^{1}H-NMR metabolomic study of Large White and Meishan pigs in late gestation: part 1- fetal placenta

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INRAE

Context: Influence of placental metabolism on piglet survival

Categories of perinatal mortality	**Percentage**
Death during farrowing	23.0%
Non- viable	21.4%
Early sepsis	17.6%
Mummified	11.0%
Crushing	7.83%
Starvation	5.58%
Other	13.59%
Total	100%

Pandolfi et al. 2017

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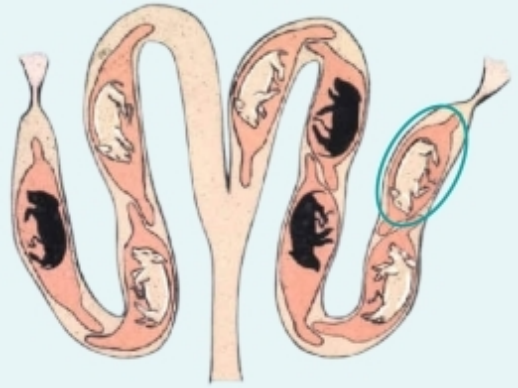
Selection for lean tissue
=> **piglets born in a less mature status**
(Herpin et al. 2002, Panzardi et al. 2013)

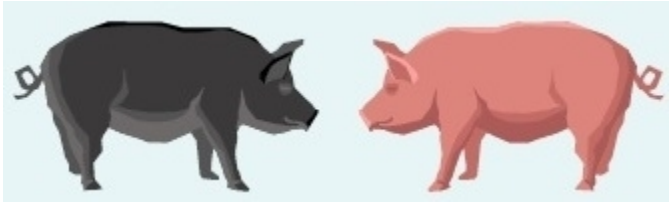
Limitation of the placental area by the litter size
=> smaller piglets
=> and lower chance of survival
(Rootwelt et al., 2013)

Placental insufficiency can impact survival from day 40 of pregnancy
(Knight et al., 1977; Marsteller et al., 1997)



Influence of placental metabolism on piglet survival

Genetic breed influences piglet survival.
In particular, piglets born from Meishan sows had a lower risk of stillbirth than piglets born from Large White sows
(Canario et al. 2006)



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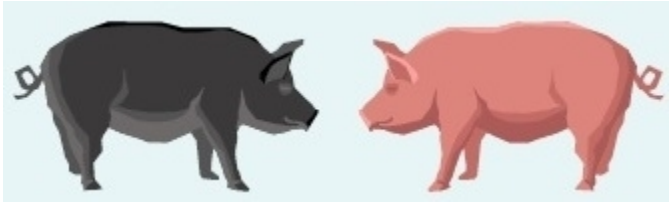
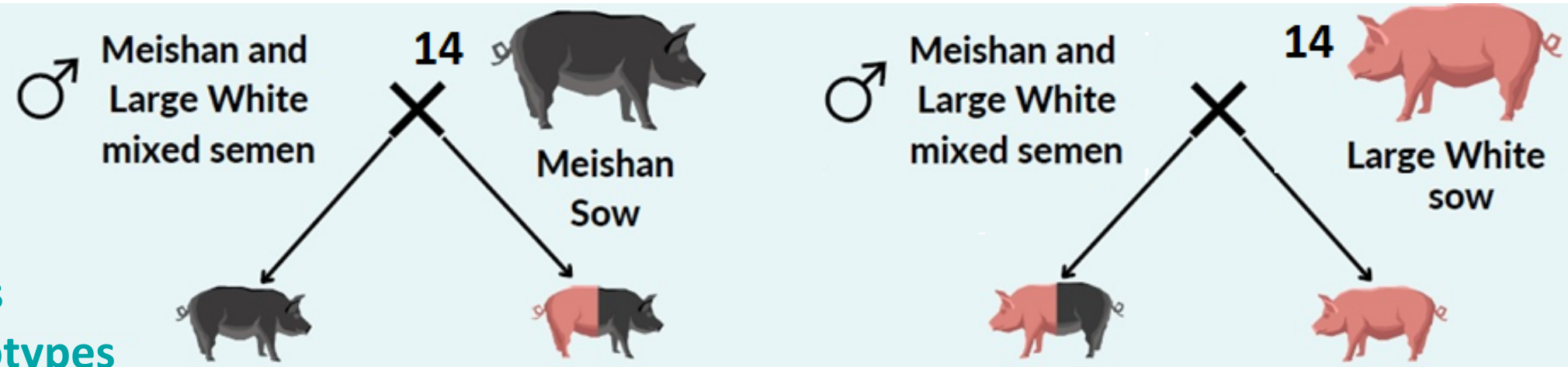


Objectives of the study:

- To study the metabolism of placenta with metabolomics analyses at the end of the gestation in both Large White and Meishan breeds

- To better understand the role of placenta in the determination of piglet maturity

Experimental design



Fetus Genotypes

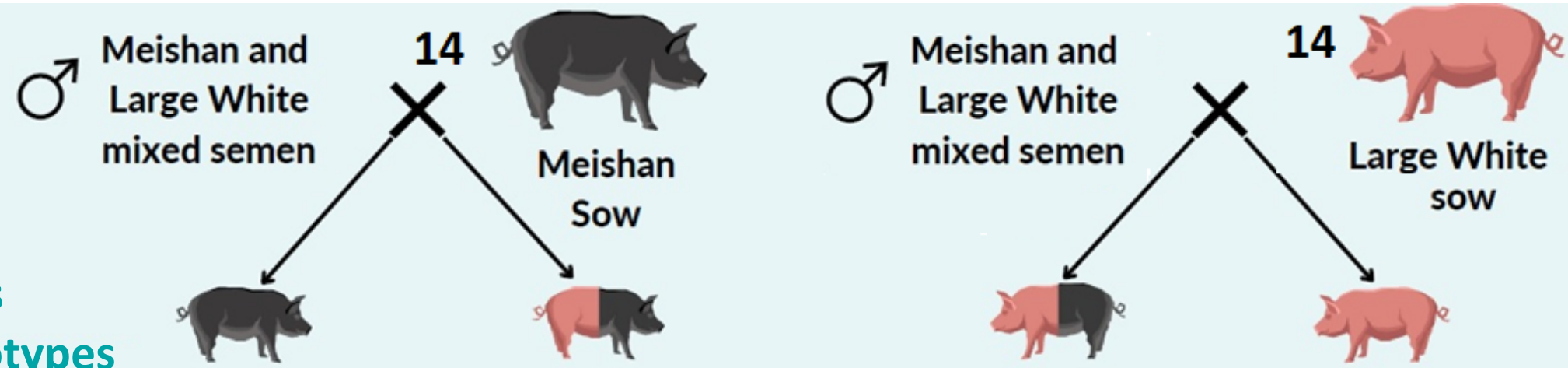
Gestation days D90 and D110 (Farrowing at D115)

Samples N=224; 4 Genotypes * 2 Days * 2 Sexes * 3 Maturity status * 7 Replicates

Tissues Placenta and Endometrium anr PORCINET

Analyses Metabolomics and Transcriptomics anr CO-LOCATION

Experimental design



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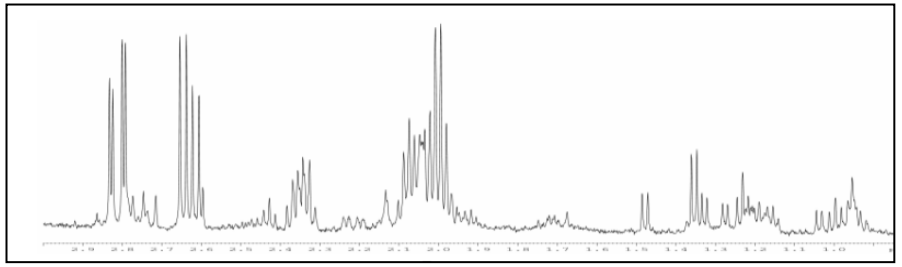
^{1}H-NMR acquisition and statistical analyses

Extraction of hydrophilic metabolites

NMR 600 MHz
Bruker Avance III HD
(MeTaToul-AXIOM)



^{1}H-NMR spectra

ASICS package
Lefort et al. 2019

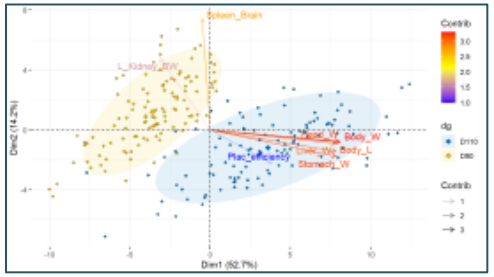
48 Metabolites

224 Samples

$$\begin{matrix} a_{1,1} & a_{1,2} & a_{1,n} \\ a_{2,1} & a_{2,2} & a_{2,n} \\ a_{m,1} & a_{m,2} & a_{m,n} \end{matrix}$$

