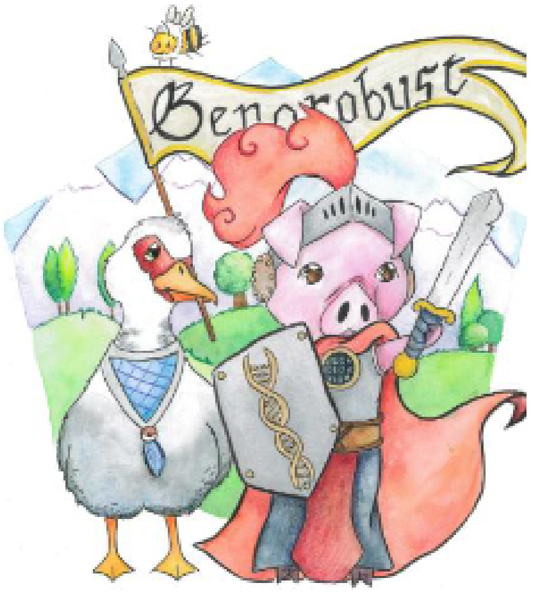
Nassim Duprat

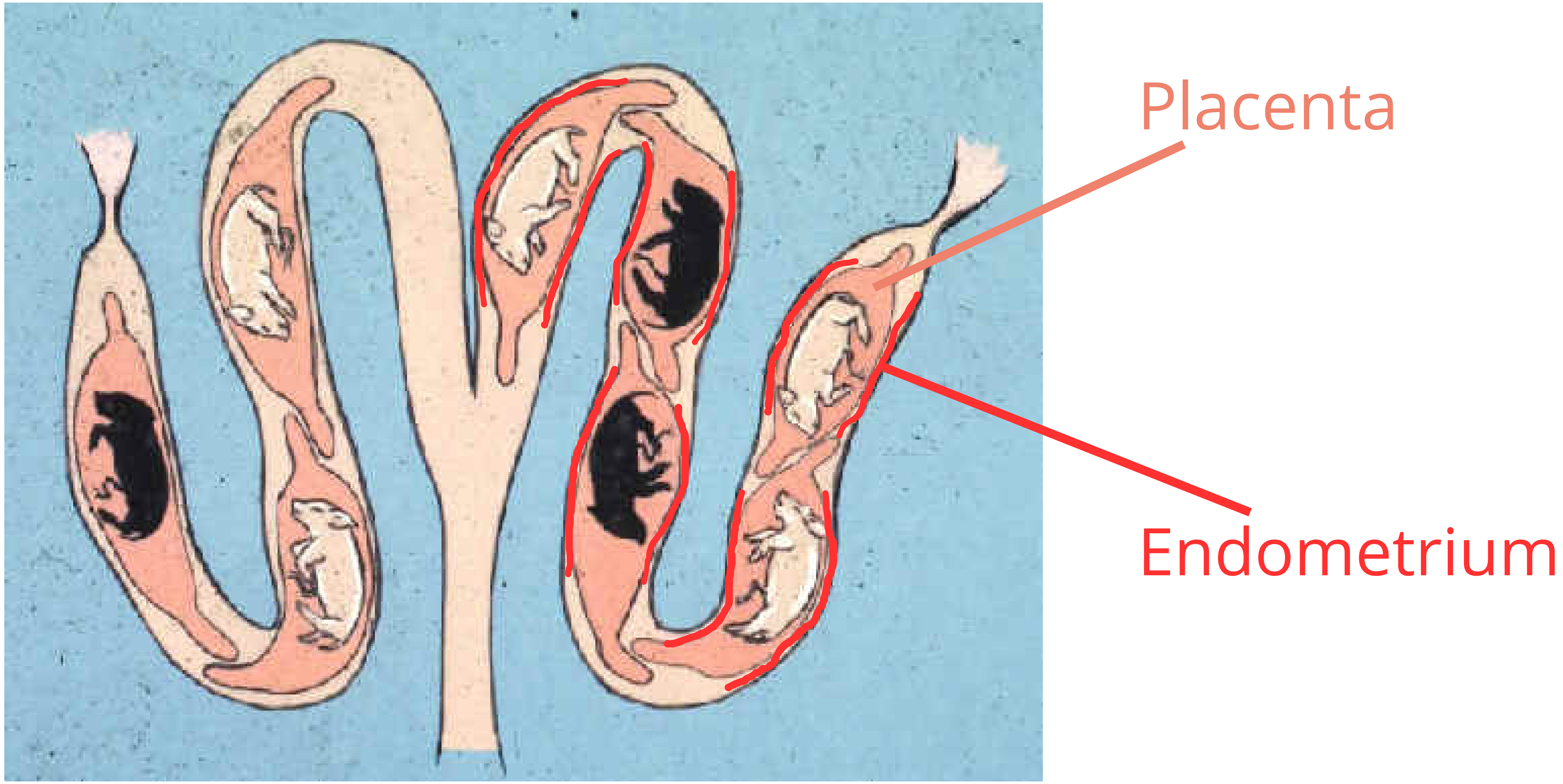
Multi-omics integration of the pig endometrium in late gestation

(Motivation : Identification of biomarkers of piglet survival)

