## Board of examiners

**Dr. Peter Ruane** Maternal and Fetal Research Group University of Manchester

**Dr. Kelly Tilleman** Centre for Reproductive Medicine UZ Gent

**Prof. Dr. Luc Leyns** Development and Cell Biology Vrije Universiteit Brussel

**Dr. Dorien Van Saen** Research Group Biology of the Testis Vrije Universiteit Brussel

**Dr. Ileana Mateizel** Centre for Reproductive Medicine Vrije Universiteit Brussel / UZ Brussel

**Prof. Dr. Rik Schots, Chair** Departement Hematology and Immunology Vrije Universiteit Brussel / UZ Brussel

**Prof. Dr. Hilde Van de Velde, Promoter** Research Group Reproduction and Immunology Vrije Universiteit Brussel / UZ Brussel

**Prof. Dr. Jan Brosens, Co-promoter** Division of Biomedical Sciences Warwick University



INVITATION to the Public defence of

## **Asma ABERKANE**

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

Early steps of human embryo implantation mimicked in a dish.

Thursday 05 July 2018 Auditorium Piet Brouwer, 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 Human embryo implantation is a synchronised cross-talk between a competent blastocyst and a receptive endometrium. The process is however poorly understood and is referred to as the "black box" of reproductive biology. The aim of this thesis was to set up in vitro models to mimic and better understand this process.

In the first study we investigated the changes in morphology and gene expression in human embryos during the initial implantation steps. For this human blastocysts were co-cultured for up to 48h in a 2D in vitro model that uses Ishikawa cells (endometrial epithelium cell line). We followed embryo implantation as it proceeded from the apposition, adhesion and the early invasion steps. Embryo development was supported in the in vitro model as both epiblast (NANOG) and trophoblast (KRT7 and hCG) markers were detected on the protein level. Upon attachment embryos upregulated the expression of different adhesion and extracellular matrix genes. Three of these genes, LAMA3, THBS1 and TNC were validated on the protein level. In the second study we analysed if implantation failure can be correlated to an aberrant in vitro decidualization reaction and how this impacts on human blastocyst development. The study was performed on primary EnSCs isolated prior to a successful (n=10) or failed (n=10) ART cycle. Secretome analysis revealed a disordered cytokine and growth factor secretion by the stromal cells from the non-pregnant patients. Culture of human blastocysts

for 24h in pooled supernatant of endometrial stromal cells showed that not the IVF outcome but the decidualization reaction impacts on blastocyst development.

## Curriculum Vitae

My life journey started on June 10th 1987 in Batna (Algeria), where alongside a joyful childhood I learned to speak and write Arabic. At the age of 10 I moved to The Netherlands. After finishing my secondary school (Edith Stein College), I moved to Belgium where I attended the Vrije Universiteit Brussel (VUB) and received a bachelor's and master's (with major distinction) degree in Biomedical Sciences (in 2012). The thesis of my master studies was on the gene expression of human preimplantation embryos following cryopreservation. I have always been fascinated by science, from the massive universe to the microscopic cell. In 2013 I obtained a PhD scholarship from the Flemish agency "The Agency for Innovation by Science and Technology". My PhD was under supervision of Prof. Hilde Van de Velde (VUB) and Prof. Jan Brosens (University of Warwick) and my research was focussed on human embryo development. more precisely the early steps of the implantation process. For this I used in vitro models, analysed the molecular profile of implanting embryos and the maternal regulation of embryo development. In line with my PhD project I was also actively involved in international collaboration projects with Prof. Jan Brosens, Dr. Yie Hou Lee (KK Research Centre, Singapore) and Prof. Guiving Nie (Hudson Institute of Medical Research, Australia). My work culminated in two first author research papers and was additionally awarded twice during national and international conferences.