48 identified, filtered and selected **metabolites**

Analyses
PCA, PLS-DA

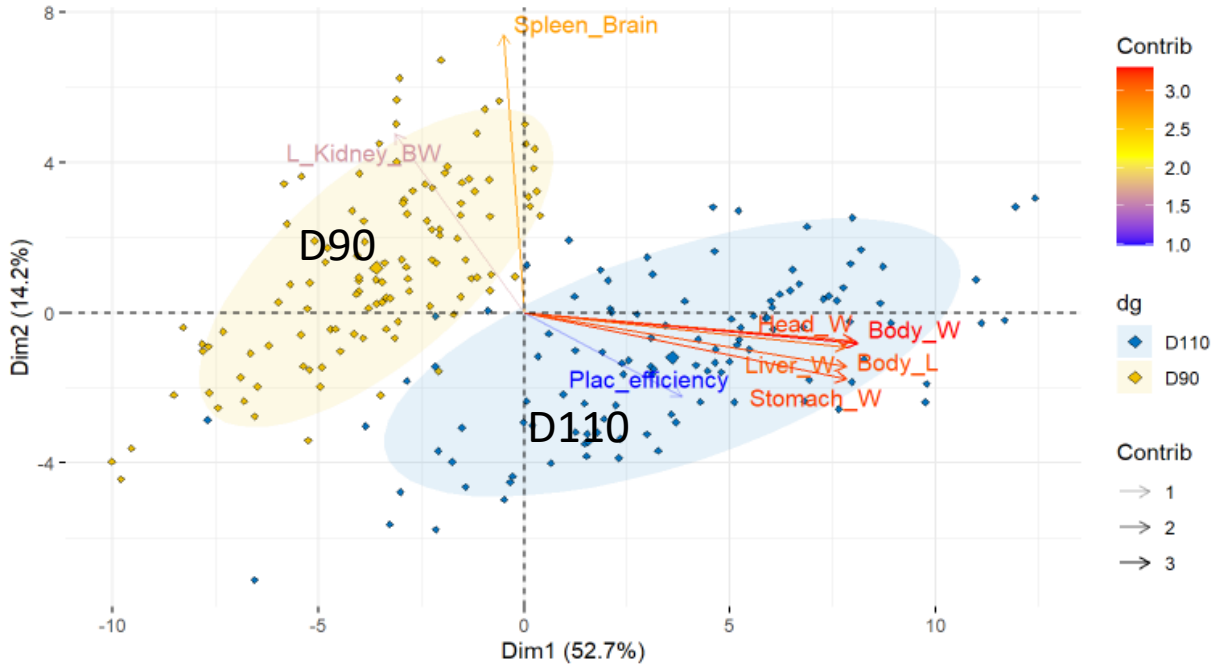


Evolution of the fetus phenotypes at the end of gestation

Strong separation between D90 and D110

Strong separation between LW and MS at D90 and D110

Data: Fetus phenotyes,
Analysis: PCA
Bi-plot



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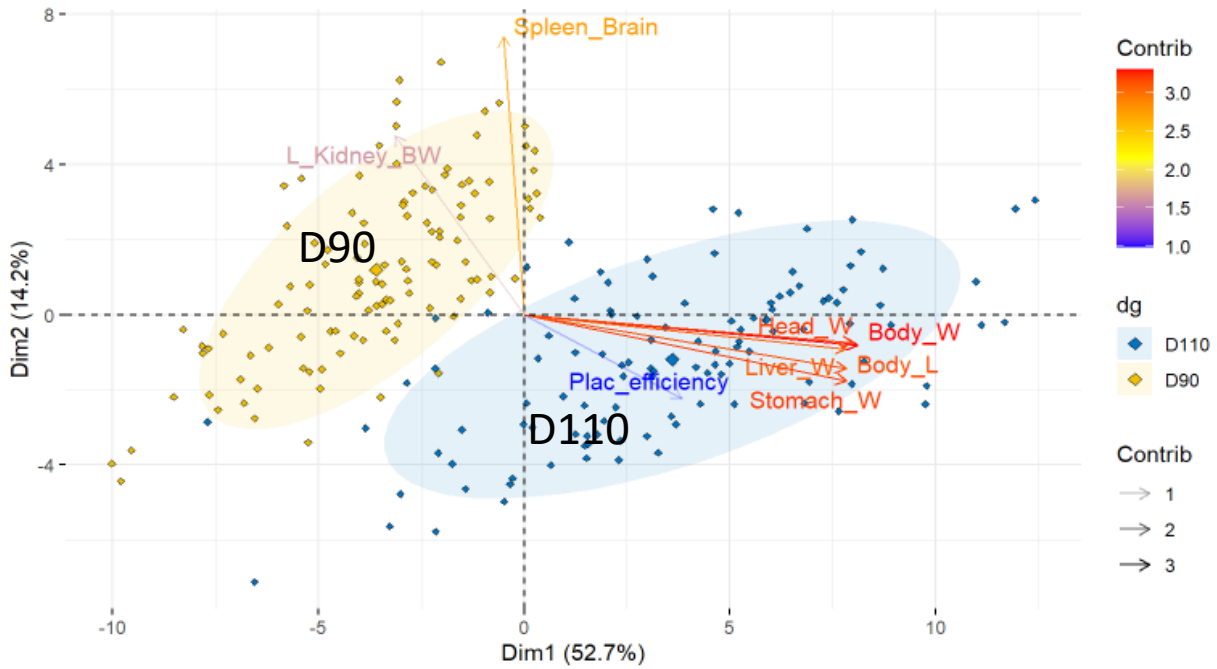