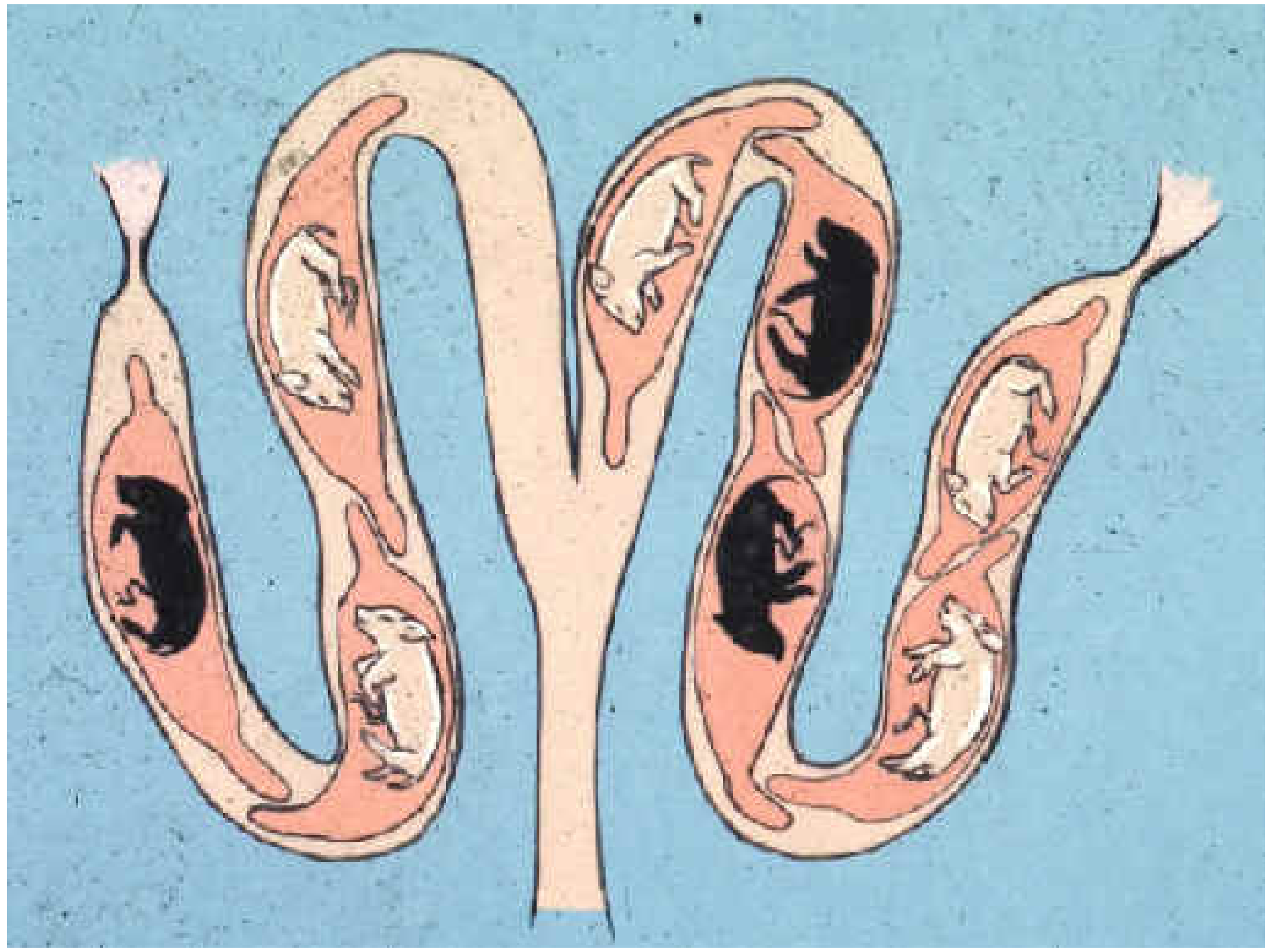


Laurence Liaubet, Cecile Bonnefont, Agnès Bonnet

Biological context



Biological context



thermoregulation

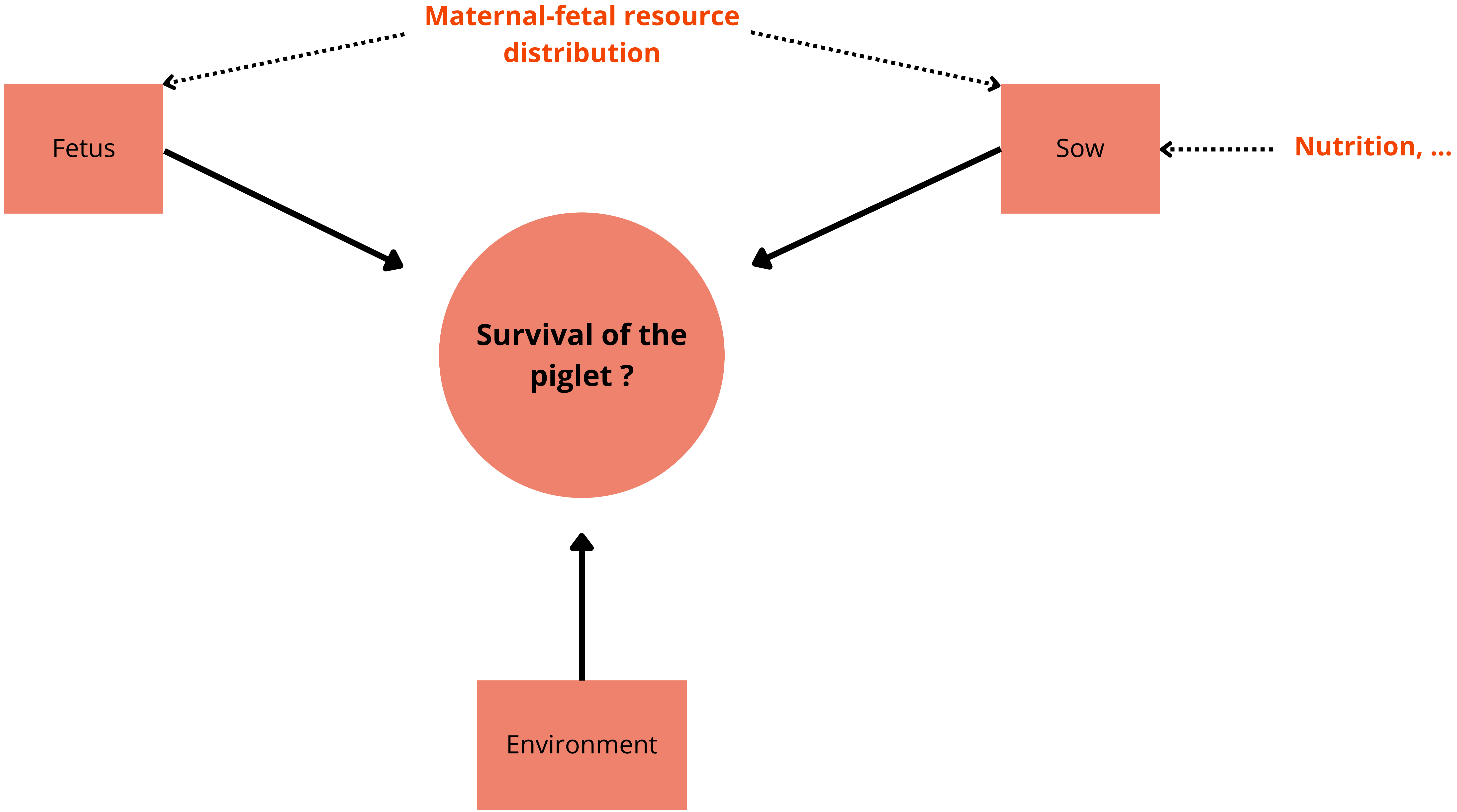
access to teats

↗ neonatal death

Gestation

Birth

Biological context



Maternal-fetal resource distribution

Fetus

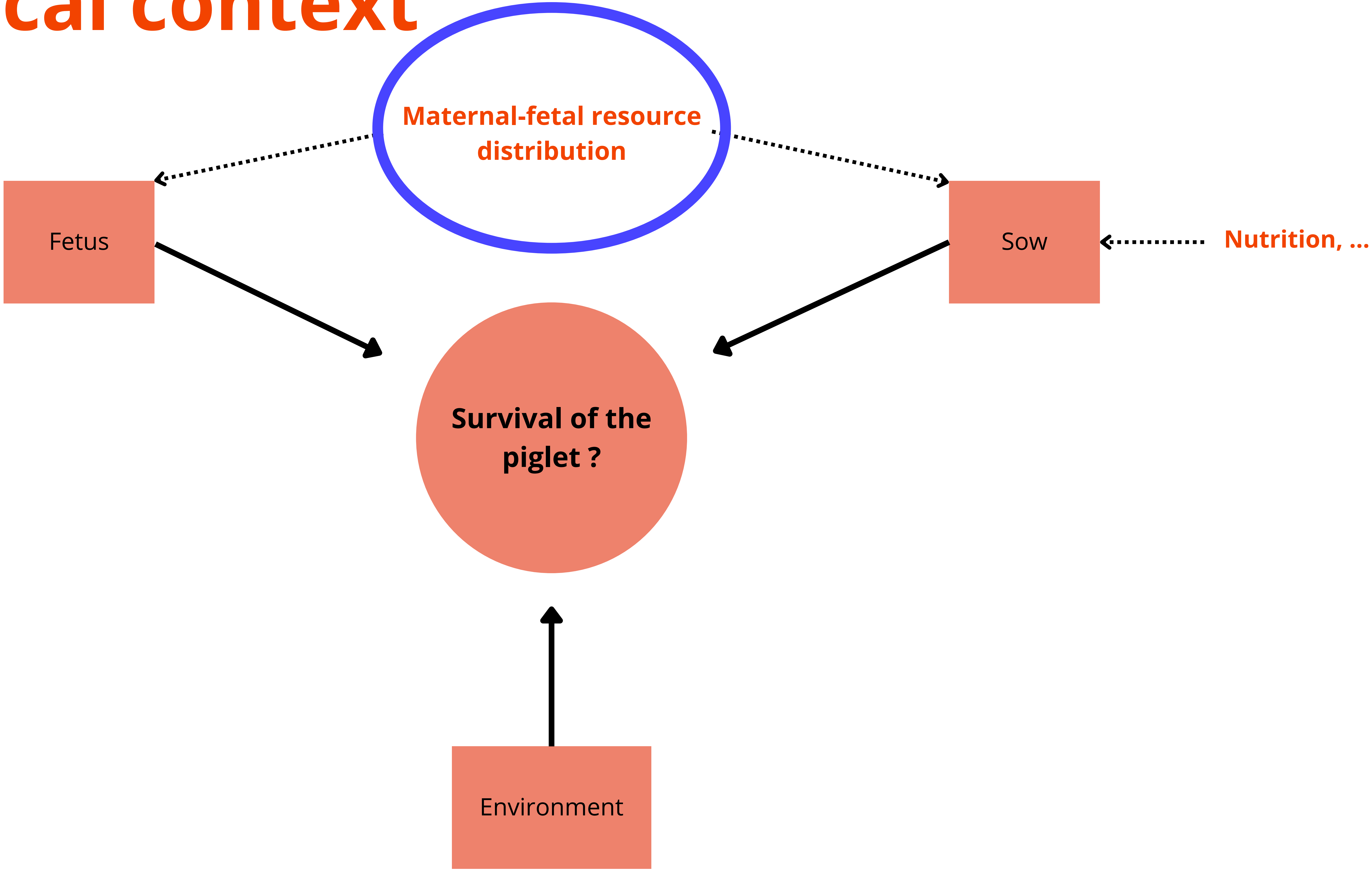
Sow

Nutrition, ...

Survival of the piglet ?

Environment

Biological context



Maternal-fetal resource distribution

Fetus

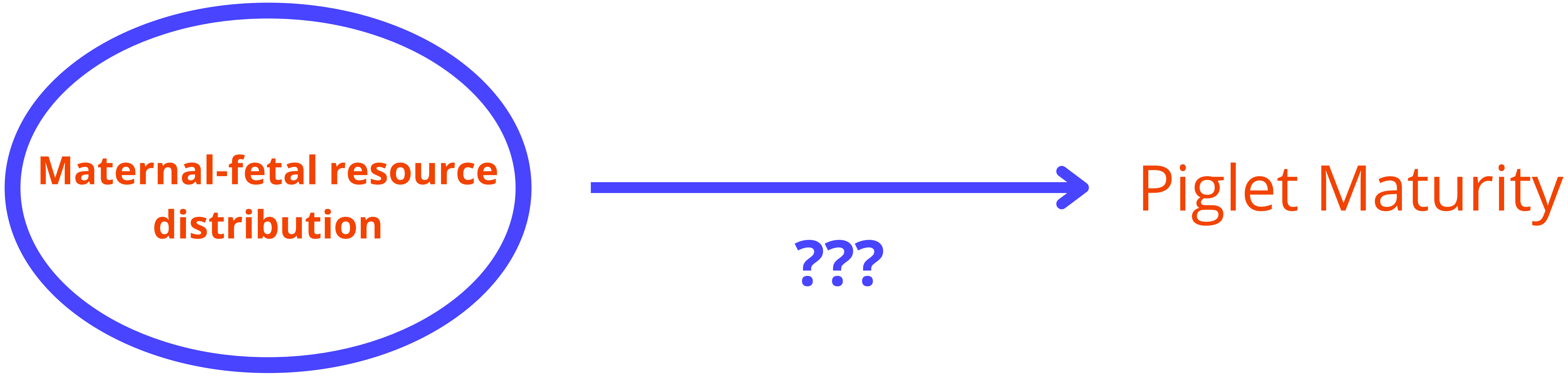
Sow

Nutrition, ...

Survival of the piglet ?

Environment

Biological context



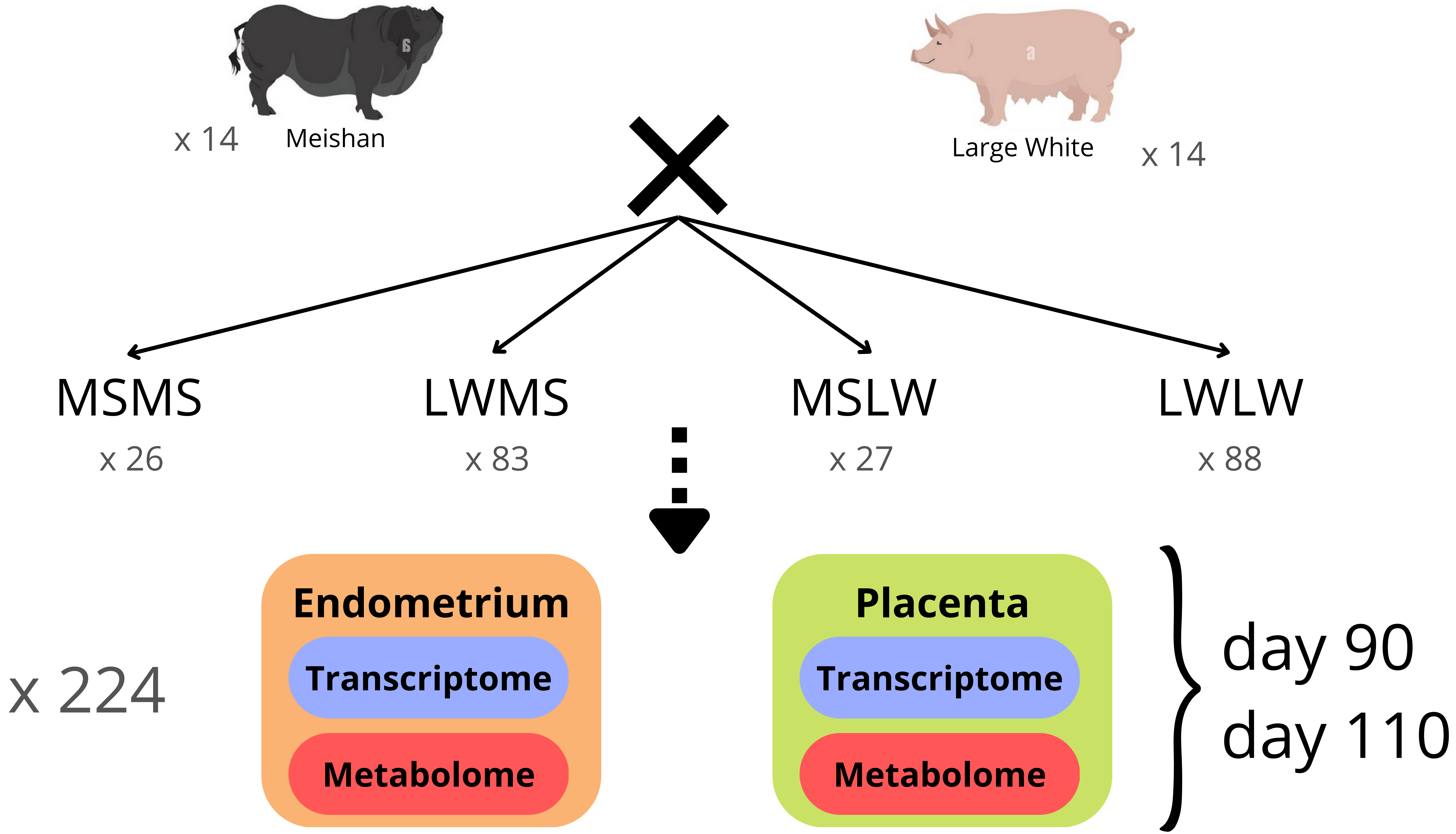
Maternal-fetal resource distribution

???

