Raman sp**e**ctroscopy characterization of extracellular **v**esicles for *in ut**e**ro* di**a**gnosis of cytomega**l**ovirus - REVEAL

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While cytomegalovirus (CMV) infection are usually benign for healthy person, it can be highly dramatic for immunocompromised person or in case of pregnancy. Indeed, if the mother contracts the virus, it can cross the placenta and affect the fetal development with risks of major impairments like congenital deafness or neurological handicap. While severe sequelae due to CMV could be avoided by antiviral therapy (if administrated at early stage of infection), the current diagnosis of fetal CMV uses a very invasive procedure through amniocentesis or trophoblast biopsy. In addition, infection of the mother by CMV is usually asymptomatic and there is no systematic screening for CMV during pregnancy.
Amniotic fluid-derived and plasma-derived extracellular vesicles (EVs) obtained by innovative purification methods, will be analyzed (1) by Raman spectroscopy (RS), to get the biomolecular signature ; (2) by nanoparticle tracking analysis (NTA), to get the particle hydrodynamic size and concentration ; (3) nanoflow cytometry (nFC), to get the phenotypic signature of the samples ; and (4) asymmetrical flow-field flow fractionation (AF4), to get the molecular masses, hydrodynamic and gyration diameters of subfractions. As it was previously performed by the team on RS data from prostate cancer tissue [1,2], Machine learning algorithms will be used to identify the specific signature of CMV infection (automated supervised classification between infected vs non-infected fetuses), and to evaluate which modality (or combination of modalities) and which sample type is the best to diagnose CMV and anticipate severe sequelae.

The trainee will have to:

- learn how to use the different modalities (Raman, NTA, nFC, AF4),
- handle biological samples while following safety rules,
- construct data collections for each modality with strict nomenclature,
- apply classification methods developed by the host team.

1. Aubertin K, Trinh VQ, Jermyn M, et al. Mesoscopic characterization of prostate cancer using Raman spectroscopy: potential for diagnostics and therapeutics. *BJU Int*. 2018;122(2):326-336. doi:10.1111/bju.14199
2. Jermyn M, Mercier J, Aubertin K, et al. Highly Accurate Detection of Cancer In Situ with Intraoperative, Label-Free, Multimodal Optical Spectroscopy. *Cancer Res*. 2017;77(14):3942-3950. doi:10.1158/0008-5472.CAN-17-0668