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Geneeskunde & Farmacie

GF

PhD in Medical Sciences
2014-2015

INVITATION to the Public defence of

Maria KRIVEGA

To obtain the academic degree of **'DOCTOR IN MEDICAL SCIENCES'**

Balancing between totipotency and differentiation in human embryos

Thursday 3 September 2015
Auditorium **Vanden Driessche**, 17:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:
http://www.vub.ac.be/english/infoabout/campuses

Vrije Universiteit Brussel

Summary of the dissertation

Today, it has become clear that the information on critical factors of human embryo development should result in the optimization of IVF techniques. The unique properties of human embryonic blastomeres, responsible for the ability of human embryos to recover after cell loss, became a target of our investigation. In this context, we analyzed two new markers - CAR and CCNE1 - and the WNT/□-catenin signaling in human preimplantation embryos *in vitro*. CAR is a gene, encoding the coxsackie and adenoviral receptor, which is induced in regenerating and developing tissues. We described a soluble CAR marking undifferentiated blastomeres and trophectoderm (TE) cells of hatching blastocysts and a transmembrane CAR relating to epithelial-like cell types via its association with tight junctions. Our further investigation was focused on CCNE1 as link between the developmental potential and the unique cell cycle characteristics. We reported ubiquitous presence of CCNE1 protein from the cleavage stages until blastocyst expansion. CCNE1 also labeled the third lineage within blastocysts' inner cell mass (ICM), which has never been described before. We associated CCNE1 with a visceral endoderm-like phenotype and proved its critical role in human embryonic cells during normal embryo development and hESC derivation. We also performed WNT/□-catenin pathway loss- and gain-of-function studies and showed relevance of the nuclear □-catenin exclusively to cleavage stages. The balanced □-catenin activity was critical for the TE fate. Similar to stabilized □-catenin, WNT3 protein, showing TE-specific expression in blastocysts, promoted trophoblast specification. The data from this work have led to a better understanding of early human embryogenesis, which is important for reproductive medicine.

Curriculum Vitae

Born: May 19, 1983, Ukraine; ***Citizanship:*** Russian

Education:

- Vrije Universiteit Brussel, Brussels, Belgium, PhD in Medical Sciences (04.2010-09.2015)
- Mount Sinai School of Medicine at New York University, USA, MS in Biomedical Sciences, 2009
- Moscow State University, Moscow, Russia, Diploma in Physiology (B.S. equivalent), specialization in Developmental Biology, 2005

Awards:

- The European Society of Human Reproduction and Embryology (ESHRE) and The Fertility Society of Australia - Australia Exchange Award, 2015
- Student Fellowship of the International Soros Science Education Program, 2002

Conferences attended:

Oral presentations at 30th (2014) and 31st (2015) Annual Meeting of ESHRE; 32nd Scientific Meeting of the Belgian Society for Reproductive Medicine (BSRM).

Poster presentations at 29th (2013) Annual Meeting of ESHRE; 28th (2012) Scientific Meeting of BSRM and EMBL conference "Germline - Immortality through Totipotency" (2012).

Publications :

- De Paepe and Krivega et al. Molecular Human Reproduction (2014) 20: 599-618. IF 3.483.
- Krivega et al. Reproduction (2014) 148: 531–544. IF 3.262.
- Krivega et al. Molecular Human Reproduction (2015) Jun 24. pii: gav036. IF 3.483.
- Krivega et al. (Conditionally accepted 2015) Molecular Human Reproduction. IF 3.483.