Piglet Maturity

Material and Methods - Co-LOcATION

Experimental design



x 14 Meishan

Large White x 14

MSMS
x 26

LWMS
x 83

MSLW
x 27

LWLW
x 88

x 224

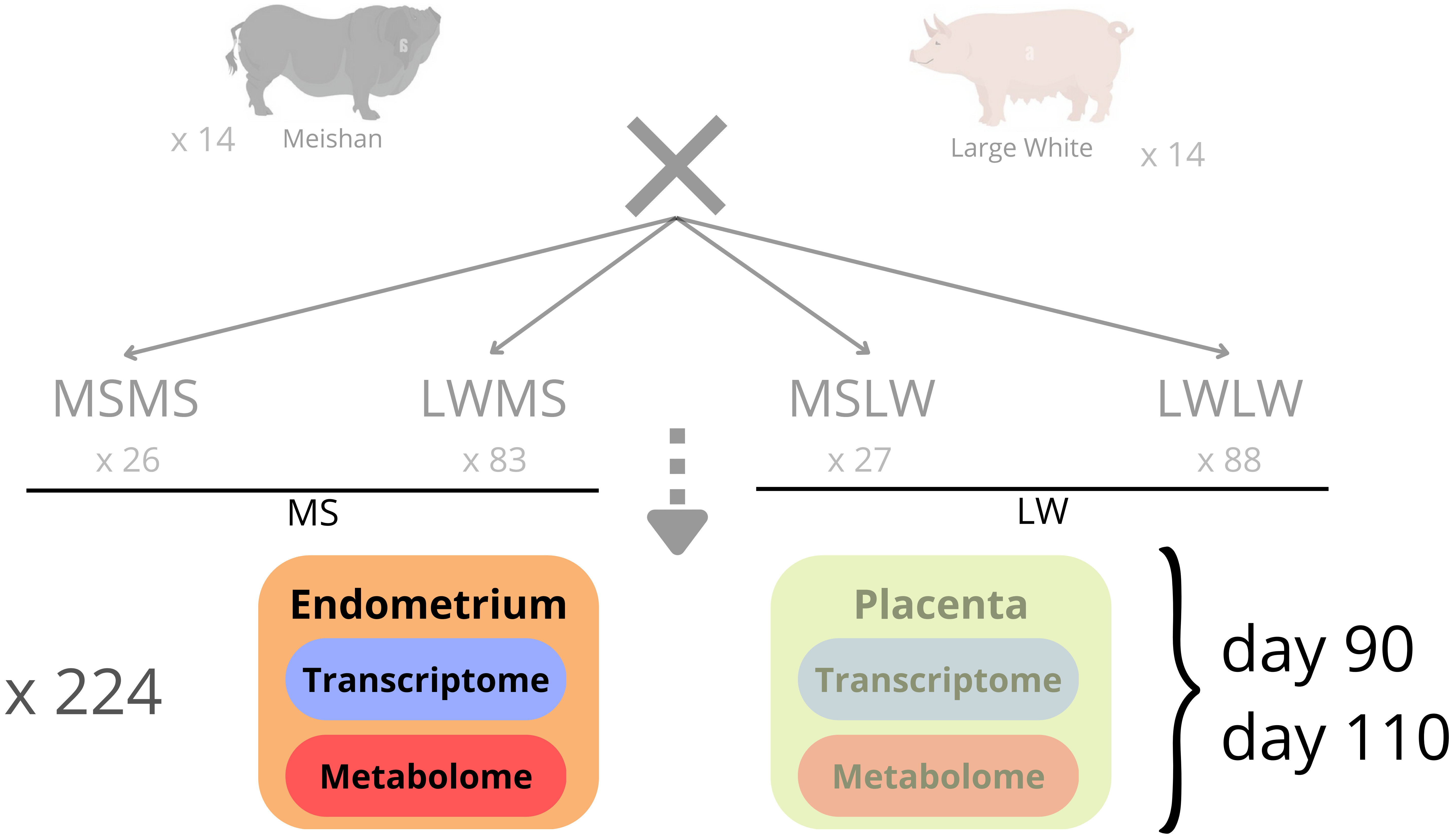
Endometrium
- **Transcriptome**
- **Metabolome**