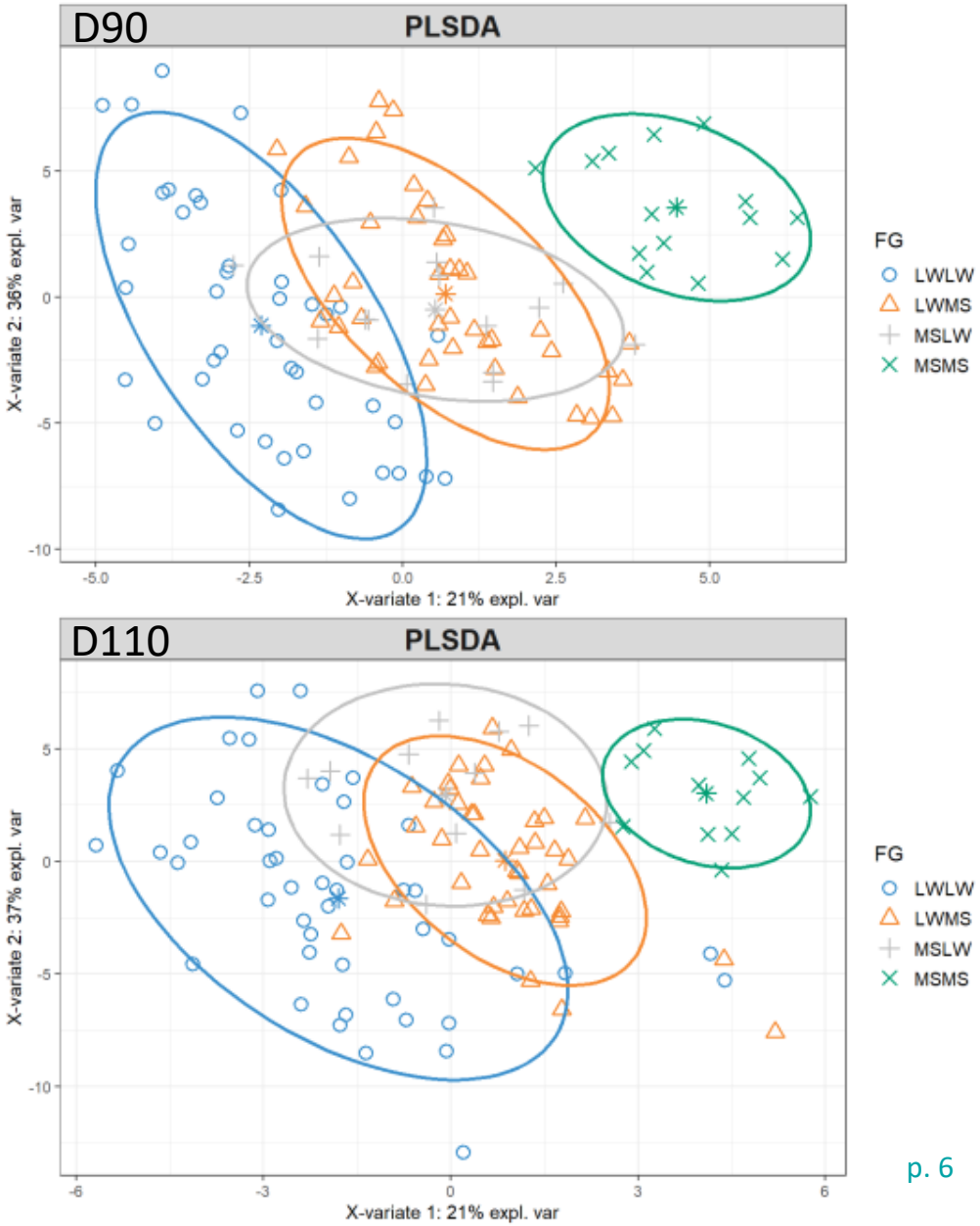

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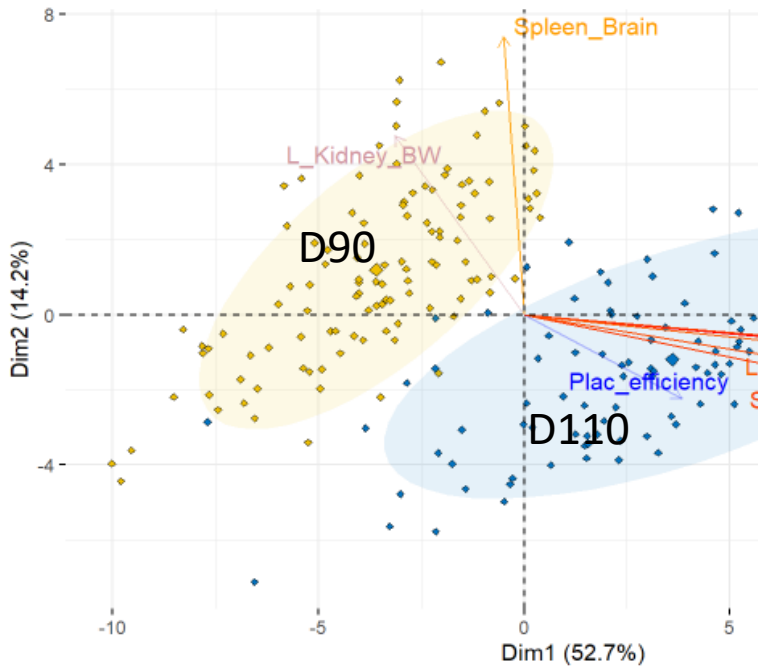
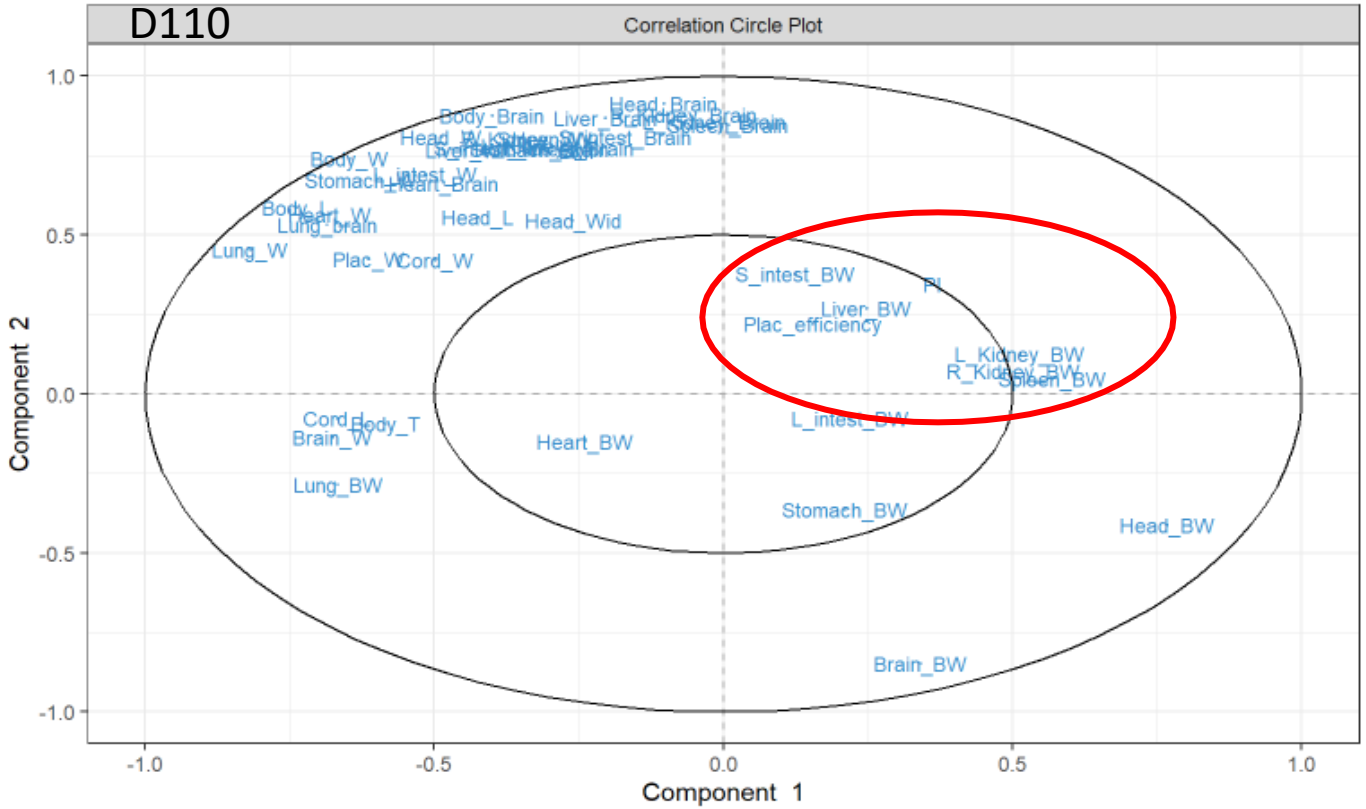
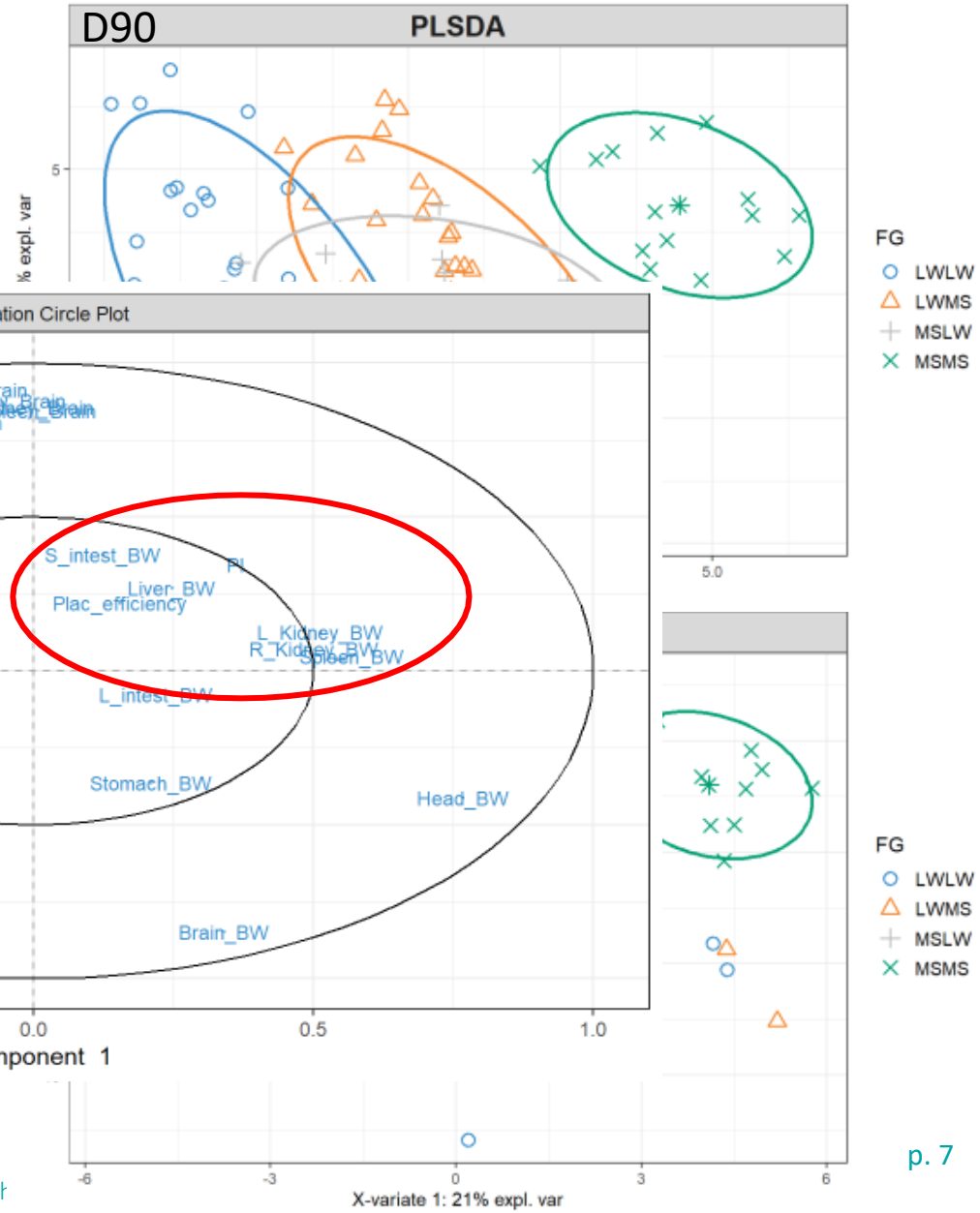




