Bioavailability of amino acids, especially of tryptophan, in human milk and infant formulas

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30/06/2021

Bioavailability of amino acids, especially of tryptophan, in human milk and infant formulas

Elise Charton
(2nd year of thesis)

Thesis directors :
Amélie Deglaire (STLO)
Isabelle Luron (NuMeCan)
Didier Dupont (STLO)

SUMMARY

01 – Scientific context

44%

Of infants are breastfed from BIRTH TO 5 MONTHS in the World

(UNICEF, 2011)

59%

Of infants are breastfed AT BIRTH in France

(Epiphane data, 2012-2013)

21%

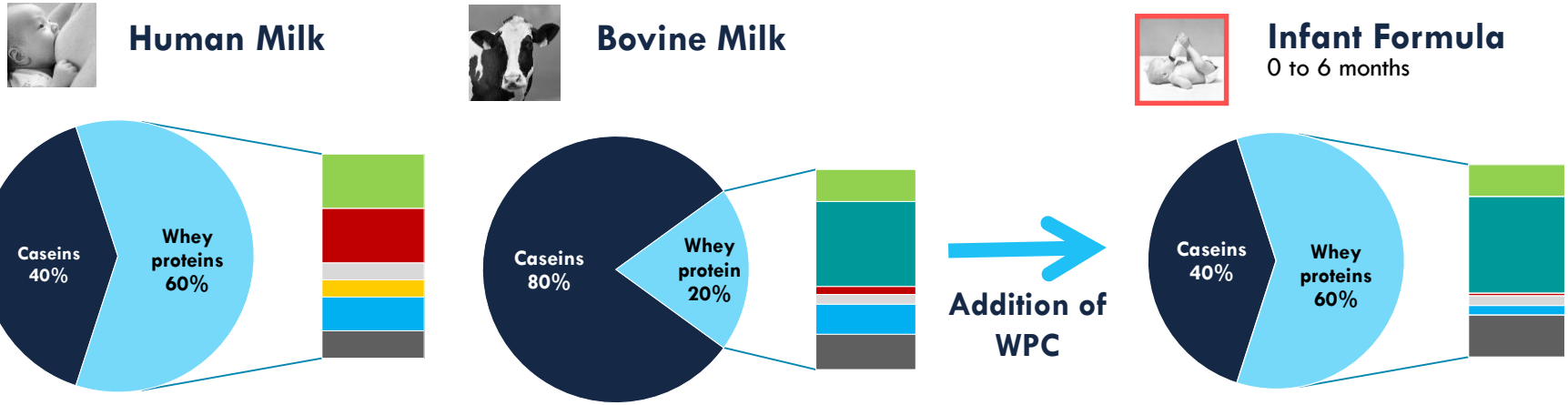
Of infants are breastfed at 3 MONTHS in France

10% Exclusive breastfeeding
11% Dominant breastfeeding

(Epiphane data, 2012-2013)

01 – Scientific context

How an Infant formula is made from Bovine milk?



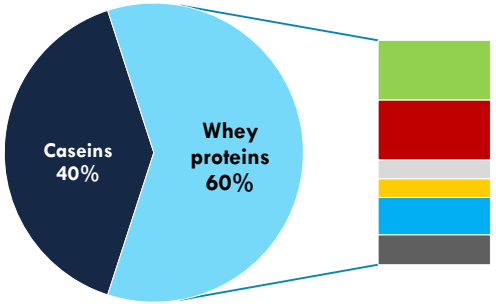
WPC : Whey proteins concentrate

Data : Chatterton et al., 2003 ; Nasirpour et al., 2005

01 – Scientific context

How an Infant formula is made from Bovine milk?

Human Milk



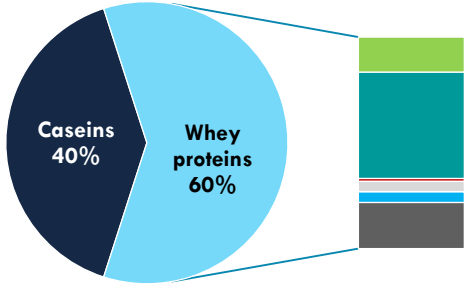
0,8 – 1,2 g protein / 100 mL

↳ **13,6 – 20,4 mg Trp/100 mL**

(min, max, WHO, 2017)