Placenta
- **Transcriptome**
- **Metabolome**

day 90
day 110

Material and Methods - Co-LOcATION

Experimental design



x 14 Meishan

Large White x 14

MSMS x 26

LWMS x 83

MSLW x 27

LWLW x 88

MS

LW

x 224

Endometrium

Transcriptome

Metabolome

Placenta

Transcriptome

Metabolome

day 90

day 110

Material and Methods - Co-LOcATION

Data Acquisition

Transcriptome

RNA-Seq

Quality control

Remove adaptaters

Mapping

Quantification

nf-core/rnasesq pipeline

Differential analysis

Limma R Package

differential transcriptome :
224 samples x 10080 transcripts

Metabolome

proton NMR

Spectrum pre-treatment

Spectrum alignment on pures spectrums library

Quantification

ASICS R Package

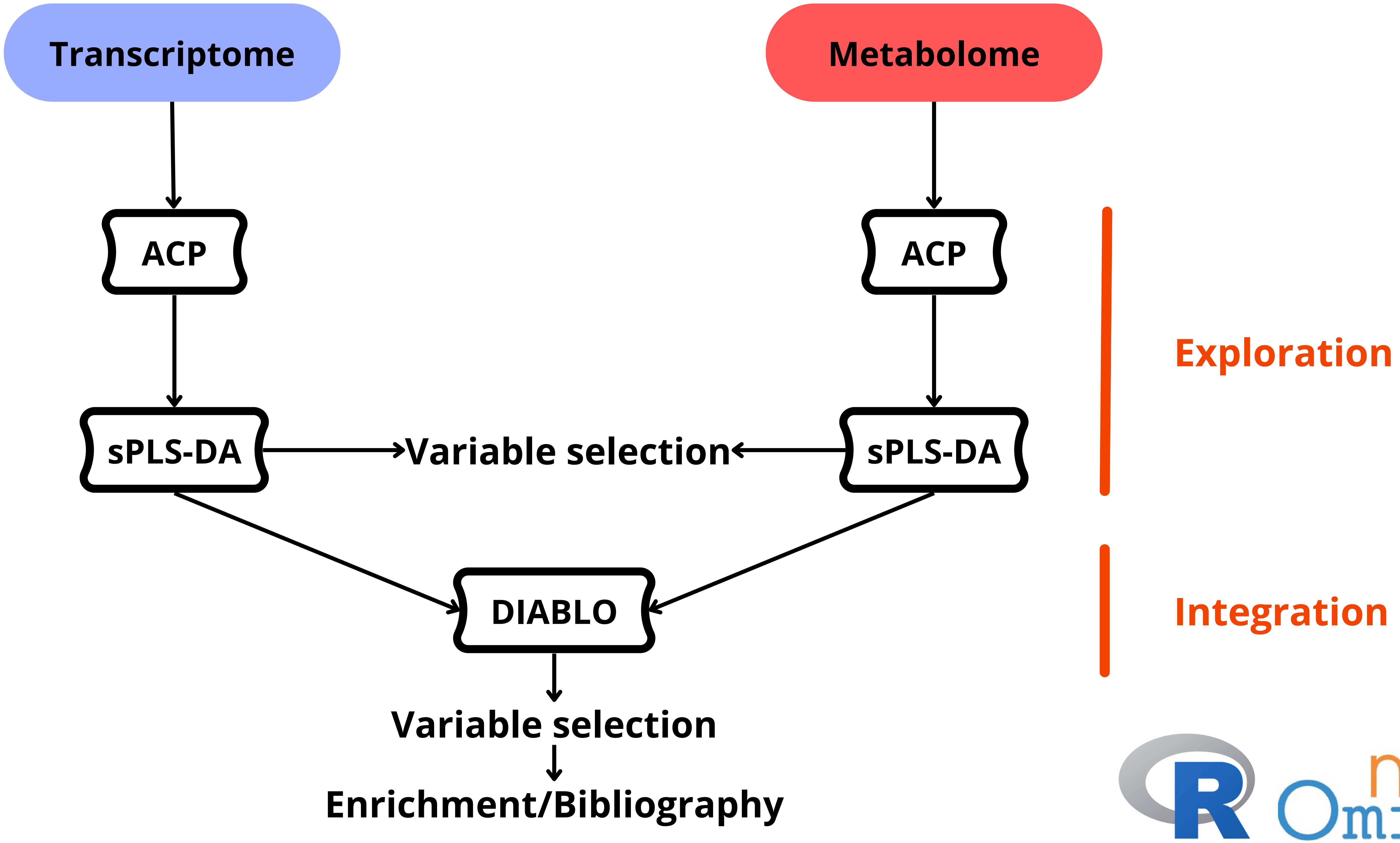
Filter

ASICS R Package

metabolome:
224 samples x 46 metabolites

Material and Methods

Pipeline



Transcriptome

Metabolome

ACP

ACP

sPLS-DA

Variable selection

sPLS-DA

DIABLO

Variable selection

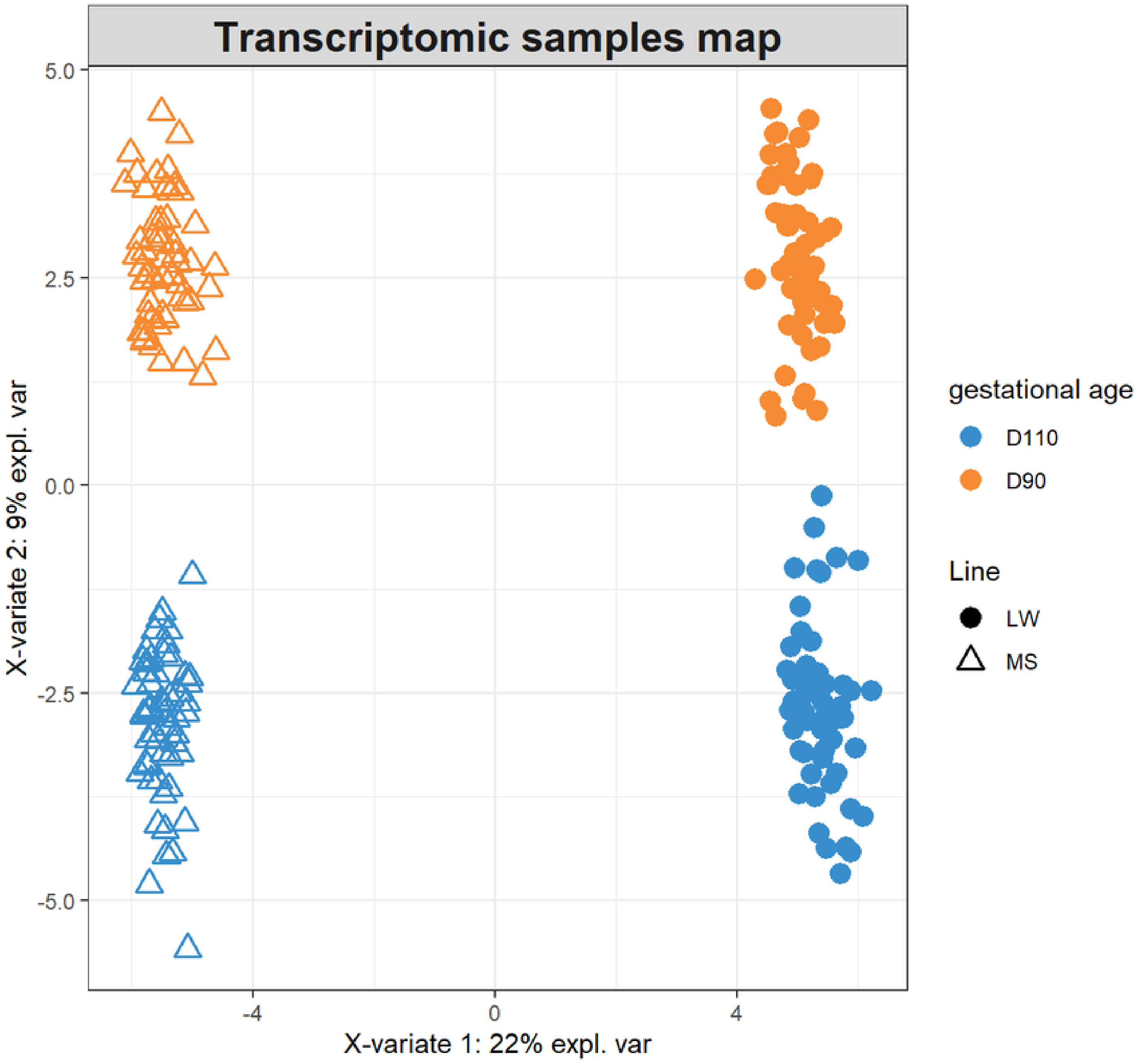
Enrichment/Bibliography

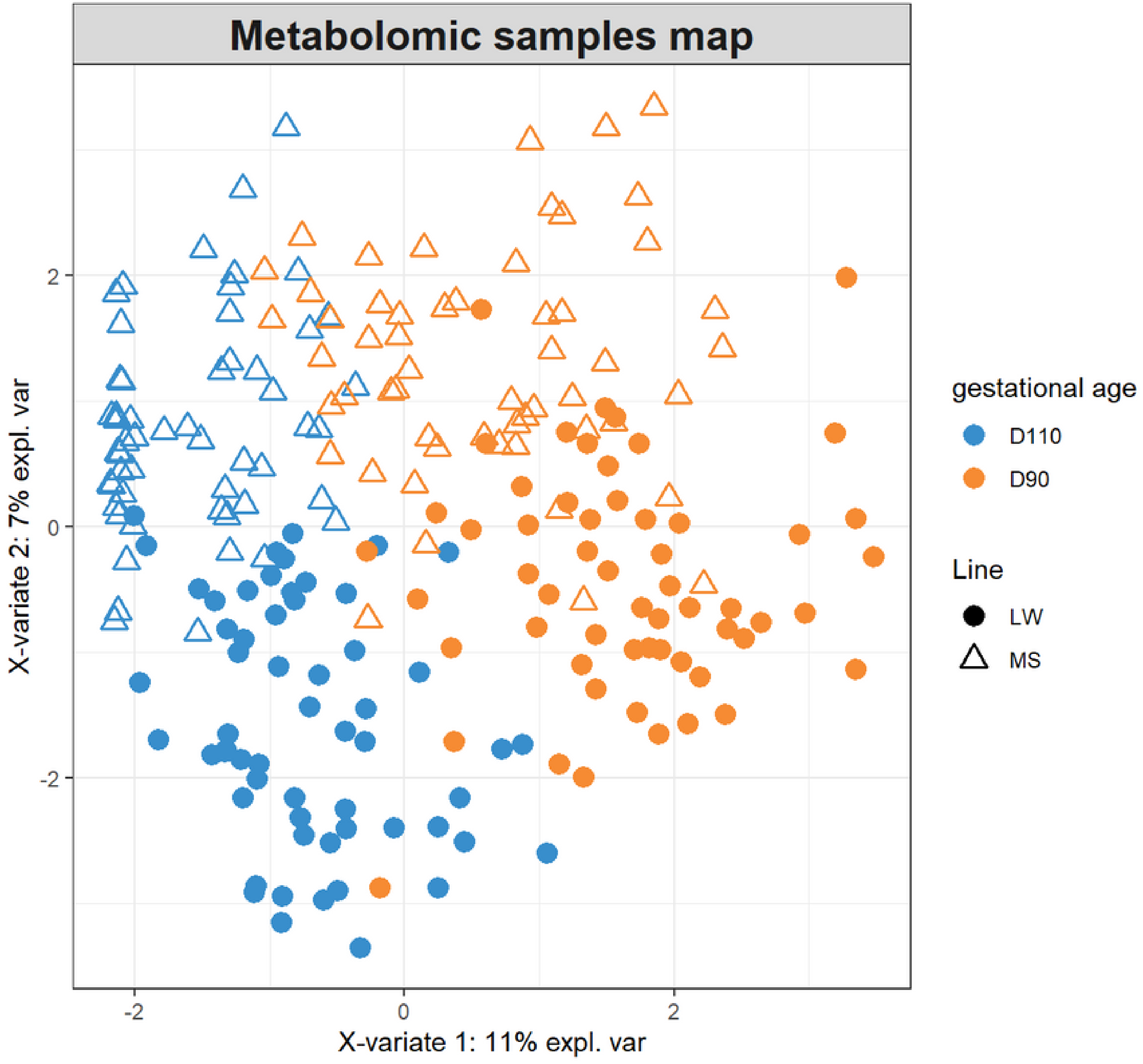
Exploration

Integration

Do the endometrium transcriptome and metabolome reflect samples classes ?

sPLS-DA


Transcriptomic samples map


Metabolomic samples map

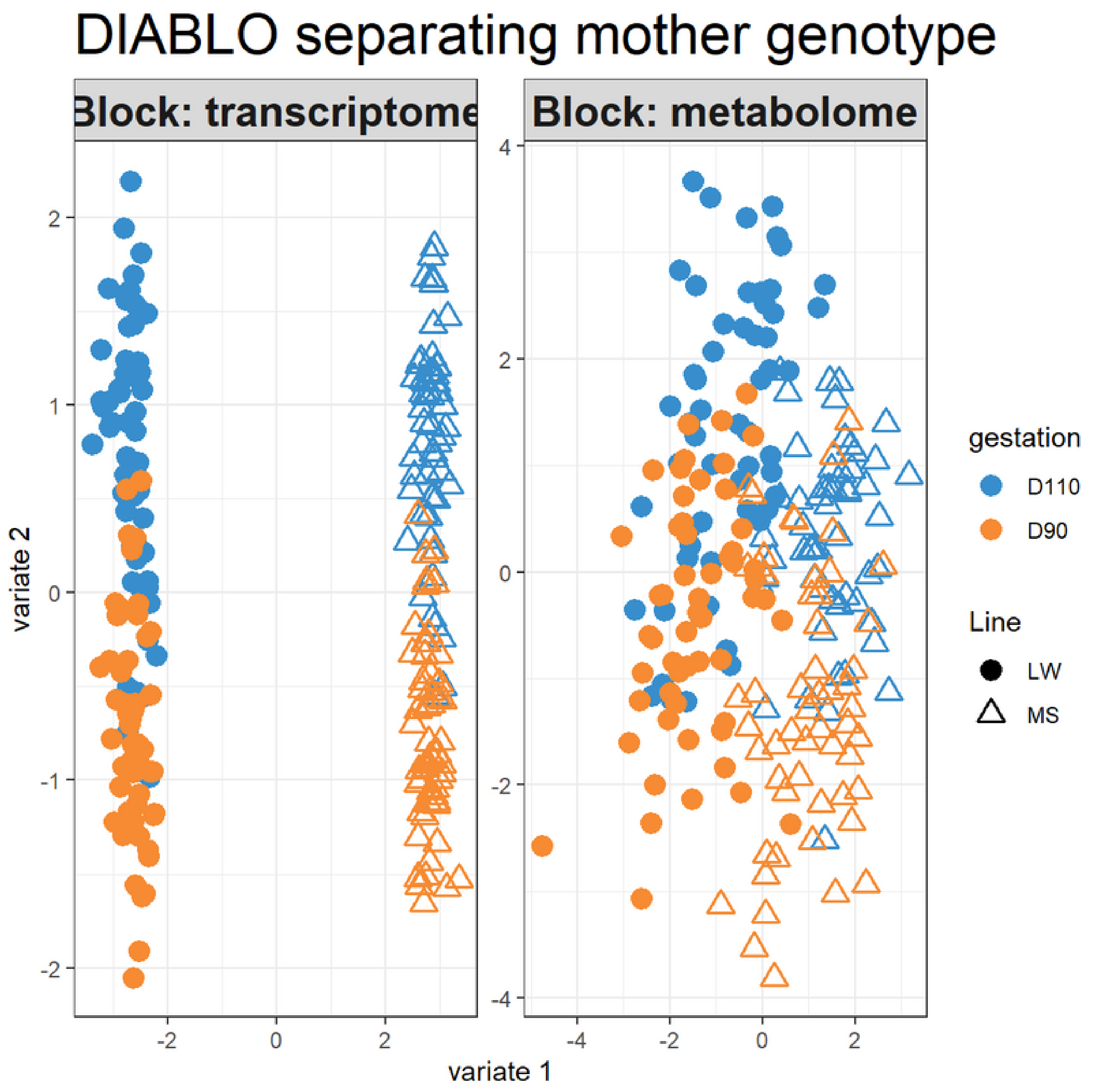
Y : Day of gestation and Mother genotype