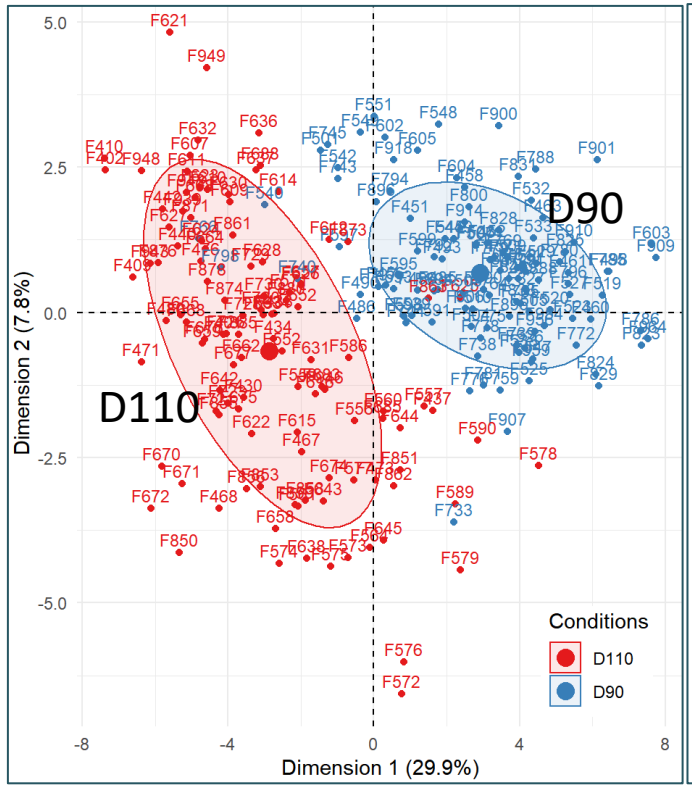


Evolution of the placental metabolome at the end of gestation

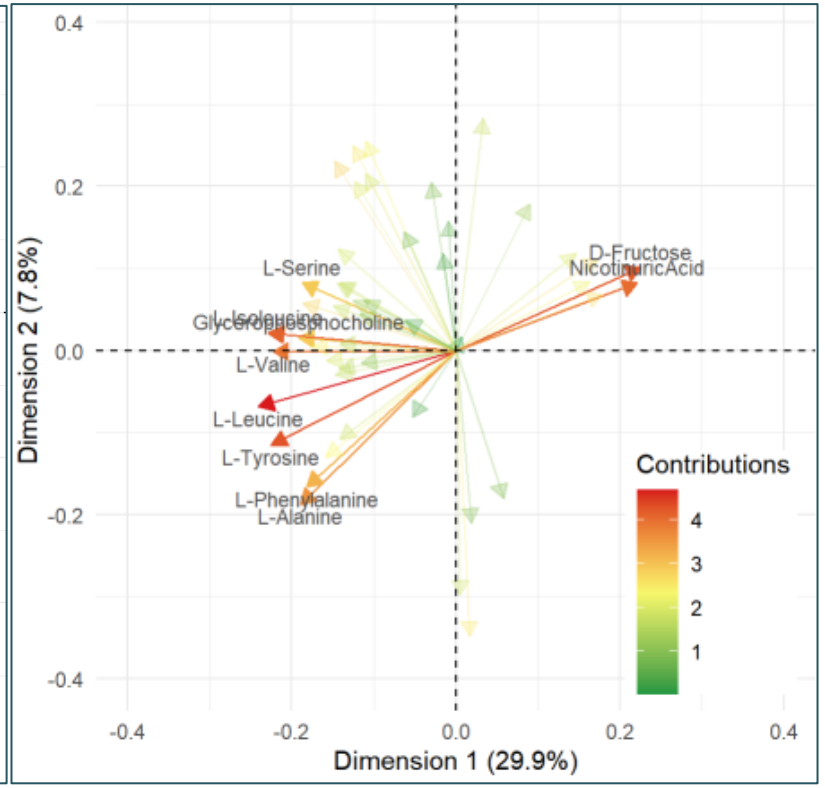
Comparison 90D vs 110D

Analysis: PCA

Individual plot



Variable plot



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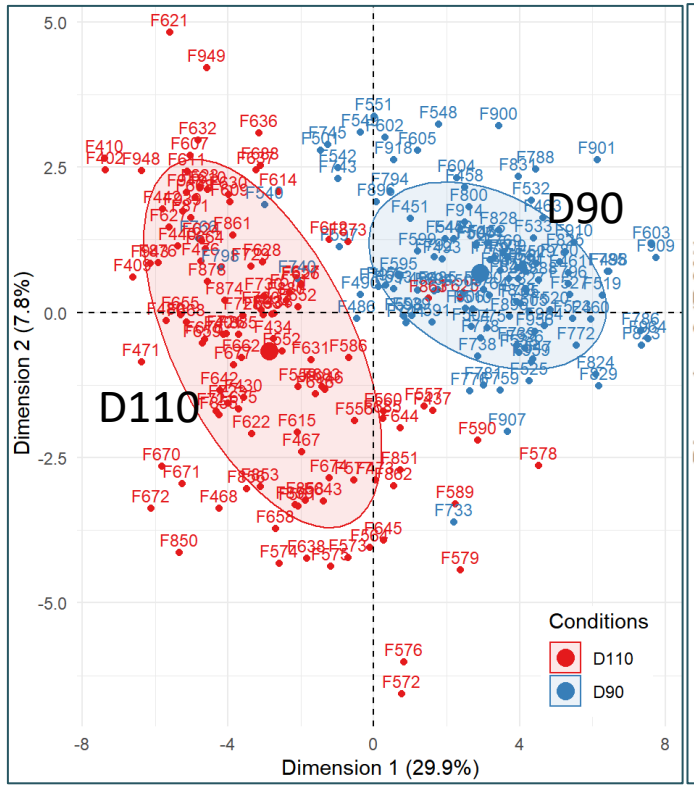

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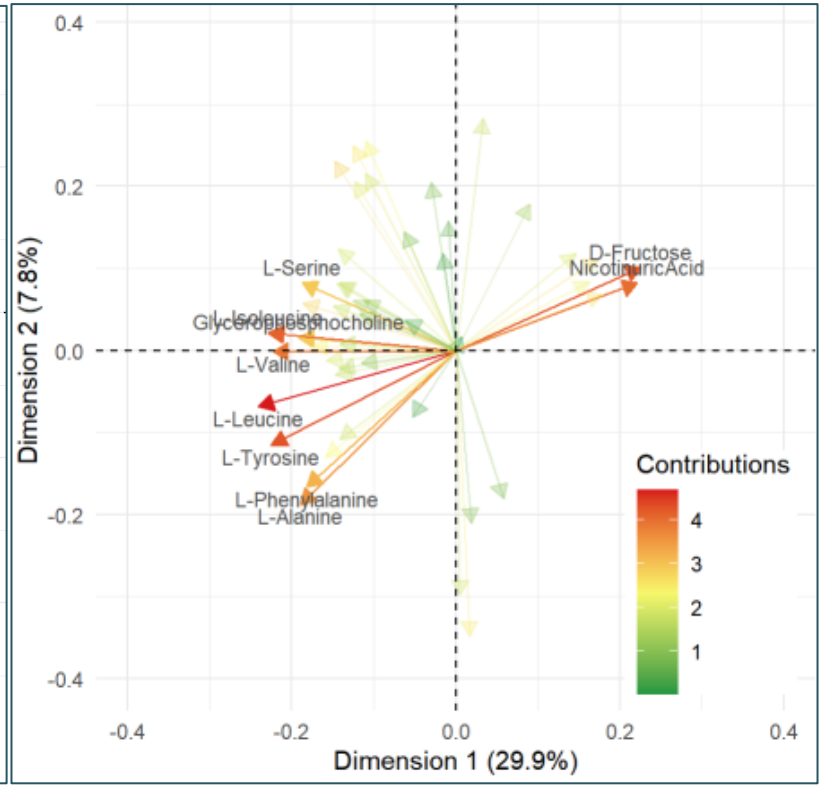
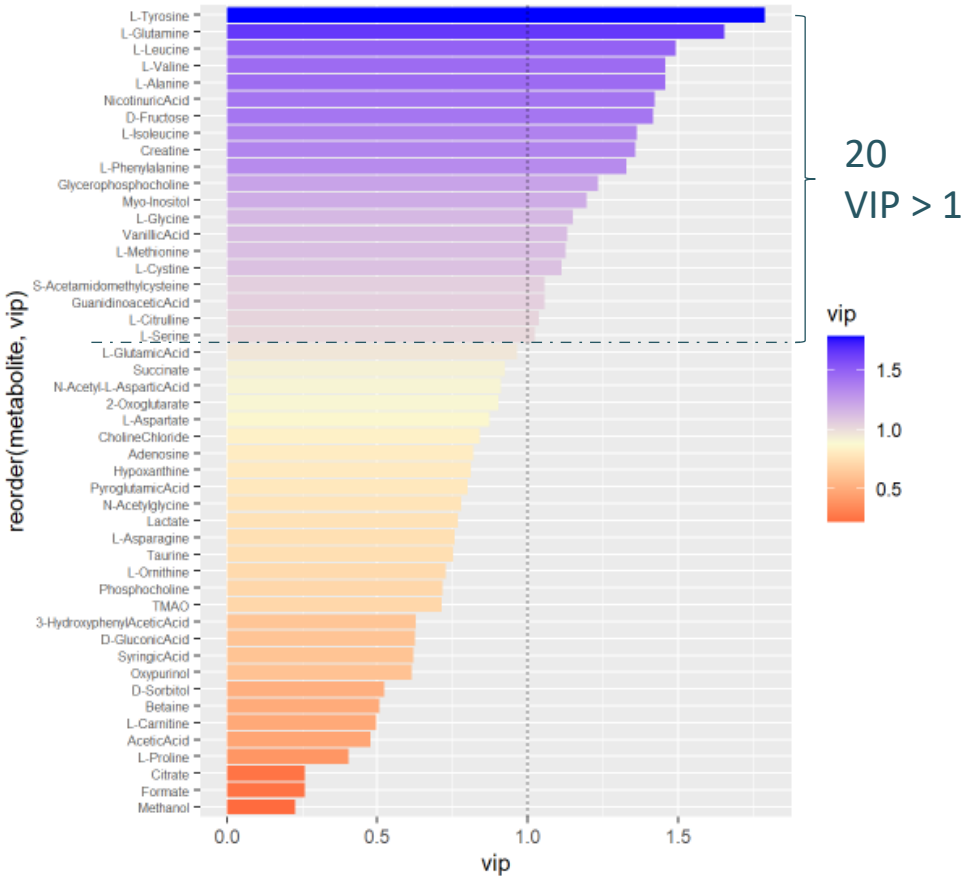