Infant Formula

0 to 6 months



1,1 – 1,8 g protein / 100 mL

(Min – Max, based on Total Nitrogen x 6.25 (EU Regulation 2016/127))

↳ **≤19,2 mg Trp/ 100 mL**

(min, EU Regulation 2016/127)

Data : Chatterton et al., 2003 ; Nasirpour et al., 2005

➔ **Trp, a limit for reducing protein content in IF** (Lönnerdal & Lien, 2003)

Only a few study on tryptophan content and its bioavailability in human milk (Darragh, Moughan, 1998 ; Maathuis *et al.*, 2017)

01 – Scientific context

BIOAVAILABILITY: nutrient fraction digested, absorbed by intestinal mucosa and available for subsequent body metabolic functions → True ileal digestibility is a good proxy (Fuller & Tomé, 2005)

DIGESTIBILITY CALCULATION:

Total N flow (g/g DMI) $= N_{ileum} \times \frac{Marker_{meal}}{Marker_{ileum}}$

Apparent ileal digestibility: Apparent ileal digestibility (%) $= \frac{Dietary\ N_{intake} - Total\ N\ flow_{ileum}}{Dietary\ N_{intake}} \times 100$

Standardised digestibility (Rutherfurd et al., 2006)**:**

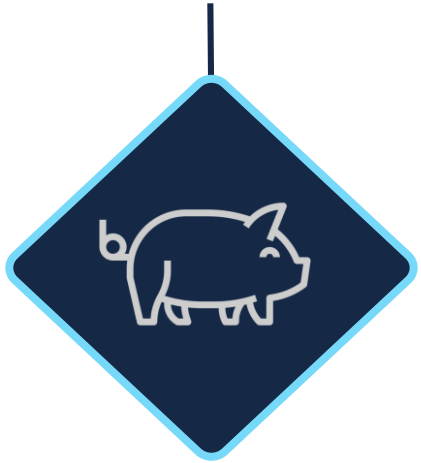
Standardized ileal digestibility (%) $= \frac{Dietary\ N_{intake} - N\ exogenous\ flow_{ileum}}{Dietary\ N_{intake}} \times 100$

Standardized ileal digestibility (%) $= \frac{Dietary\ N_{intake} - (Total\ N\ flow_{ileum} - N\ endogenous\ flow_{ileum})}{Dietary\ N_{intake}} \times 100$

02 – Objectives

Measure of AAs and Total Nitrogen ileal digestibility in human milk and IF

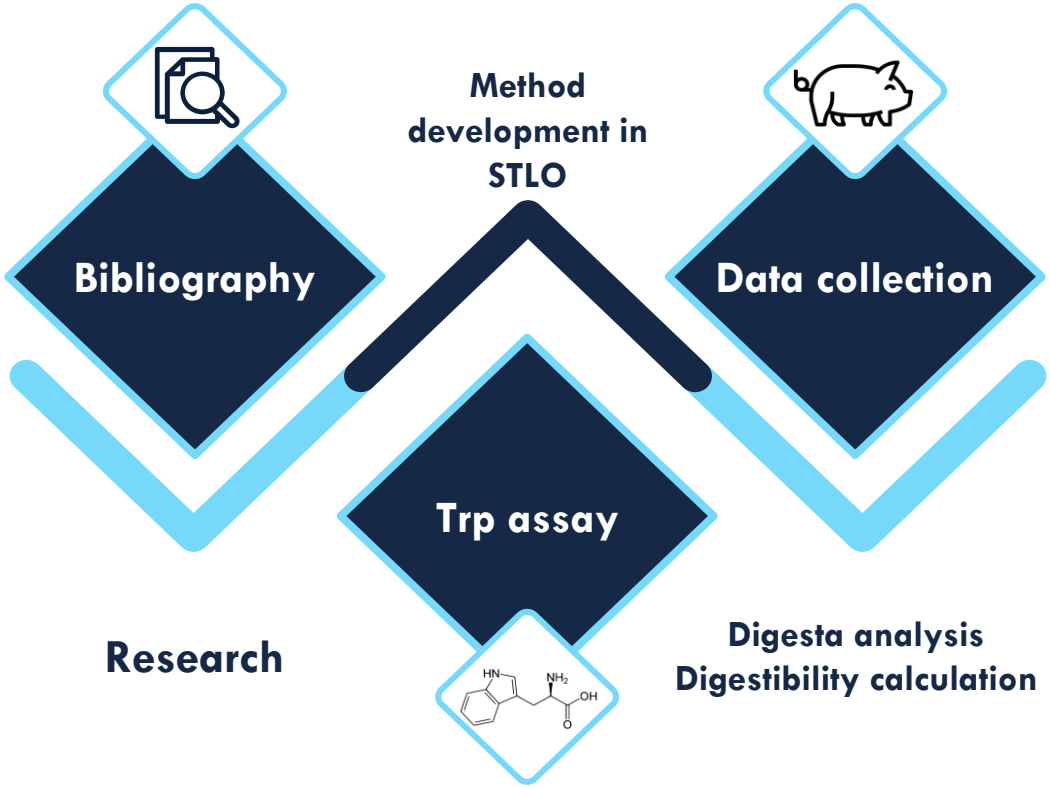
- In vivo experiment
- Digestibility calculation