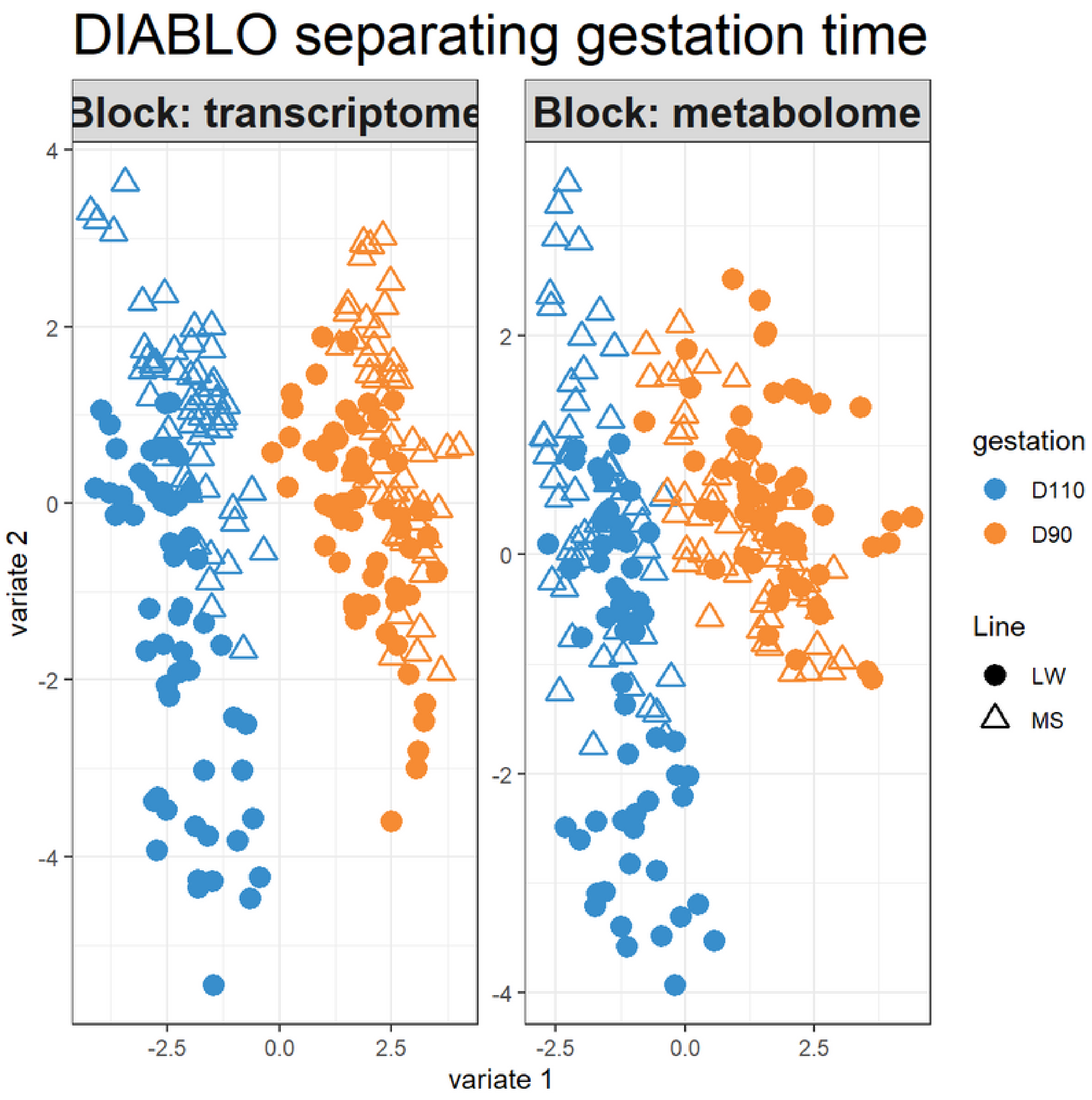
number of selected transcripts: 50, 20

number of selected metabolites: 6, 10

Endometrium transcriptome and metabolome integration

DIABLO



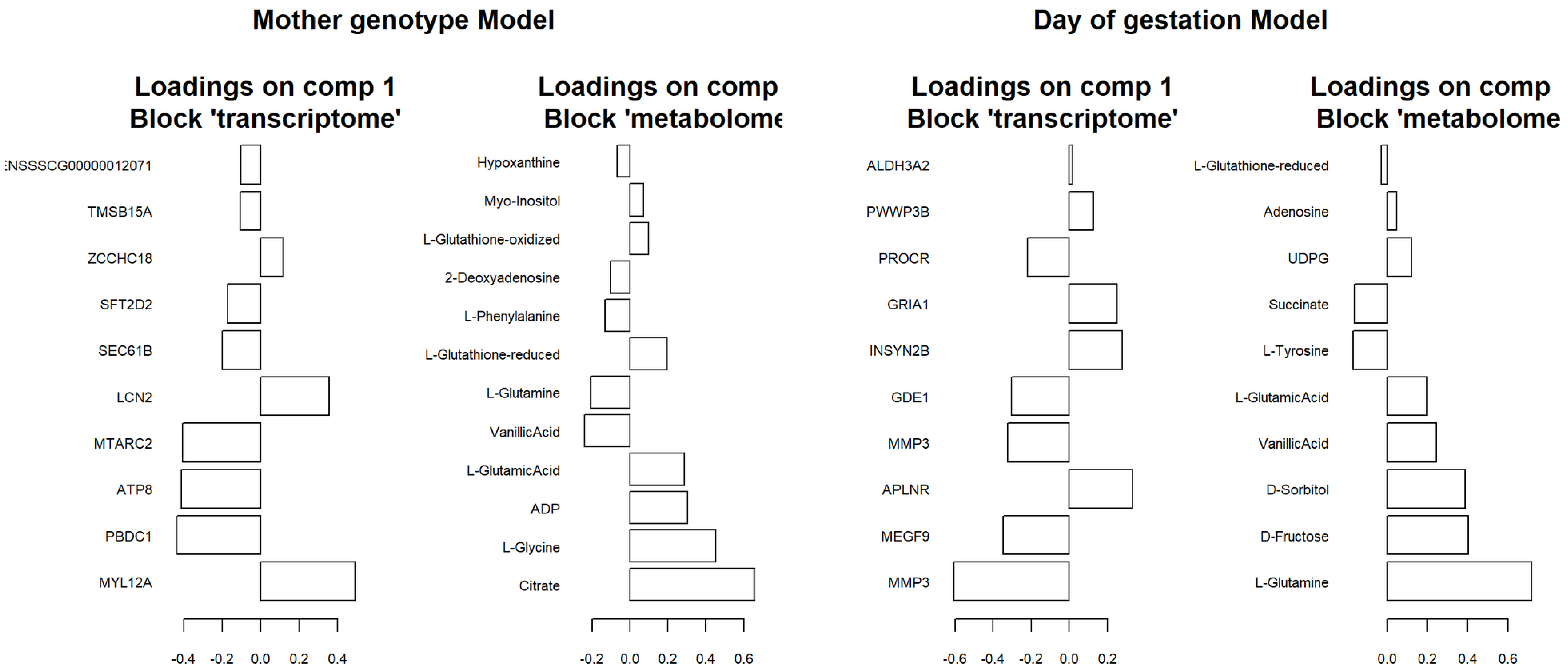


number of selected transcripts: 10, 1
number of selected metabolites: 12, 10

number of selected metabolites: 10, 11
number of selected transcripts: 10, 10

Endometrium transcriptome and metabolome integration

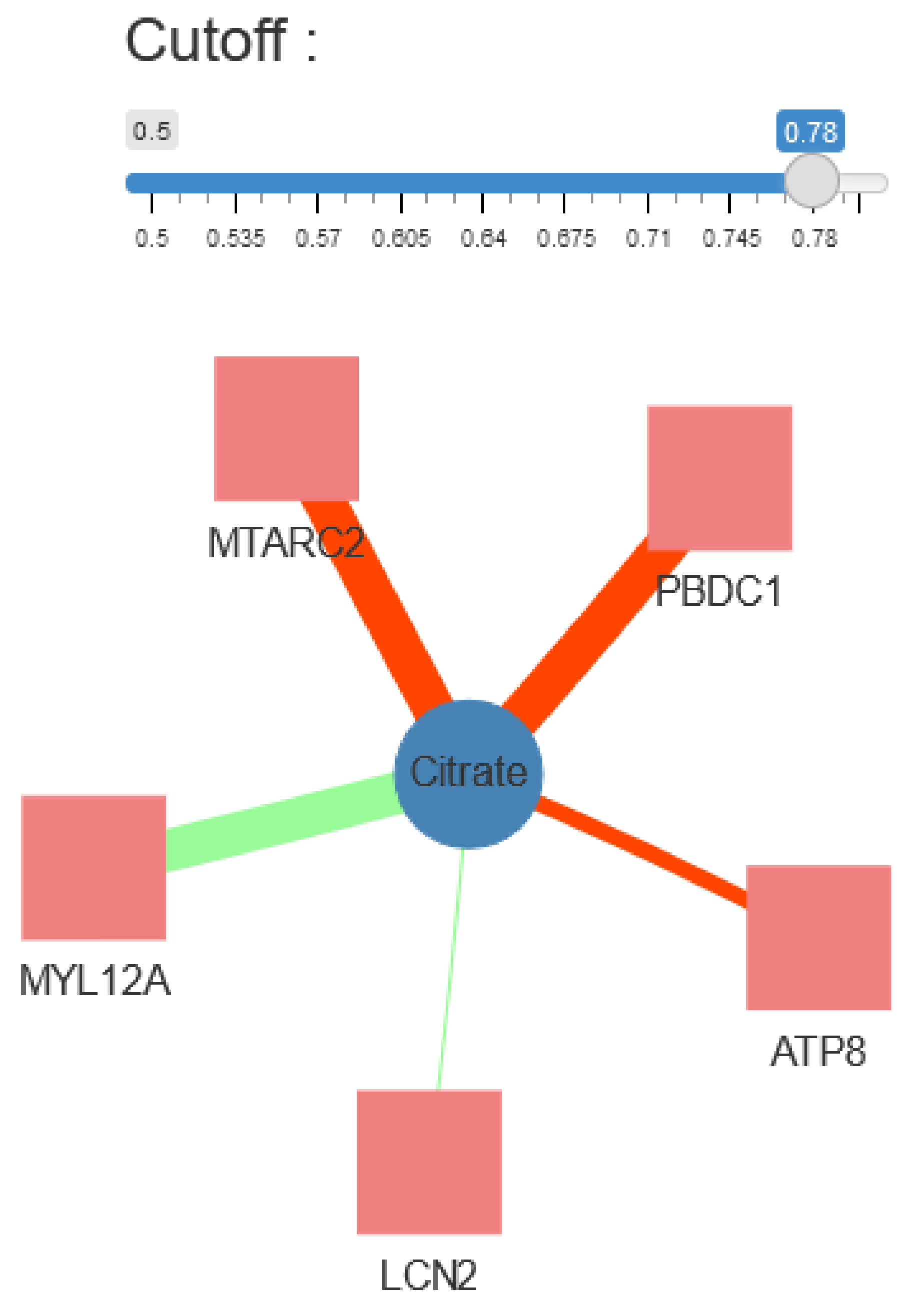
Loadings



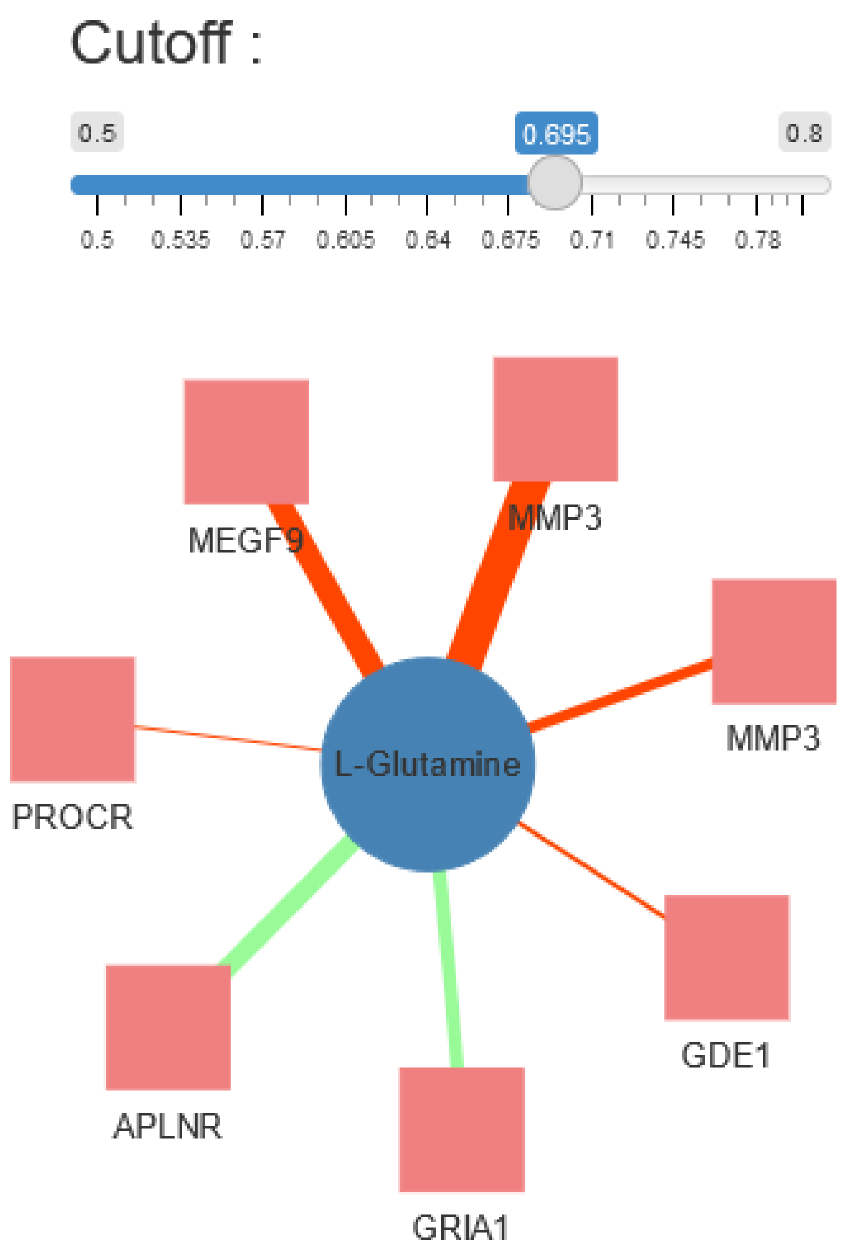
assessment of the robustness of variables using the mixomics "perf" function