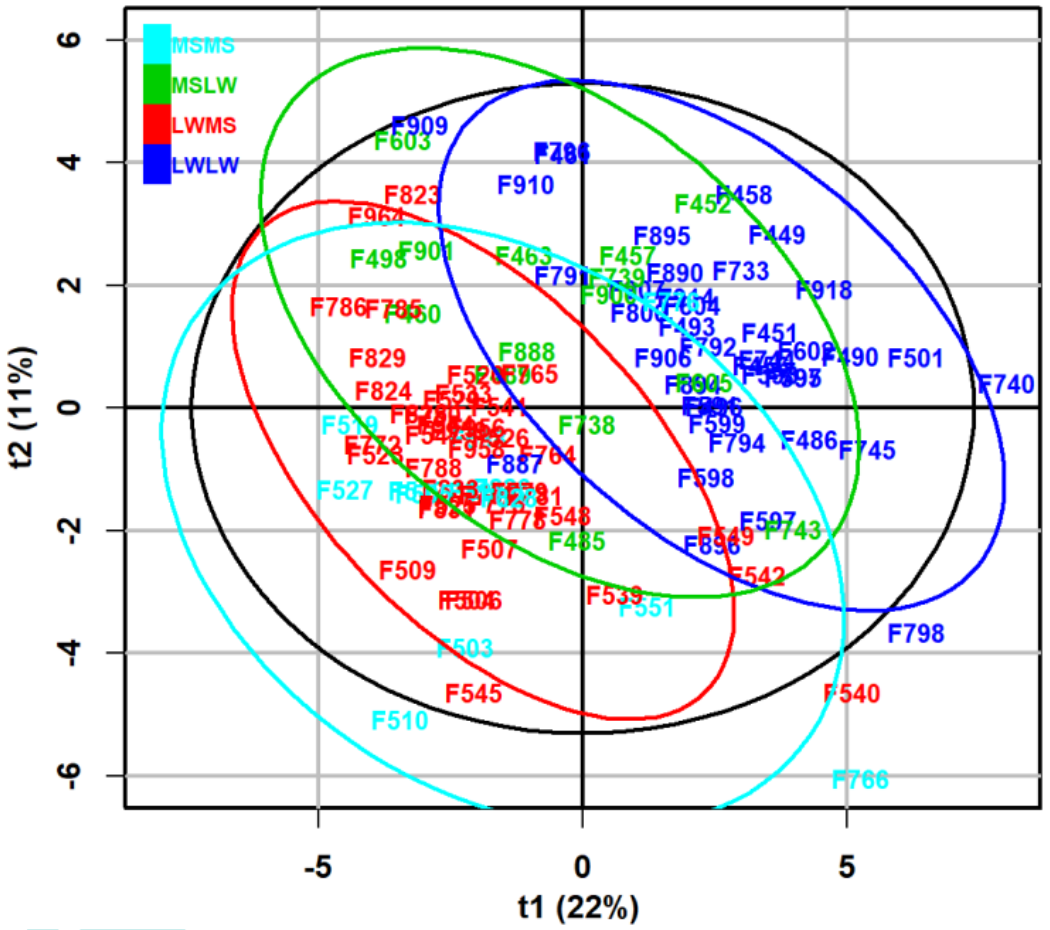
Analysis: PLS-DA



Comparison of the placental metabolome between genotypes

Analysis: PLS-DA

D90



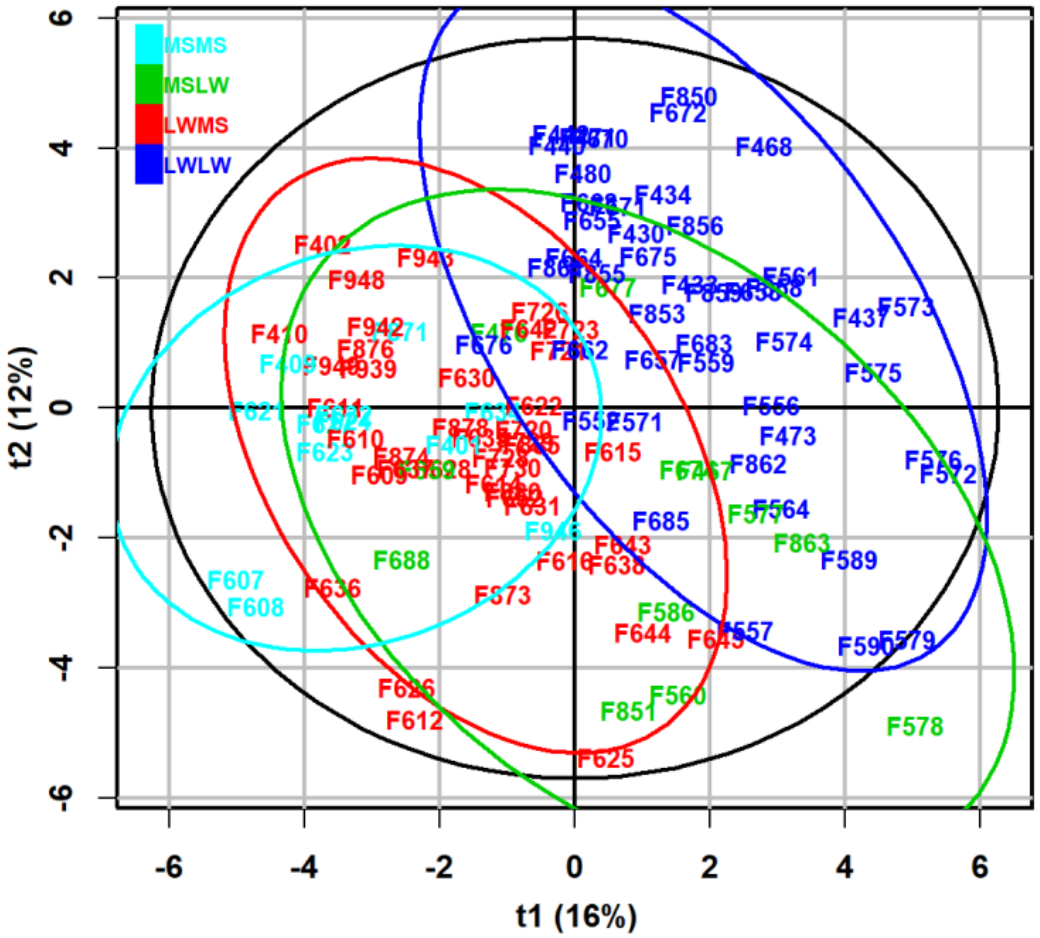
19 metabolites
VIP > 1

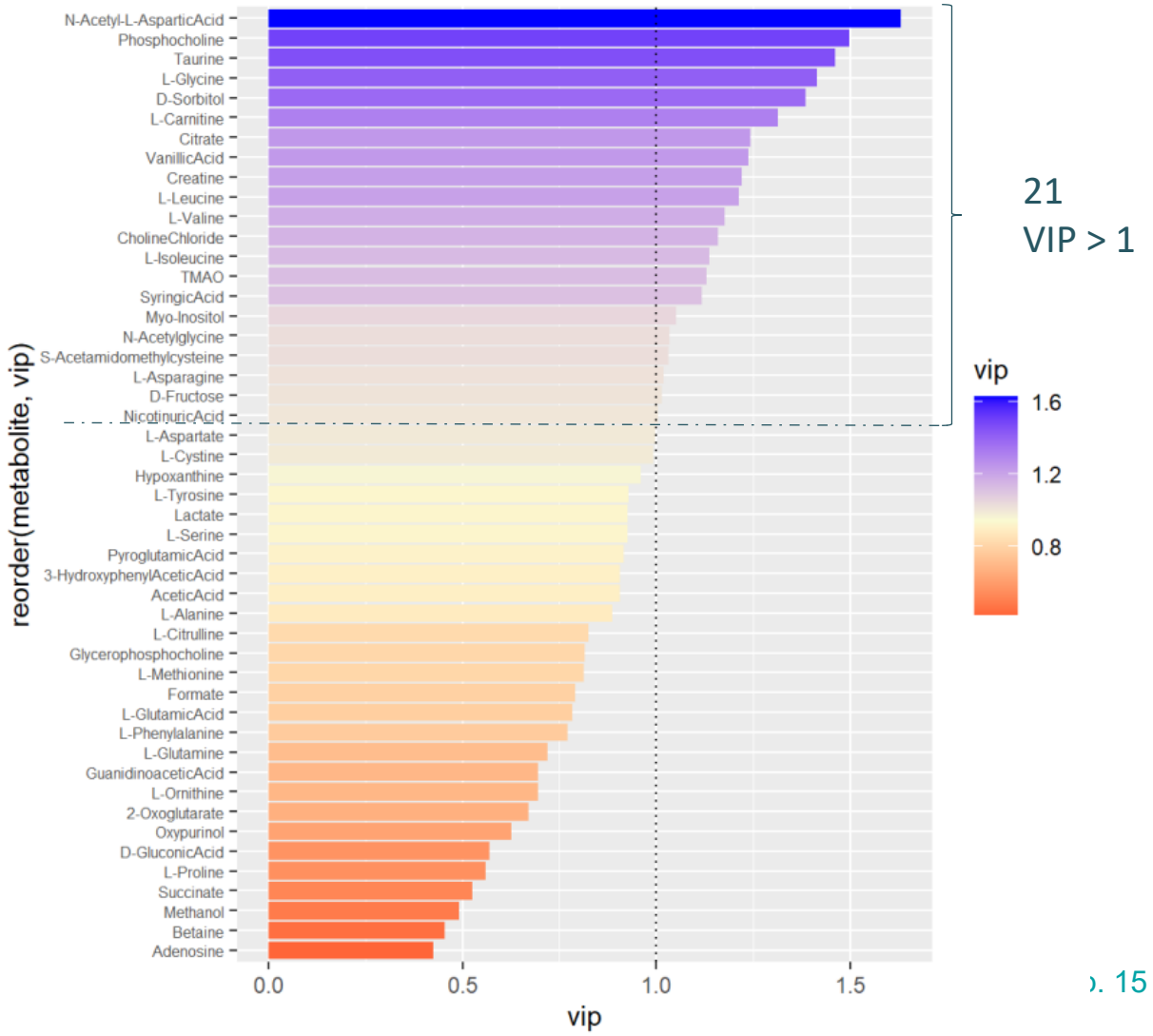
- 2-oxoglutarate
- D-Fructose
- Glycerophosphocholine
- GuanidinoaceticAcid
- L-Alanine
- L-Citrulline
- L-Cystine
- L-Glutamine
- L-Glycine
- L-Isoleucine
- L-Leucine
- L-Methionine
- L-Phenylalanine