Effect of Trp on infant development and diet effect

- Trp metabolites
- Intestinal and brain development

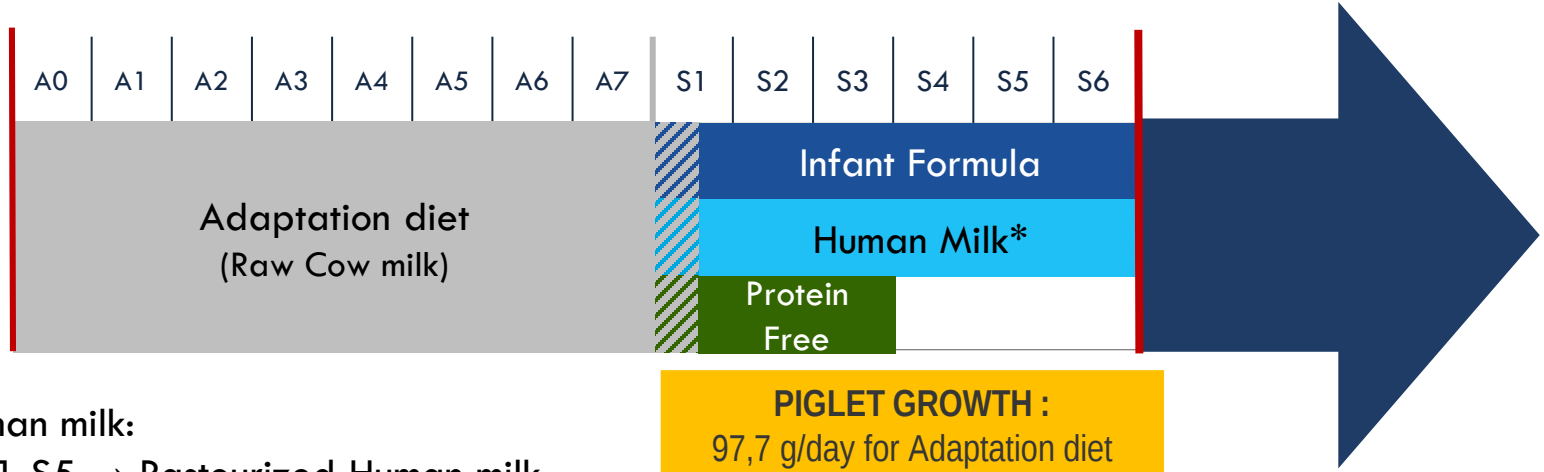
02 – Strategy


Method development in STLO
Bibliography
Data collection
Trp assay
Research
Digesta analysis
Digestibility calculation
HN
NH2
OH
O

02 – Strategy

Ethical committee agreement needed for HM collection and Animal experiment

Model: Yucatan piglets (10 days old)
Meal intake : 345 g/ kg BW/ day
HM: n=9 IF: n=9 PF: n=6