Endometrium transcriptome and metabolome integration

Networks



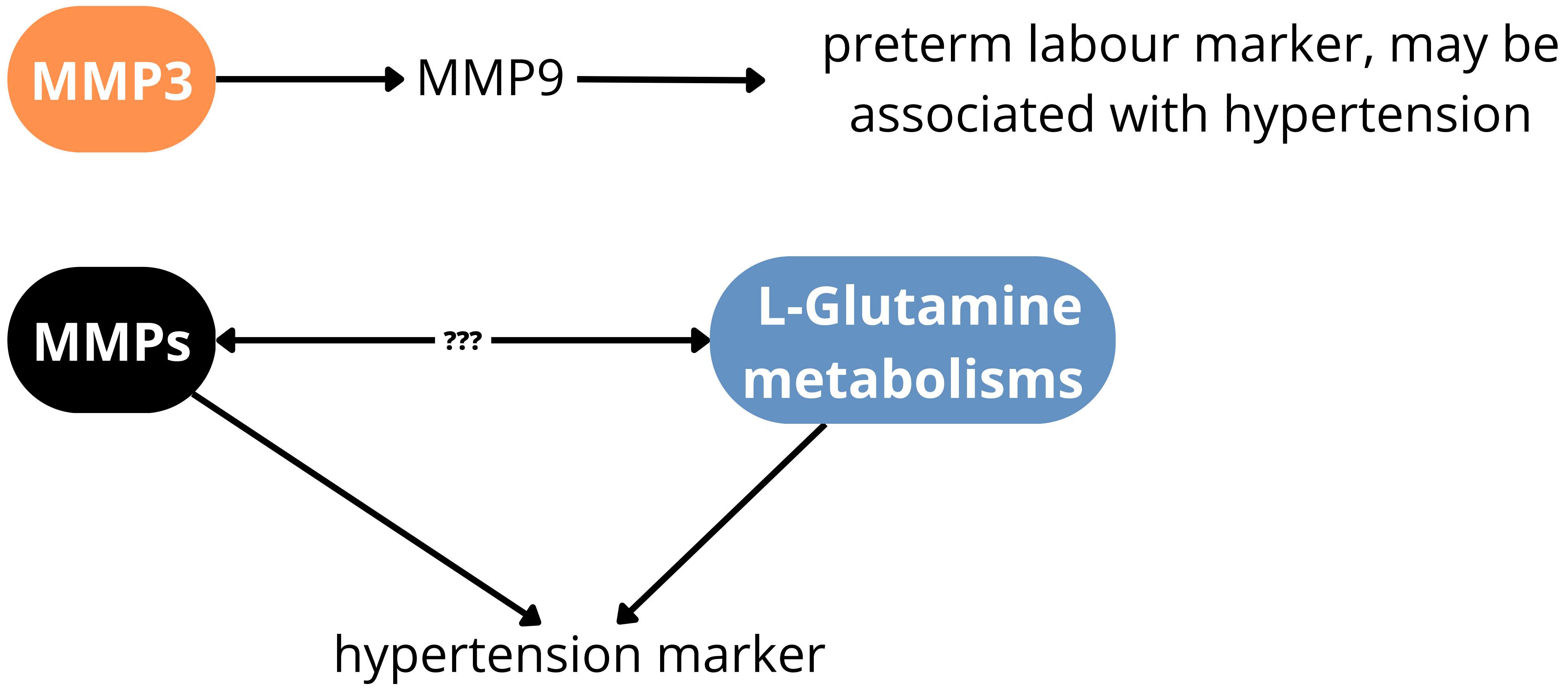
mother genotype model



day of gestation model

Discusion

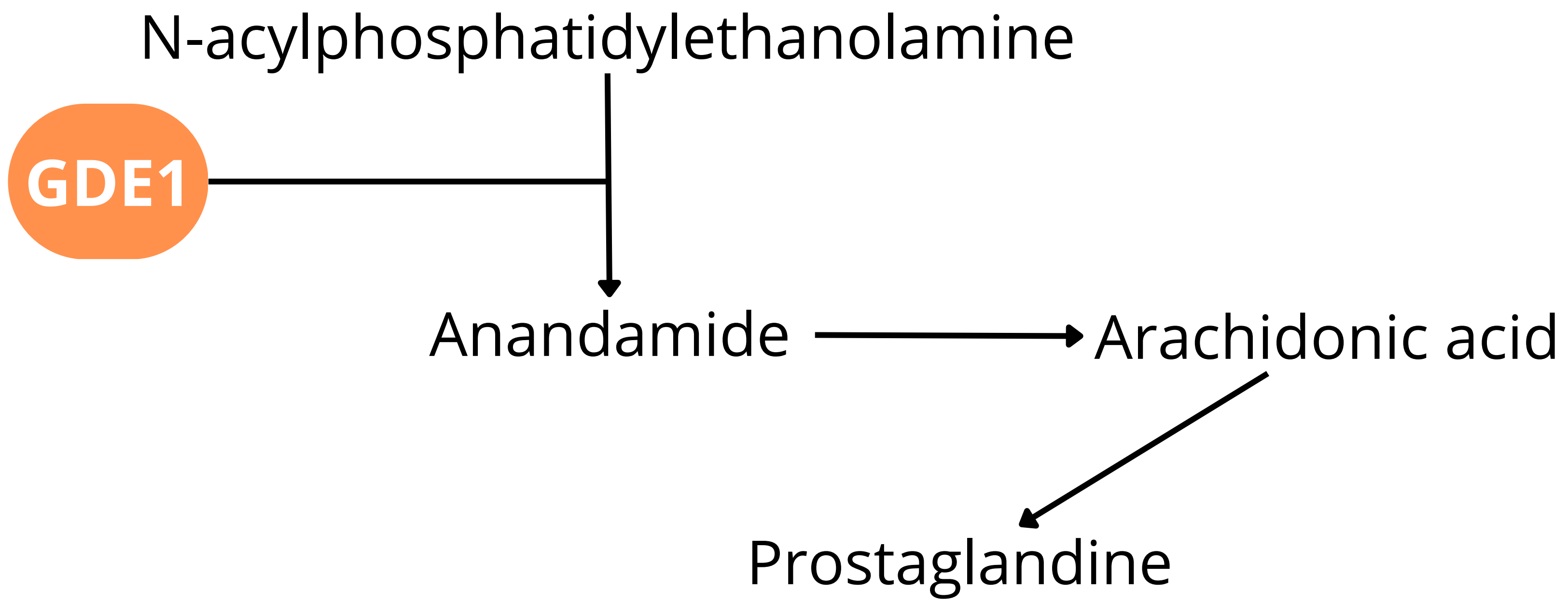
Day of gestation



MMP3 → MMP9 → preterm labour marker, may be associated with hypertension

MMPs ↔ ??? ↔ **L-Glutamine metabolisms**

hypertension marker



N-acylphosphatidylethanolamine

GDE1

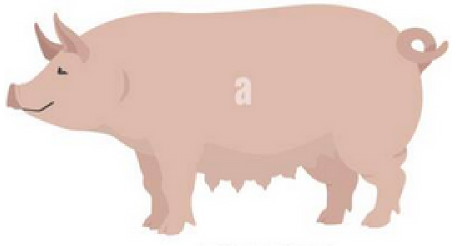
Anandamide → Arachidonic acid

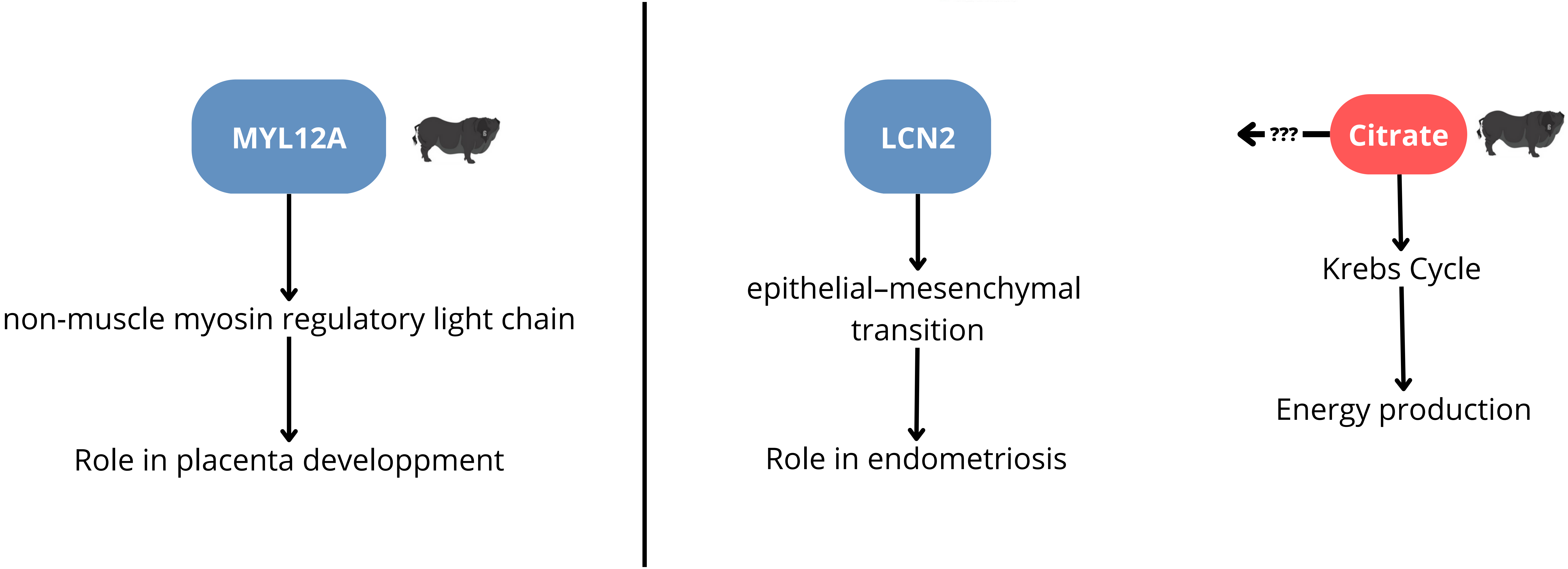
Prostaglandine

Flores-Pliego Et al., 2015 ,Bisogni Et al., 2020, Raffetto Et al., 2007, Durante, 2019, Pandey Et al., 2019, M.Simon Et al., 2008, Maccarrone Et al., 2017