- L-Tyrosine
- L-Valine
- Myo-Inositol
- NicotinuricAcid
- S-Acetamidomethylcysteine
- VanillicAcid

Comparison of the placental metabolome between genotypes

Analysis: PLS-DA

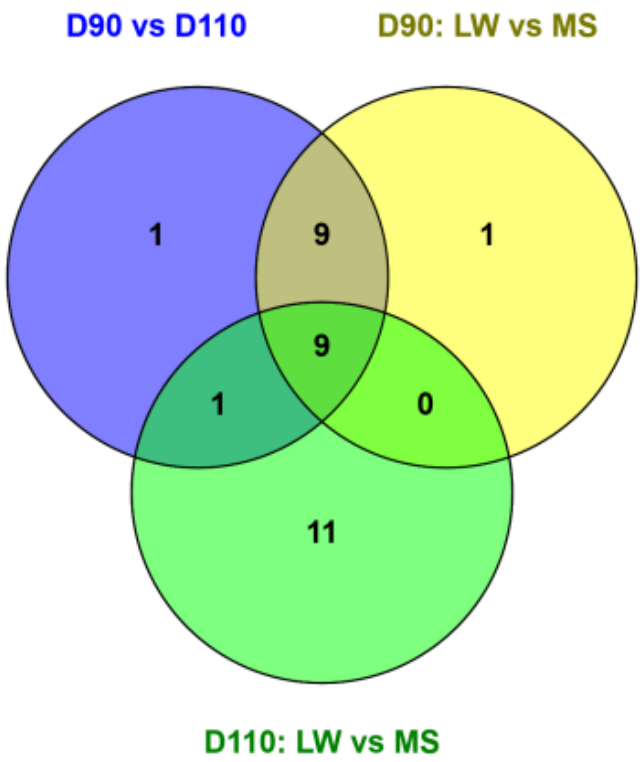
D110





Characteristics of a placenta associated with higher maturity

Venn diagram of discriminant metabolites previously identified



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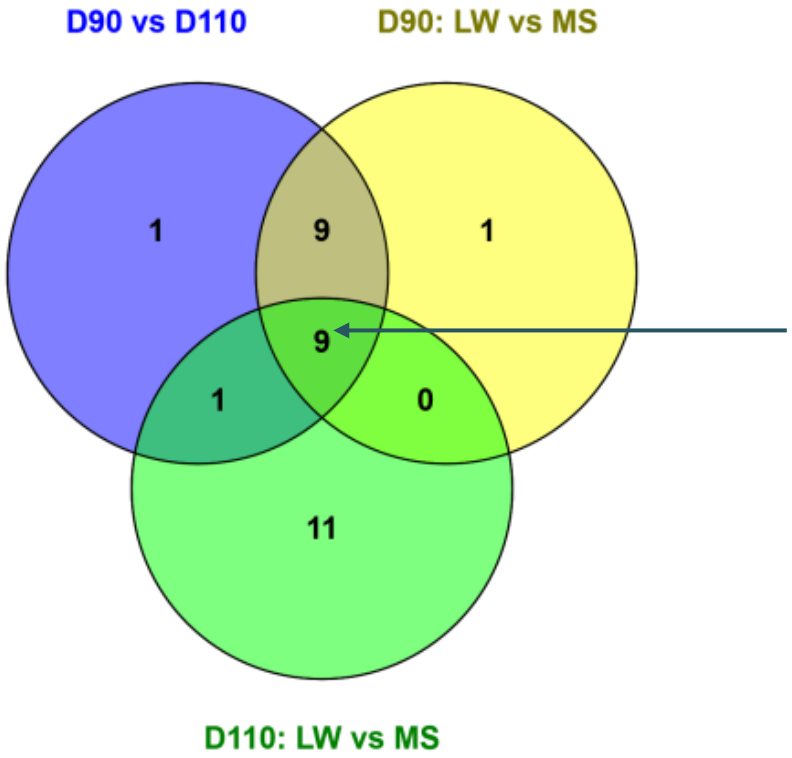

