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Host laboratory:

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Host group/team:

MAB2

Title of the M2 research internship:

Characterization of the prokineticin1-mediated protection of the fetal brain in preterm pregnancies: case of chorioamnionitis.

Project summary:

Chorioamnionitis (CA) is a common infection of pregnancy. Optimal management of clinical CA includes antibiotic therapy and premature delivery of the fetus. However, this strategy did not show significant improvements of the pregnancy outcome and consequences of the premature birth (PTB) on fetal brain development that causes cerebral palsy. To date, clinicians are still missing a reliable early biomarker and efficient treatments to attenuate and/or prevent the occurrence of CA and its associated consequences on fetal development.

During the last decade, our team demonstrated that Prokineticin1 (PROK1), the canonical member of the PROK family could constitute a reliable biomarker of the occurrence of preterm birth. This result has been patented by Inserm transfert and PROK1 is now considered as a quiescent factor in case of PTB. We hypothesize that by preventing the occurrence of PTB, PROK1 may prevent other developing tissues such as the fetal brain.

Given these encouraging results, we aim in the proposed Master2 project to characterize the impact of infection on fetal brain development and to decipher the mechanism by which PROK1 may prevent the development of harmful effects on the developing fetal brain.

First the M2 student will characterize the brains of fetuses collected gravid mice treated with LPS (Lipopolysaccharide of bacteria E-Coli), in the absence or presence of PROK1. Immunohistochemical, Western-blotting, RNAseq and Cytokine array analyses will be performed to answer fundamental questions such as, histopathological characterization of the fetal brains; characterization of the prokineticins status in same brains and characterization of their inflammatory status. The in vivo characterization of the impact of LPS and PROKS treatments on the developmental of the fetuses' brains with a focus on the study of the cortical development will be conducted in collaboration with GIN institute and will involve the Synchrotron and IRMAGE platforms.

Keywords:

preterm birth, inflammation, fetal brain

Relevant publications of the team:

1. Raia-Barjat T, Chauleur C, Collet C, Rancon F, Hoffmann P, Desseux M, Lemaître N, Benharouga M, Giraud A, Alfaidy N. EG-VEGF maternal levels predict spontaneous preterm birth in the second and third trimesters in pregnant women with risk factors for placenta-mediated complications. *Sci Rep.* 2023 Nov 14;13(1):19921.
2. Raia-Barjat T, Digonnet M, Giraud A, Ayash T, Vancolen S, Benharouga M, Chauleur C, Sébire G*, Alfaidy N*. Animal Models of Chorioamnionitis: Considerations for Translational Medicine. *Biomedicines.* 2022 Mar 30;10(4):811. 3. Abi Nahed R, Elkhoury Mikhael M, Reynaud D, Collet C, Lemaître N, Michy T, Hoffmann P, Sergent F, Marquette C, Murthi P, Raia-Barjat T, Benharouga M*, Alfaidy N*. Role of NLRP7 in Normal and Malignant Trophoblast Cells. *Biomedicines.* 2022 Jan 24;10(2):252.
3. Reynaud D, Abi Nahed R, Lemaître N, Bolze PA, Traboulsi W, Sergent F, Battail C, Filhol O, Sapin V, Boufettal H, Hoffmann P, Aboussaouira T, Murthi P, Slim R, Benharouga M, Alfaidy N. NLRP7 Promotes Choriocarcinoma Growth and Progression through the Establishment of an Immunosuppressive Microenvironment. *Cancers.* 2021 Jun 15;13(12):2999.
4. Reynaud D, Sergent F, Abi Nahed R, Traboulsi W, Collet C, Marquette C, Hoffmann P, Balboni G, Zhou QY, Murthi P, Benharouga M, Alfaidy N. Evidence-Based View of Safety and Effectiveness of Prokineticin Receptors Antagonists during Pregnancy. *Biomedicines.* 2021 Mar 17;9(3):309.
5. Alfaidy N, Baron C, Antoine Y, Reynaud D, Traboulsi W, Gueniffey A, Lamotte A, Melloul E, Dunand C, Villaret L, Bessonnat J, Mauroy C, Boueïhl T, Coutton C, Martinez G, Hamamah S, Hoffmann P, Hennebicq S, Brouillet S. Prokineticin 1 is

a new biomarker of human oocyte competence: expression and hormonal regulation throughout late folliculogenesis. *Biol Reprod.* 2019 Oct 25;101(4):832-841.