Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

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Host laboratory:
Lab : Biosanté Laboratory. INSERM U1292

Host group/team:
MAB2: Mechanism of Angiogenesis in Biological Barriers

Title of the M2 research internship:

PFAS exposure and its consequences on the development of the placenta

Project summary:
Several studies reported that pregnancy exposure to per-and polyfluoroalkyl substances (PFAS) may have adverse impact on the health of mothers and fetuses. Recent human and animal studies suggested that PFAS-mediated effects may involve placental (PL) perfusion and development. However, further in-depth research is necessary to explore the effect of maternal PFAS exposure on placental structure and on the functioning of cells that compose the placental villi, *ie*: the trophoblast and fetal endothelial cells. In a very recent study that included 367 pregnant women (SEPAGES, mother-child cohort, https://cohorte-sepages.fr/en), we demonstrated an association between exposure to the following PFAS: PFHxPA, PFTrDA, PFHpA and alterations in key placental structures known to ensure nutrient and oxygen exchange and placental perfusion (*1*). We also demonstrated that the PFAS, 6:2diPAP was associated with alterations of capillary density within the placental villi, suggesting a direct effect of these PFAS on the placental development and vascularization. The objective of the Master2 project is i) to validate this observation using immunohistochemistry analyses of markers of endothelial cells (CD34 marker) and trophoblast cells (Cytokeratin 7) of human placental explant treated with individual or mixture of these PFAS. Quantification and scoring of the intensities of such stainings is routinely used by our team. Human placenta is routignly collected in our laboratory under the following authorization/**NCT05188066**; ii) *to* characterize the effects of individual or mixture PFAS on the proliferation, migration and invasion of primary PL cells and on two cell lines HTR8/SVneo and BeWo that represent the invasive and endocrine trophoblast cells, respectively. Primary placenta microvascular endothelial cells (HPEC) will also be used to determine the effect of these PFAS on their permeability and viability. 3D spheroids culture will also be used to determine the effect of these PFAS on cells apoptosis, genotoxicity, inflammation and oxidative stress.

Keywords:
PFAS, placenta, pregnancy, SEPAGES cohort, 3D culture system, environmental health

Relevant publications of the team:

1. Khan S, Ouidir M, Lemaitre N, Jovanovic N, Bayat S, Lyon-Caen S, Hoffmann P,Desseux M, Thomsen C, Couturier-Tarrade A, Småstuen Haug L, Valmary-Degano S,Siroux V, Slama R, **Alfaidy N**, Philippat C. PFAS exposure during pregnancy:Implications for placental health and functioning. Environ Int. 2025 Jan30;197:109308. doi: 10.1016/j.envint.2025.109308. Epub ahead of print. PMID:39986002.
2. Jovanovic N, Mustieles V, Althuser M, Lyon-Caen S, **Alfaidy N**, Thomsen C,Sakhi AK, Sabaredzovic A, Bayat S, Couturier-Tarrade A, Slama R, Philippat C.Associations between synthetic phenols, phthalates, and placentalgrowth/function: a longitudinal cohort with exposure assessment in earlypregnancy. Hum Reprod Open. 2024 Apr 1;2024(2):hoae018. doi:10.1093/hropen/hoae018. PMID: 38689737; PMCID: PMC11057944.
3. Sergent F, Vaiman D, Raia-Barjat T, Younes H, Marquette C, Desseux M, NahedRA, Kieu TL, Dung NV, Keck M, Hoffmann P, Murthi P, Benharouga M, **Alfaidy N**. Antagonisation of Prokineticin Receptor-2 Attenuates Preeclampsia Symptoms. JCell Mol Med. 2025 Jan;29(2):e70346. doi: 10.1111/jcmm.70346. PMID: 39817714;PMCID: PMC11736873.

4. Josserand V, Lavaud J, Keramidas M, Collet C, Traboulsi W, Hoffmann P, FeigeJJ, Benharouga M, Coll JL, **Alfaidy N**. RGD-Based Fluorescence to Assess PlacentalAngiogenesis. Methods Mol Biol. 2024;2728:131-136. doi:10.1007/978-1-0716-3495-0_11. PMID: 38019397.
5. Traboulsi W, Reynaud D, Abi Nahed R, Sergent F, **Alfaidy N**, Benharouga M. InVivo Quantitative Assessment of Gestational Choriocarcinoma Development andProgression Using Luminescent Trophoblast Cells. Methods Mol Biol.2024;2728:77-85. doi: 10.1007/978-1-0716-3495-0_6. PMID: 38019392.
6. Raia-Barjat T, Chauleur C, Collet C, Rancon F, Hoffmann P, Desseux M, Lemaitre N, Benharouga M, Giraud A, **Alfaidy N**. EG-VEGF maternal levels predictspontaneous preterm birth in the second and third trimesters in pregnant womenwith risk factors for placenta-mediated complications. Sci Rep. 2023 Nov14;13(1):19921. doi: 10.1038/s41598-023-46883-6. PMID: 37963927; PMCID:PMC10645734.
7. Vincenzi M, Kremić A, Jouve A, Lattanzi R, Miele R, Benharouga M, **Alfaidy N**, Migrenne-Li S, Kanthasamy AG, Porcionatto M, Ferrara N, Tetko IV, Désaubry L,Nebigil CG. Therapeutic Potential of Targeting Prokineticin Receptors inDiseases. Pharmacol Rev. 2023 Nov;75(6):1167-1199. doi:10.1124/pharmrev.122.000801. Epub 2023 Sep 8. PMID: 37684054; PMCID:PMC10595023.
8. Philippat C, Heude B, Botton J, **Alfaidy N**, Calafat AM, Slama R; EDENMother–Child Cohort Study Group. Prenatal Exposure to Select Phthalates andPhenols and Associations with Fetal and Placental Weight among Male Births inthe EDEN Cohort (France). Environ Health Perspect. 2019 Jan;127(1):17002. doi:10.1289/EHP3523. PMID: 30624098; PMCID: PMC6381819.