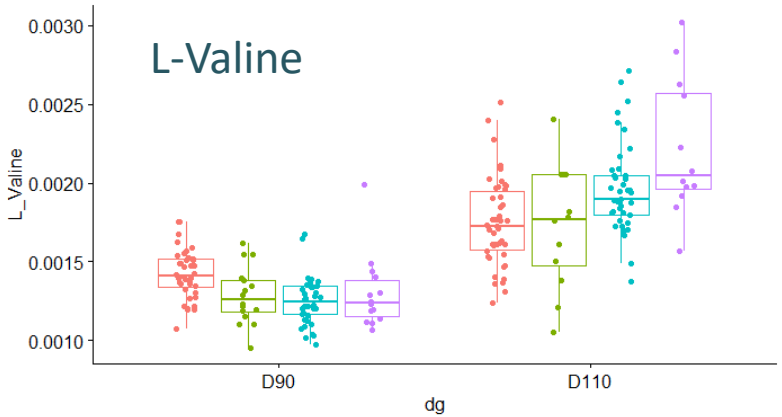

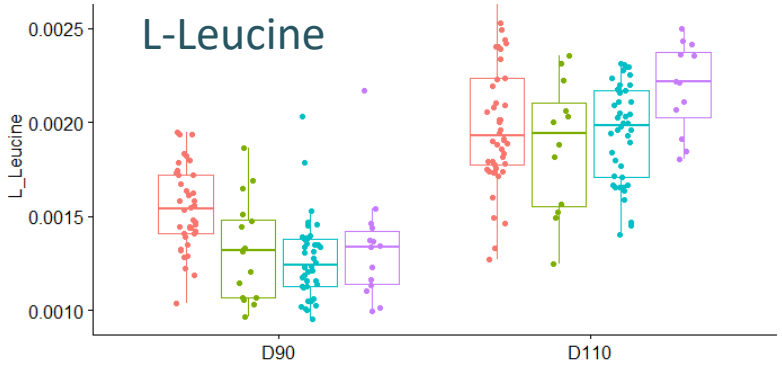

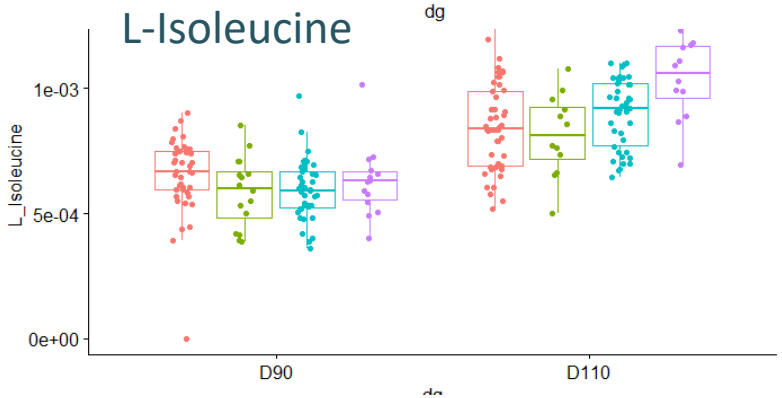

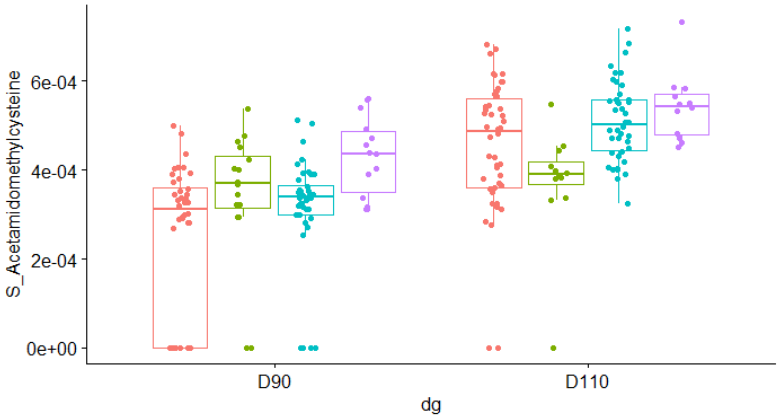

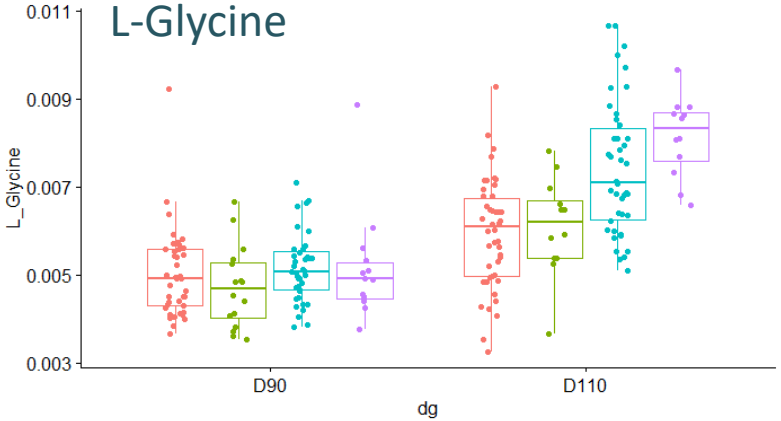

FG LWLW MSLW LWMS MSMS

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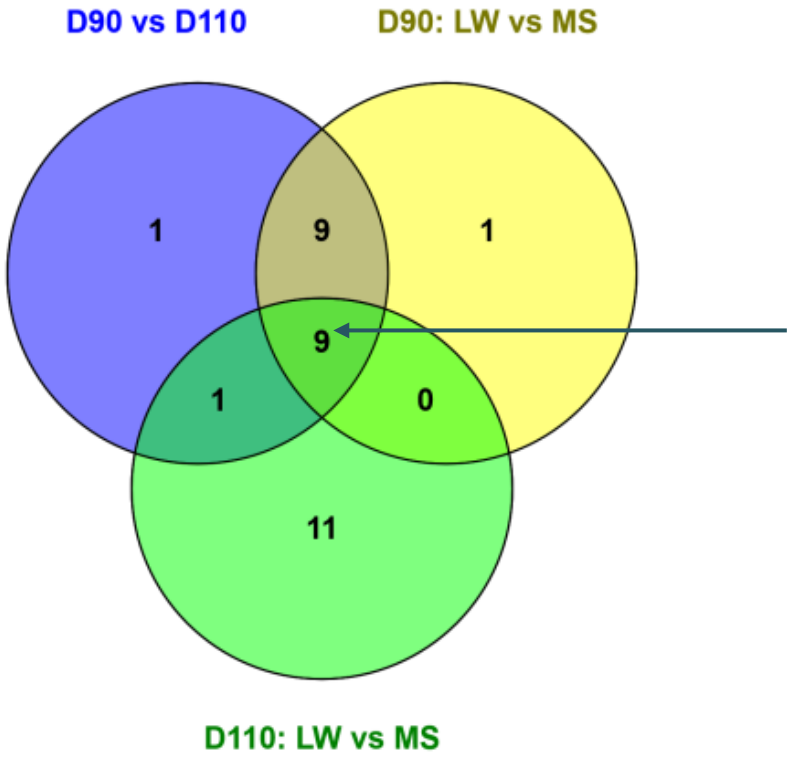
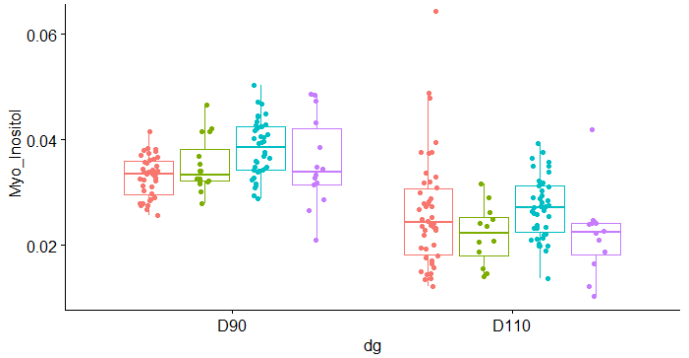
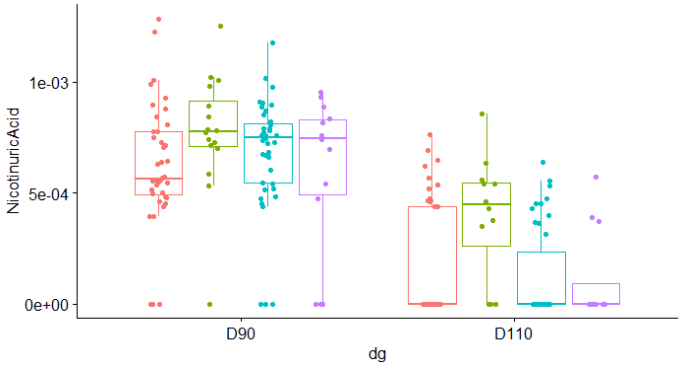


