

Proposal for a 6-month internship in 2022 (Master 2 degree): Integrated analyses of NMR spectra to model the feto-maternal crosstalk at the end of gestation in pigs

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Context: CO-LOCATIOn project (funding: ANR)

The CO-LOCATIOn project aims to answer the following question: how do the maternal and fetal genomes affect the metabolism and the gene expression to drive fetal maturity? The feto-maternal crosstalk associated to fetal maturity are explored, using an integrative omics approach (metabolome, lipidome and transcriptome) and by simultaneously questioning the two adjacent tissues (placenta/endometrium) that are players of feto-maternal interactions. The fetuses were already sampled at 2 dates of gestation (90 vs 110 days of gestation), from sows of 2 genotypes: Meishan (MS) or Large White (LW) mated with boars of the 2 genotypes (MS and LW). The neonatal piglet mortality is known to be lower in MS breed than in LW breed. Around 20 phenotypes were registered on all fetuses and the fetuses were split into 3 maturity status.

Internship work: NMR spectra analyses and interpretation

The objective of the internship is to analyze the ¹H-NMR spectra of endometrium and placenta of 224 fetuses. The NMR spectra have already been acquired. The student will participate to:

- Identify the metabolites present in the endometrium and in the placenta
- Identify the differential metabolites for the gestation dates, for the 3 maturity status and for the interaction genotype x maturity status in both tissues to characterize the biological pathways involved in a better maturity status
- Analyze the correlations between the metabolites and the phenotypes of the fetuses for both tissues
- And then study the covariations between endometrium and placenta to characterize the crosstalk between these both tissues.

Methodology: Statistical analyses

The ¹H-NMR spectra will be analyzed by 2 different methods: bucket analyses and metabolite analyses with the ASICS package of R. Unsupervised analyses (such as PCA, classification HAC) and supervised analyses (as PLS-DA) will be done. Linear models will be applied to identify differential metabolites. Then methods of data integration as PLS will be realized. All analyses will be performed with R software. The R script should be easy to read. The R markdown will be used.

Then the interesting metabolites will be identified (Human Metabolite Database, HMDB) and a biological interpretation of the results will be expected (Reactome, ...).

Skills: NMR spectra analyses, statistics, R software utilization (R markdown), biological interpretation

References :

Lefort G, Servien R, Quesnel H, Billon Y, Canario L, Iannuccelli N, Canlet C, Paris A, Vialaneix N, Liaubet L. The maturity in fetal pigs using a multi-fluid metabolomic approach. *Sci Rep.* 2020 Nov 16;10(1):19912. doi: 10.1038/s41598-020-76709-8.

Mozduri Z, Marty-Gasset N, Lo B, Masoudi AA, Morisson M, Canlet C, Arroyo J, Bonnet A and Bonnefont CMD (2021) Identification of Plasmatic Biomarkers of Foie Gras Qualities in Duck by Metabolomics. *Front. Physiol.* 12:628264. doi: 10.3389/fphys.2021.628264