*Human milk:
S1-S5 → Pasteurized Human milk
S6 → Fresh Human milk

PIGLET GROWTH :
97,7 g/day for Adaptation diet
53,2 g/day for IF and HM groups

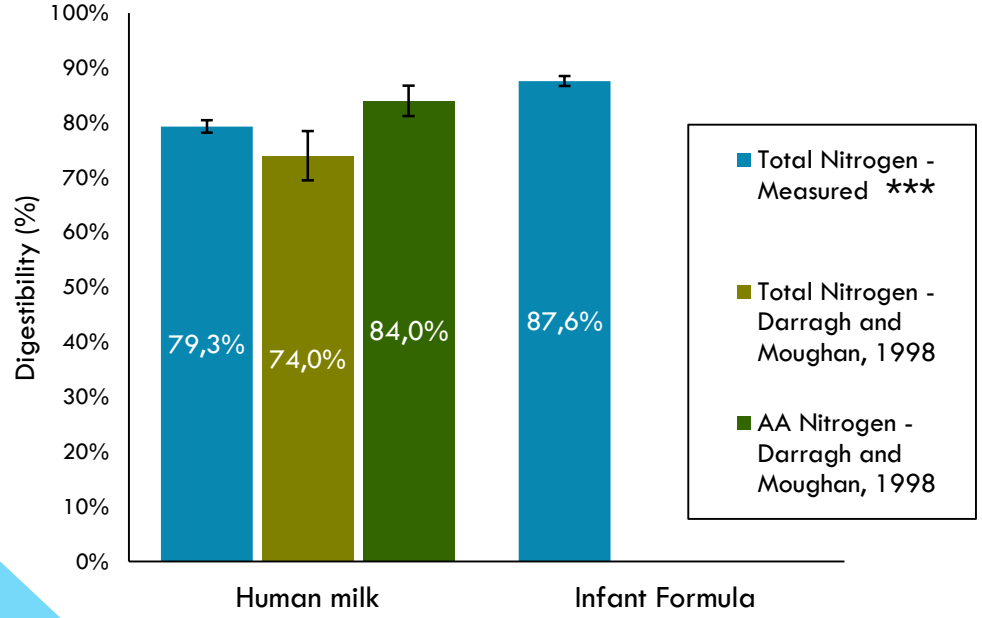
03

Results

Digestibility, Microbiota, Gut-brain axis

03 – Results: Ileal Digestibility – Total nitrogen

Total Nitrogen apparent digestibility



*** p-value<0,001

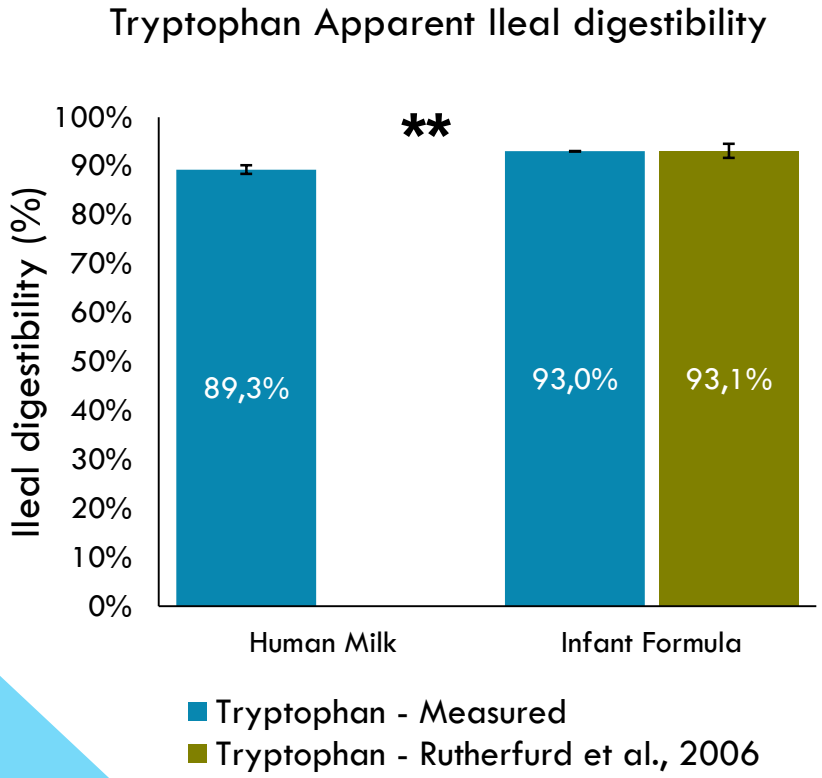
EFFECT OF Non Proteic Nitrogen (NPN) on Apparent total Nitrogen digestibility

HM : **25%** Ntot | IF : **5%** Ntot

NPN is composed by:

- *Urea*
- *Glucosamine*
- *Free Amino acids*
- *NH_3/creatin/ureic acid*
- *Peptides*
- …

03 – Results: Ileal Digestibility - Tryptophan



Does the use of Trp is similar between both diets ?

