UNIVERSITÉ Clermont Auvergne

MASTER
BIOLOGIE SANTE

Track « Integrative Biology, Physiopathologies »

Proposal for a Master 2 internship – 2023-2024

Title: Study of environmental pollutants (phthalate and alternative plasticizers) influence on nuclear receptors pathways in human fetal membranes regarding their pathological premature rupture.

Laboratory: iGReD, Universite Clermont Auvergne, CNRS, INSERM (team « Translational Approach to Epithelial Injury and Repair »)
Laboratory director: Krzysztof Jagla (team leaders: Pr. Sapin & Dr. Blanchon)
Address : CRBC, UFR de Médecine et des Professions Paramédicales, Place Henri Dunant,

Internship tutor: Dr. Loïc BLANCHON
Tel: +33 4 73 17 81 74
E-mail : loic.blanchon@uca.fr

Summary : The rupture of fetal membranes (FM) is a physiological phenomenon that is programmed towards the end of pregnancy (after 37 weeks of gestation (WG)). It's the consequence of weakening and loss of elasticity of FM resulting from cellular and molecular events such as extracellular matrix degradation, apoptosis and sterile inflammation. Throughout pregnancy, many cellular actors, including the nuclear receptors, are of primary importance for an harmonious gestation in order to prevent a premature rupture of FM (before 37 WG), occurring in 3 to 4% of pregnancies and responsible for 1/3 of prematurity.
In September 2019, "Santé Publique France" communicated the results of the Esteban study, which confirms the exposure of the French population, including pregnant women to pollutants such as phthalates (for example MEHP). Up to date, little is known about their potential negative actions on nuclear receptors signalling pathways in such FM context. This project aims to better understand the potential links between exposure of pregnant women to phthalates and alternative plasticizers (develop to replace phthalates) and premature rupture of fetal membranes (FM). Previous experiments and tests already published by the team (see below pub 1) demonstrate a MEHP dysregulation of the PPARγ nuclear receptor signalling pathway in MF. Following that, this project will extend such tests to others nuclear receptors pathways such as: Retinoic Acid receptor (RAR), Vitamin D receptor (VDR), Liver X receptor (LXR), Retinoid X Receptor (RXR, heterodimeric partner of PPARγ, RAR, VDR, LXR), Progesterone Receptor (PR) or AhR (Aryl hydrocarbon Receptor/known as a pollutant receptor). To achieve that, MEHP or MINCH (most used alternative plasticizer) will be used and studies will be conducted in all cell types present in the FM to decipher globally the negative action of both pollutants on such pathways in this tissue.

Methodologies (key words) : *Cell culture (primary and cell lines), qRT-PCR, Western-blot, luciferase gene reporter, Immunofluorescence, multiplex quantification, scratch assay*

Publications of the research group on the proposed topic (3 max.)

1. Antoine A. *et al*. (2022) Dysregulation of the amniotic PPARγ pathway by phthalates: A new hypothesis to explain the premature rupture of fetal membranes. *Life* 12(4):544.
2. Belville C *et al*. (2022) Physiological TLR4 regulation in human fetal membranes as an explicative mechanism of a pathological preterm case. *Elife*. 11:e71521.
3. Choltus H *et al*. (2021) Cigarette Smoke Condensate Exposure Induces Receptor for Advanced Glycation End-Products (RAGE)-Dependent Sterile Inflammation in Amniotic Epithelial Cells.