Discusion

Mother Genotype





MYL12A

non-muscle myosin regulatory light chain

Role in placenta developpment

LCN2

epithelial–mesenchymal transition

Role in endometriosis

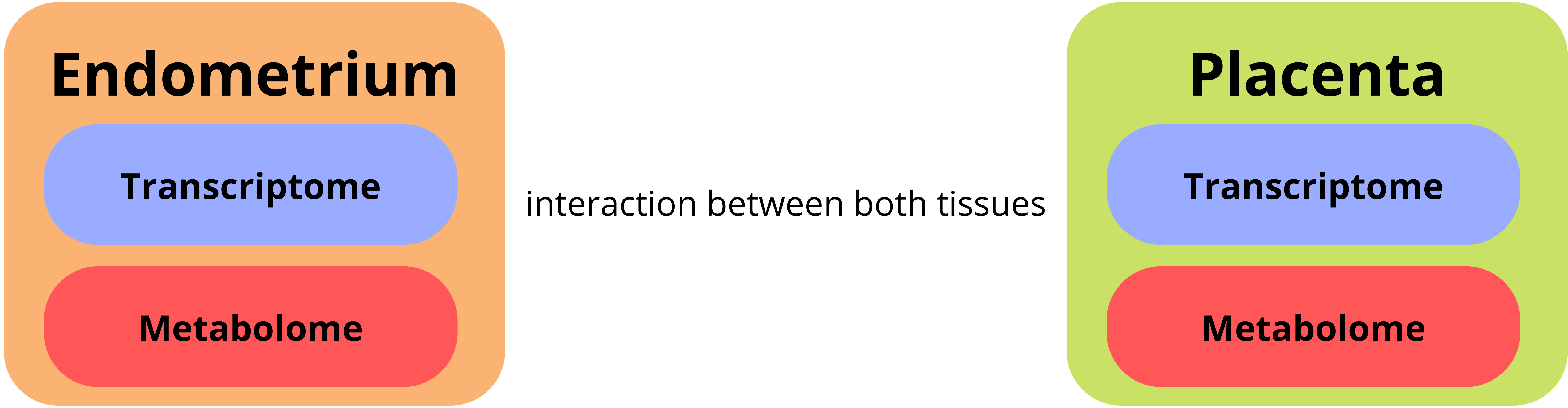
← ??? — **Citrate**

Krebs Cycle

Energy production

Liao Et al., 2014, Wang Et al., 2010, Park Et al., 2011

Perspectives



Endometrium

Transcriptome

Metabolome

interaction between both tissues

Placenta

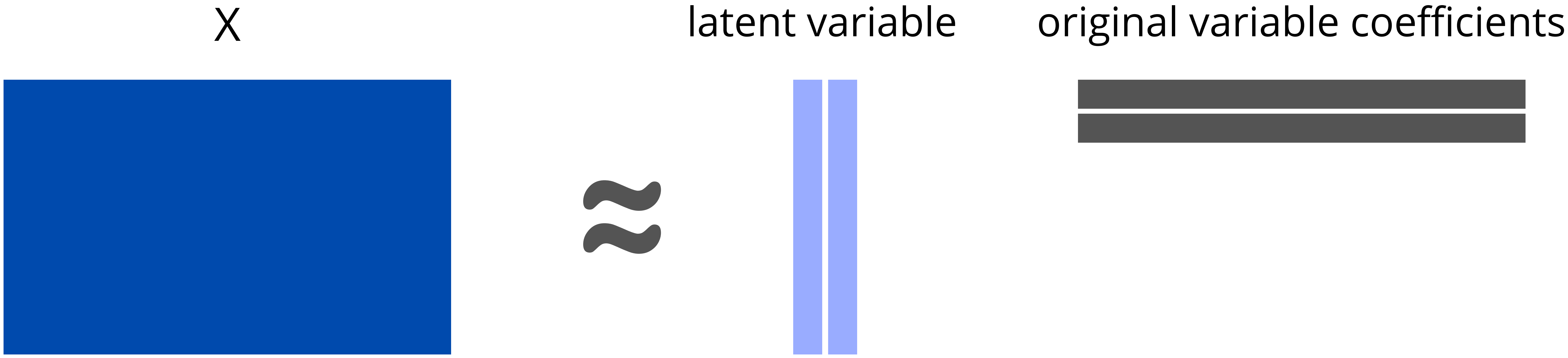
Transcriptome

Metabolome

- Metabolome and Transcriptome integration of the placenta
- Integration of the Transcriptome or Metabolome between tissues

Any questions ?

