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PhD in Medical Sciences  
2017-2018

INVITATION to the Public defence of

**Caroline DE PAEPE**

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

**Totipotency versus differentiation in human embryonic cells.**

**Wednesday 24 January 2018**

Auditorium **Piet Brouwer**, 17:30

Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:

<http://www.vub.ac.be/english/infoabout/campuses>

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## Summary of the dissertation

The aim of this PhD thesis was to study the differentiation of early human embryonic cells.

Our study on human preimplantation embryos was focused on two major topics. First, we determined whether TE cells display plasticity. Therefore, we isolated and reaggregated TE cells from full human blastocysts and showed that they are able to develop into blastocysts with ICM cells expressing the pluripotency marker NANOG. Moreover, we showed that the majority of the isolated TE cells which were repositioned in the center of the embryo do not sort back to their original position but integrate within the ICM and start to express NANOG. These results show that full blastocyst TE cells are not yet committed. This suggests that in the future hESC could be derived from these TE cells without destroying the embryo.

Second, we determined whether supplementation of BMP4 affects the first lineage differentiation in the human. Therefore, we supplemented human day 3 cleavage stage embryos for 24 h, 48 h or 72 h with recombinant BMP4 or control medium. After culture, gene expression for ICM and TE markers and a PE marker was analyzed and compared with control embryos. No differences in the expression of NANOG, CDX2, GATA3 and GATA6 were found between BMP4-treated embryos and controls. Instead we found that BMP4 supplementation triggered apoptosis in the human blastocyst. An induction of MSX2 expression, a transcriptional regulator in the programmed cell death pathway, preceded apoptosis. In BMP4-treated embryos, the apoptosis was induced through a mitochondrial pathway. All together our findings suggest that BMP4 plays a role in apoptosis rather than in lineage differentiation during human preimplantation development.

## Curriculum Vitae

A well-presented, self-motivated and confident biomedical graduate who has knowledge of three languages (French, Dutch, English). Obtained her Master degree in Biomedical sciences at the Vrije Universiteit Brussel in 2010.