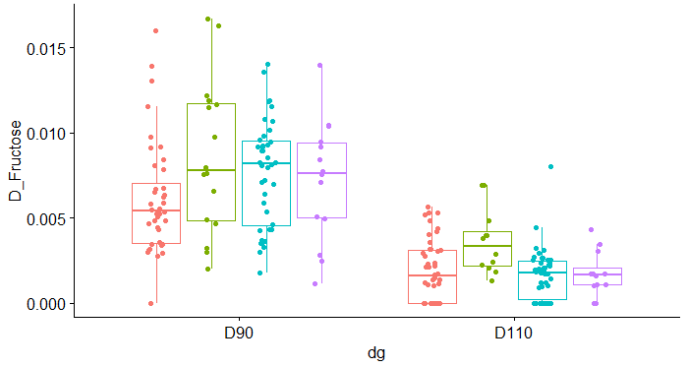
Myo-Inositol



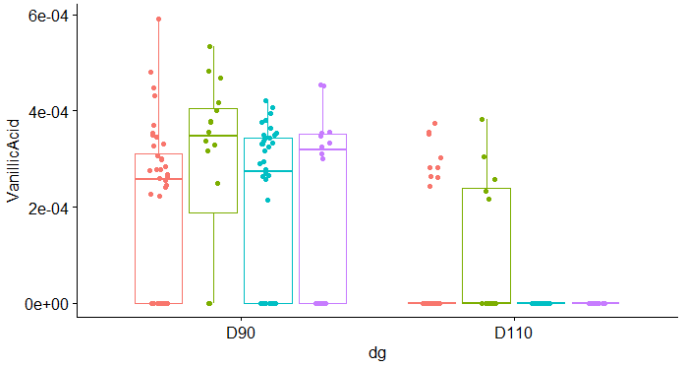
Nicotinuric acid



D-Fructose



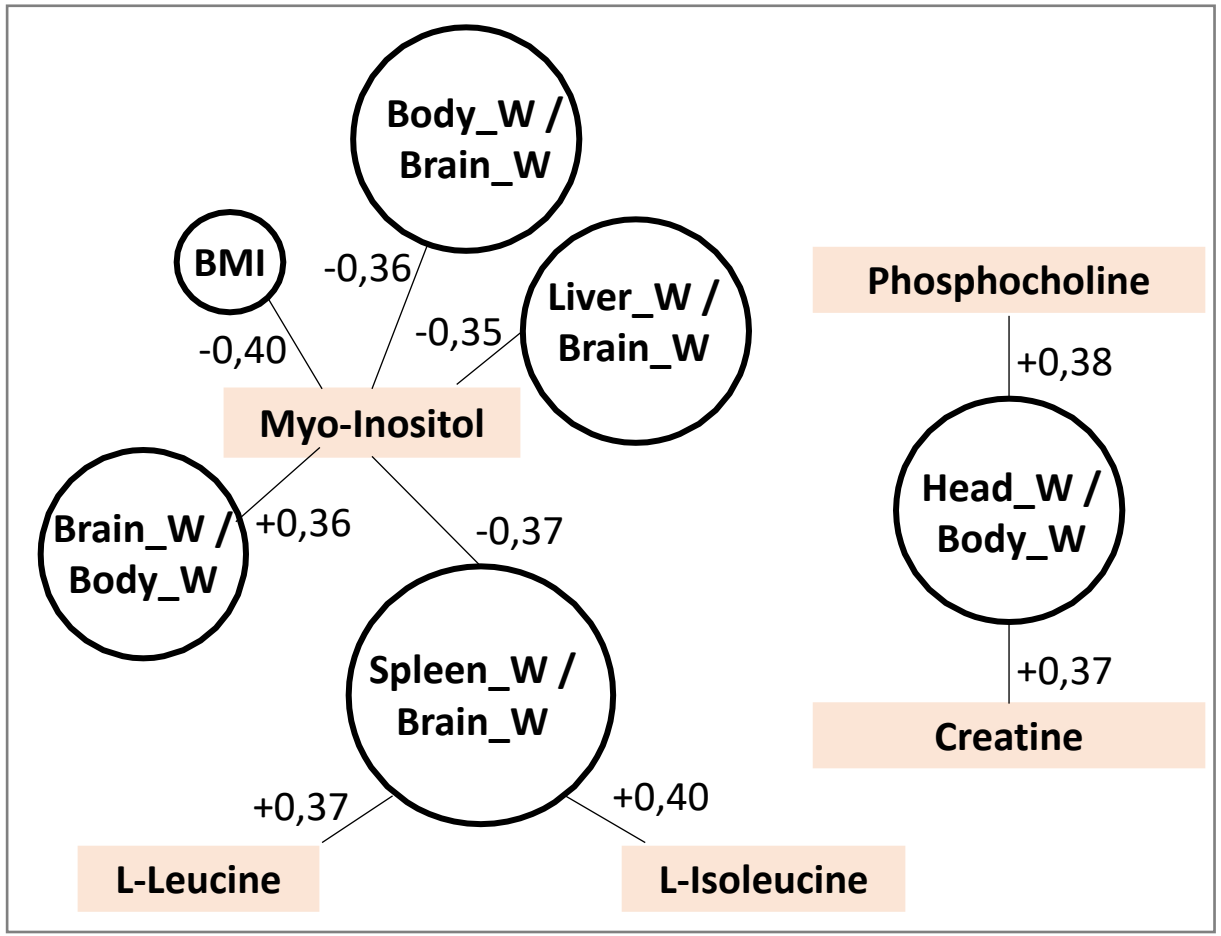
Vanillic acid



FG LWLW MSLW LWMS MSMS

Correlations between fetus phenotypes and placental metabolites

Bi-partite plot



Conclusion and perspectives

A new step in the knowledge of the role of placenta in piglet maturity development

Metabolites associated with intra-uterine fetal growth restriction (IUGR):
- Myonisitol : confirmation in both humans (Dessi & Fanos, 2013; Barberini et al., 2014) and pigs (Nissen et al. 2011; Lefort et al. 2020)
- Fructose: confirmation in pigs (Lefort et al. 2020)
- Nicotinuric acid and vanillic acid: new potential biomarkers of IUGR

Further analyses are required to confirm their potential role in IUGR

The long term perspectives of this work will be to slightly modify the diet of the gestant sows at the end of the gestation to improve the piglet maturity at birth and to increase the survival rate of piglets.

Conclusion and perspectives

Foeto-maternal interactions

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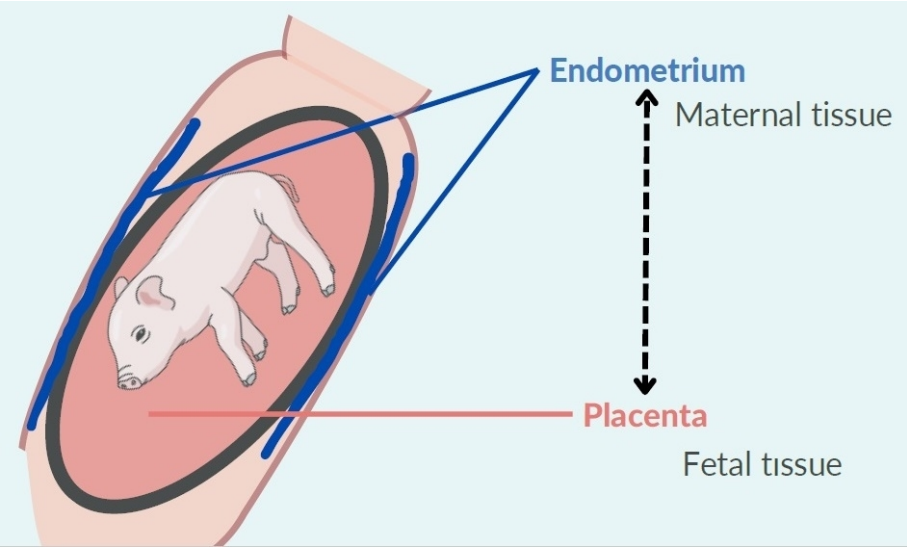
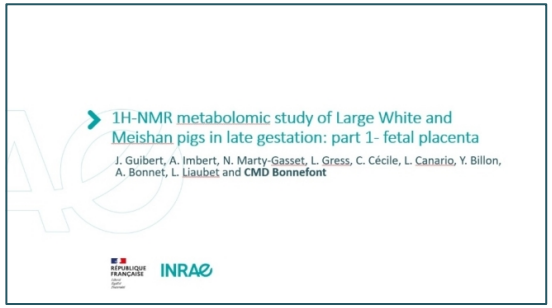
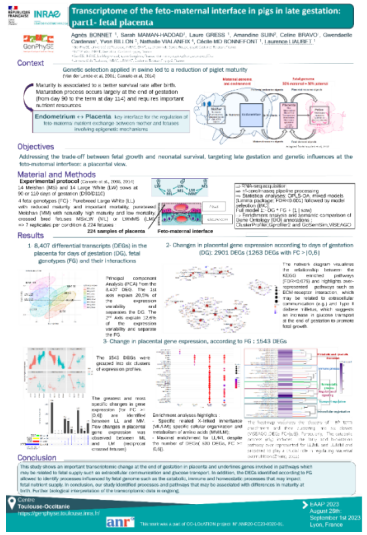


Placenta Metabolomics

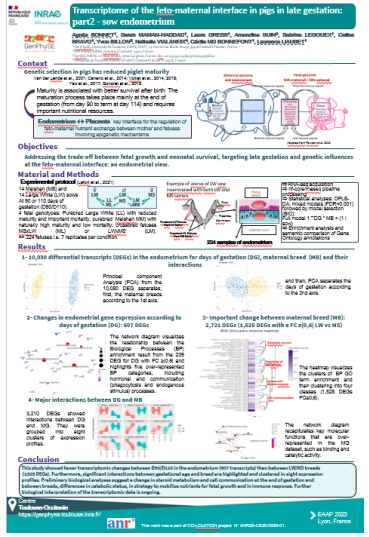


Placenta Transcriptomics



Endometrium Metabolomics

Endometrium Transcriptomics



Thanks to

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Nassim DUPRAT
Nathalie MARTY-GASSET

METATOUL platform

Cécile CANLET

anr® **PORCINET**

anr® **CO-LOCATION**

Thank you for your attention

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