Matrix factorization



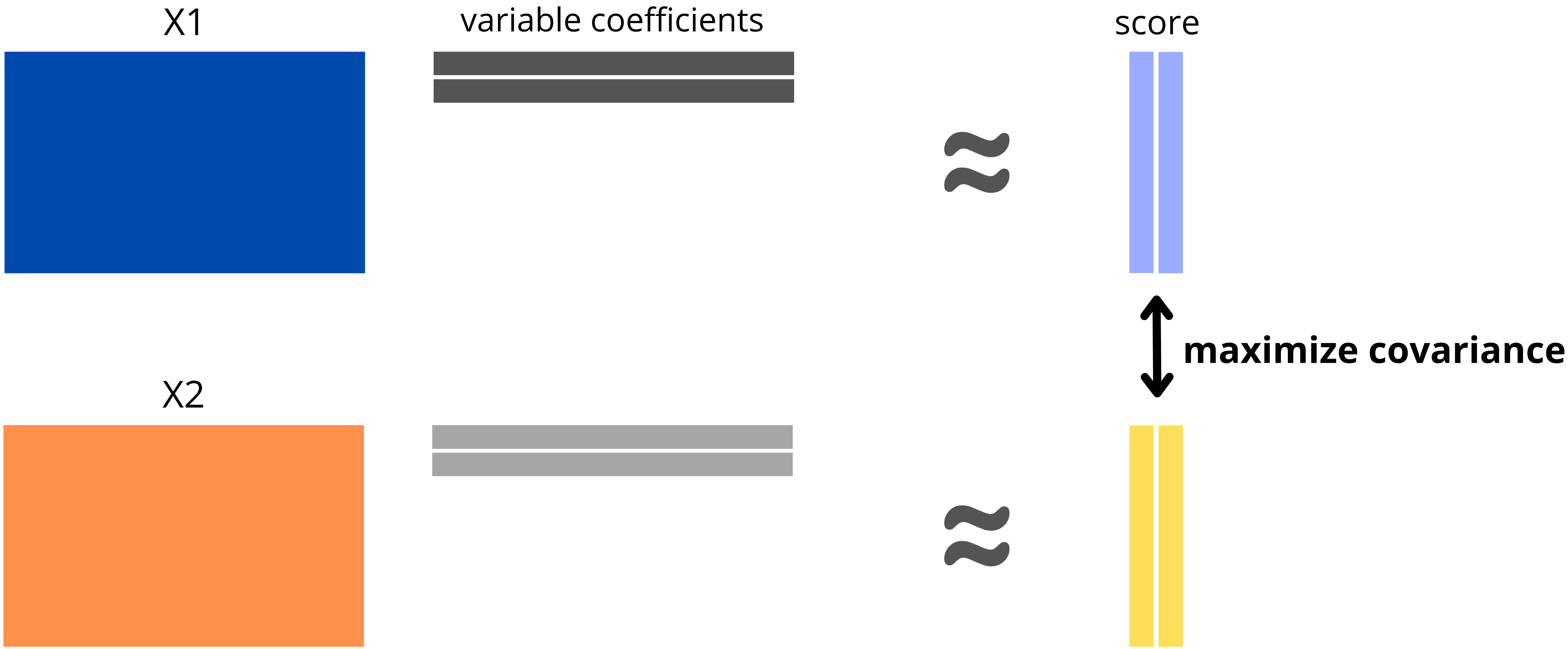
X

≈

latent variable

original variable coefficients

DIABLO



X1

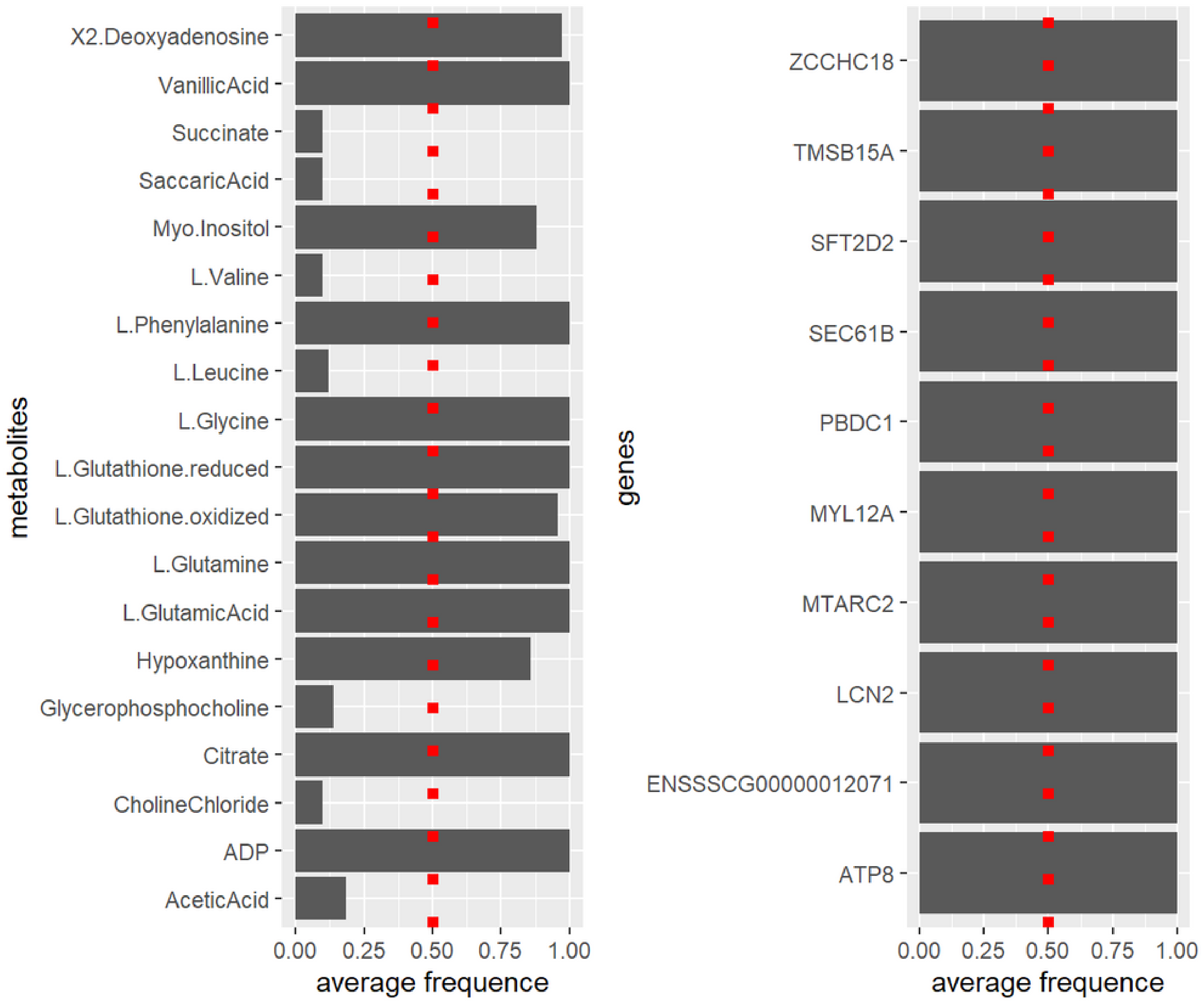
variable coefficients

score

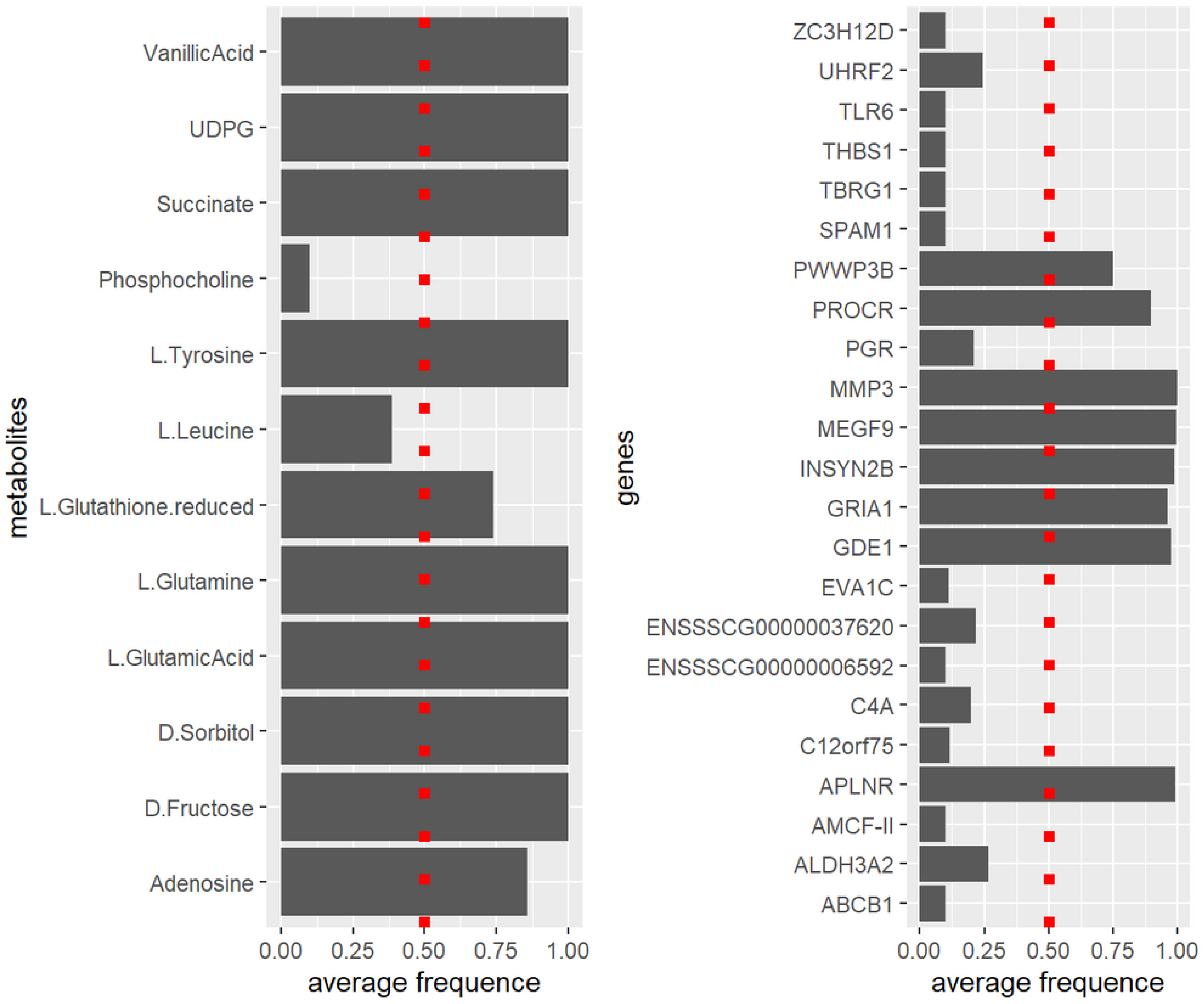
maximize covariance

X2

Robustness/Stability of the selected variables



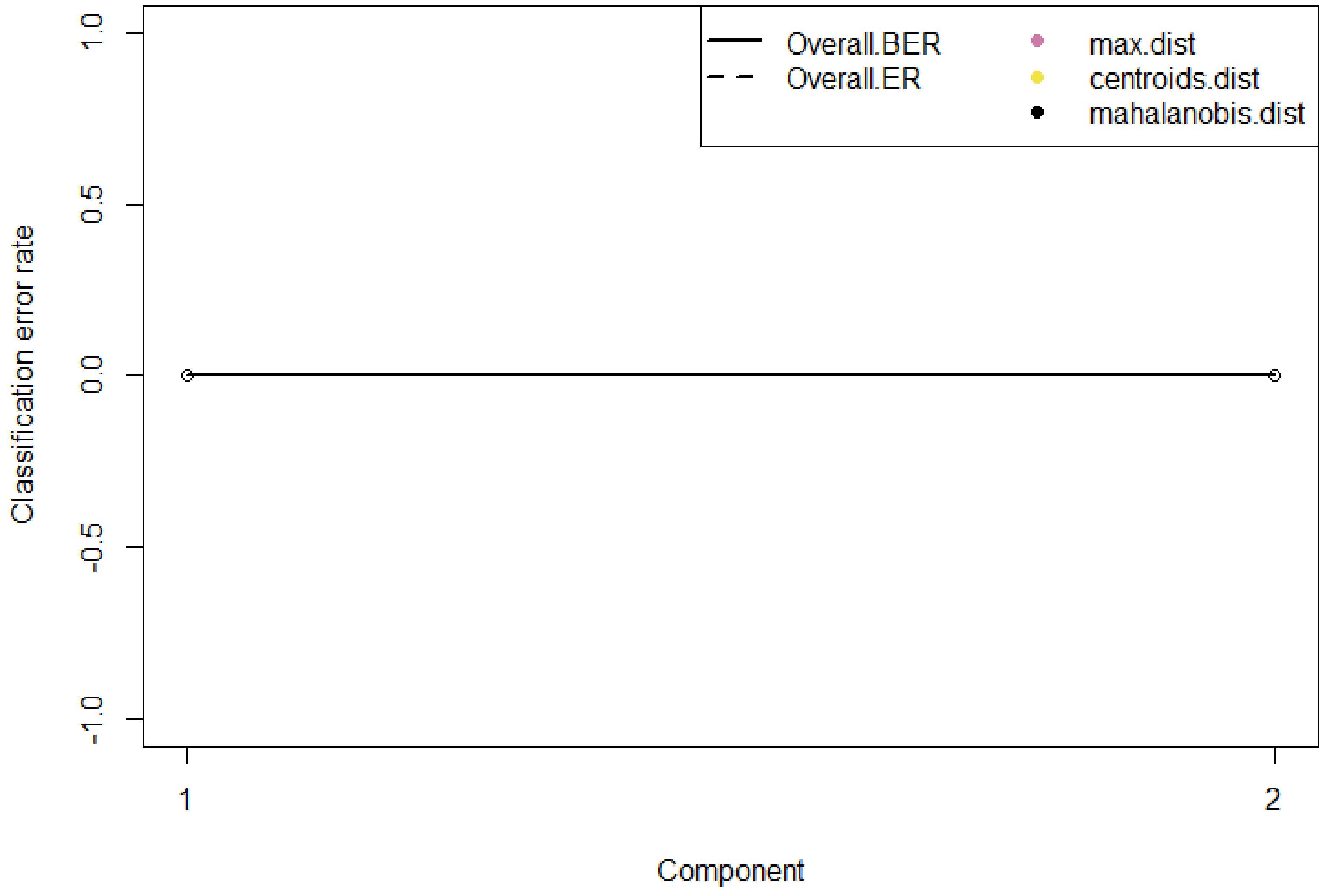
Mother genotype



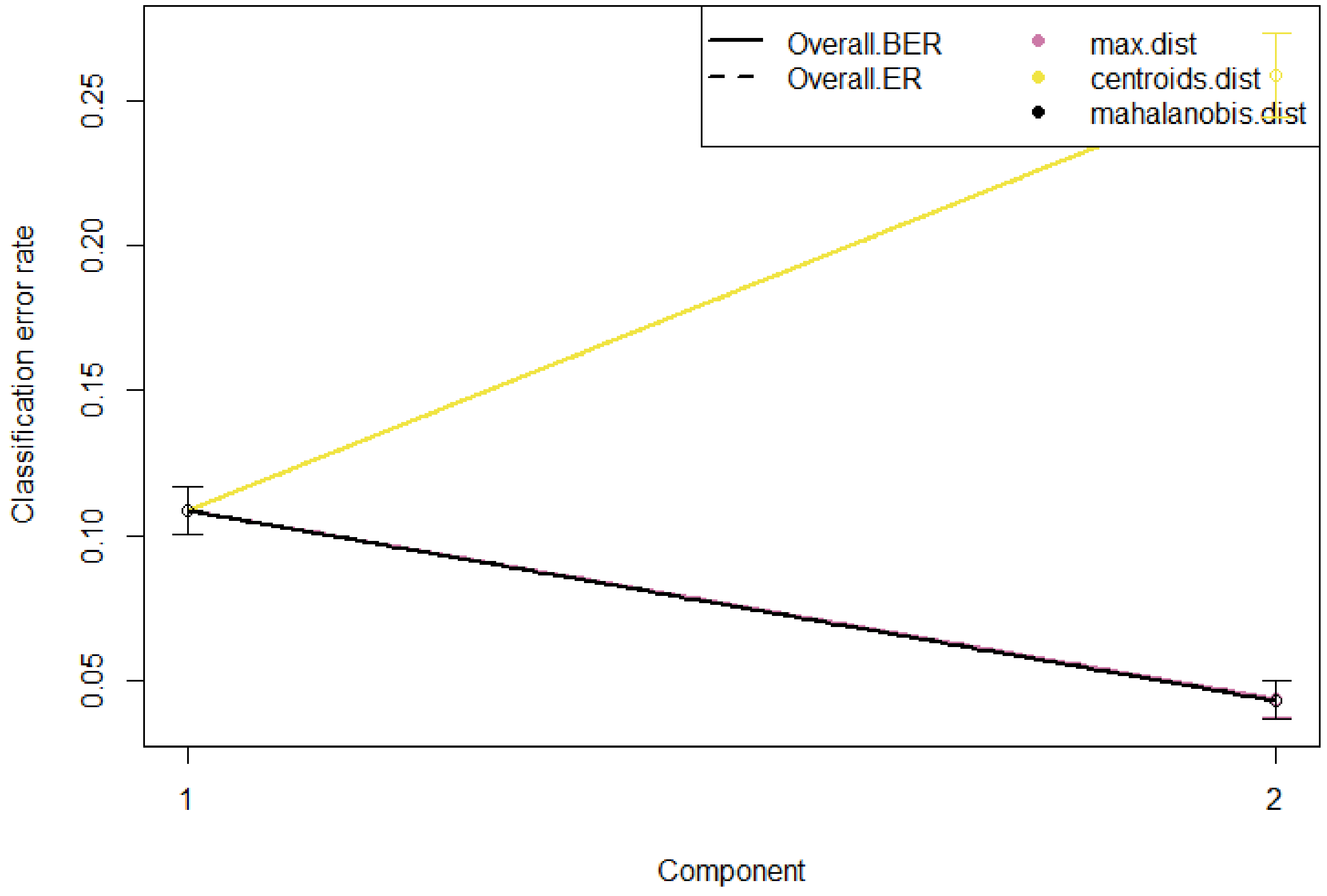
Gestational age

Performation of the DIABLO models

Mother genotype



Gestation day



Comparison of the

Mother genotype

Gestation day