
- 23 February 2024, 16:30-18:30; University of Florence (Florence, Italy)
  Prof.ssa E. Cerbai - Prof. R. Coppini: *Effects of SGLT-2 inhibitors in diseased myocardium.*
- 11 April 2024, 9:00-13:00; University of Pisa (Pisa, Italy)
  Prof. Massimo Dal Monte: *The beta-adrenergic system in the retina: targeting beta adrenoceptors against retinal neovascular diseases. Part 1.*
- 11 April 2024, 14:00-18:00; University of Pisa (Pisa, Italy)
  Prof.ssa Rosario Amato: *The beta-adrenergic system in the retina: targeting beta adrenoceptors against retinal neovascular diseases. Part 2.*
- 20 May 2024, 14:00-18:00; University of Siena (Siena, Italy)
  Prof. S. Cagnin: *Beyond the proteome: non-coding regulatory RNAs in cell pathophysiology.*
- 21 May 2024, 10:00-14:00; University of Siena (Siena, Italy)
  Prof. S. Cagnin: *Beyond the proteome: non-coding regulatory RNAs in cell pathophysiology.*

Traineeship in other Italian or foreign laboratories:

- Karolinska Institutet, Solna, Sweden
  From 1st April 2024 to 31st December 2024 *(on-going)*.
  To carry out the following activity: study the effect of endocrine disruptors on the embryonic and postnatal male reproductive system.