- ↳ Metabolomic analysis
- ↳ Transcriptomic analysis

03 – Results: Ileal Digestibility – Tryptophan

Principal use of Trp : anabolism
Secondary use of Trp : catabolism
- Major pathway
- Minor pathway

TRYPTOPHAN

PROTEIN SYNTHESIS

SEROTONIN

Neuronal development contribution *(Heine, 1996)*

Link between serotonin and behaviour regulation *(Fernstrom, 2012; Young et al.,1985)*

Effect of serotonin on sleep, food intake and digestion *(Le Floc'h et al., 2011)*

KYNURENINE

Niacin
(vit. B3)
↳ **NAD/NADP**
(metabolism co factor)

Acetoacetyl CoA
↳ **Acetyl CoA**
role in energetic metabolism
→ glycolysis
(Puy, 2017)

Bacterial metabolism

INDOLE

↘ **inflammation** *(Shimada et al., 2013)*

Epithelial barreer integrity *(Bansal et al., 2010 ; Shimada et al., 2013)*

⚠ **High concentration: ↗ anxious and depressed behaviour**
(Hayatt MIR, 2018 ; Jaglin et al., 2018)

Pineal gland

MELATONIN

sleep/-wake balance *(Aparicio et al., 2013)*

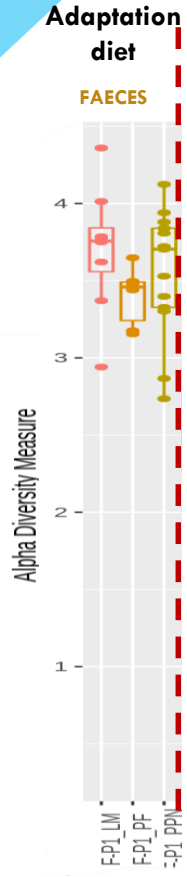
Behaviour *(Le Floc'h et al., 2011)*

Memory and learning *(Macchi and Bruce, 2003)*

Immune activity *(Szczepanik, 2007)*

Antioxydant properties *(Heine, 1995)*

03 – Results : Microbiota



Alpha diversity / Shannon = Number of OTUs and evenness

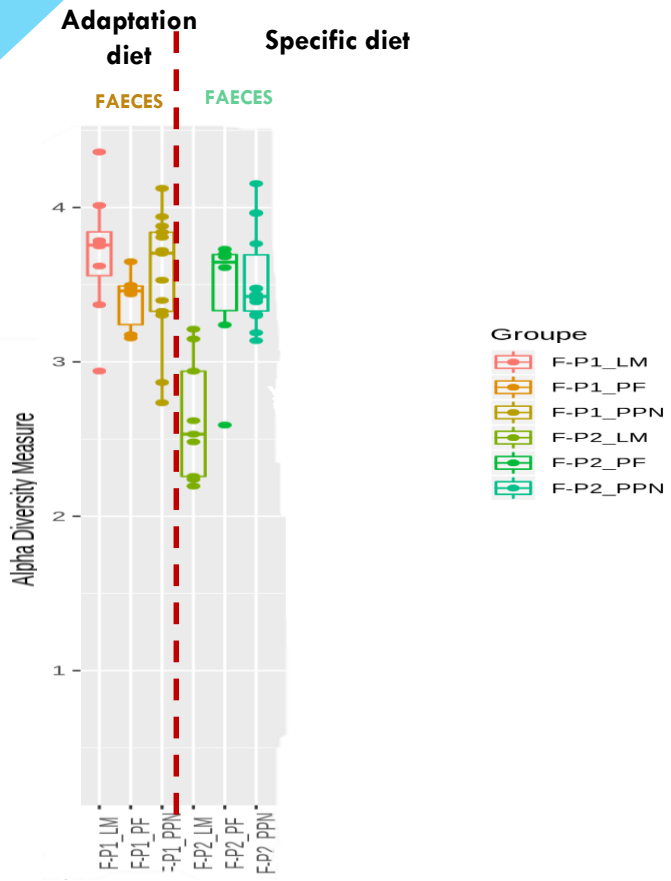
F-P1 = Faecal collection during adaptation diet
F-P2 = Faecal collection at slaughtering

LM = Human Milk
PF = Protein Free
PPN = Infant formula

C = Colon

AFTER ADAPTATION DIET : in faeces, no differences between piglets

03 – Results : Microbiota



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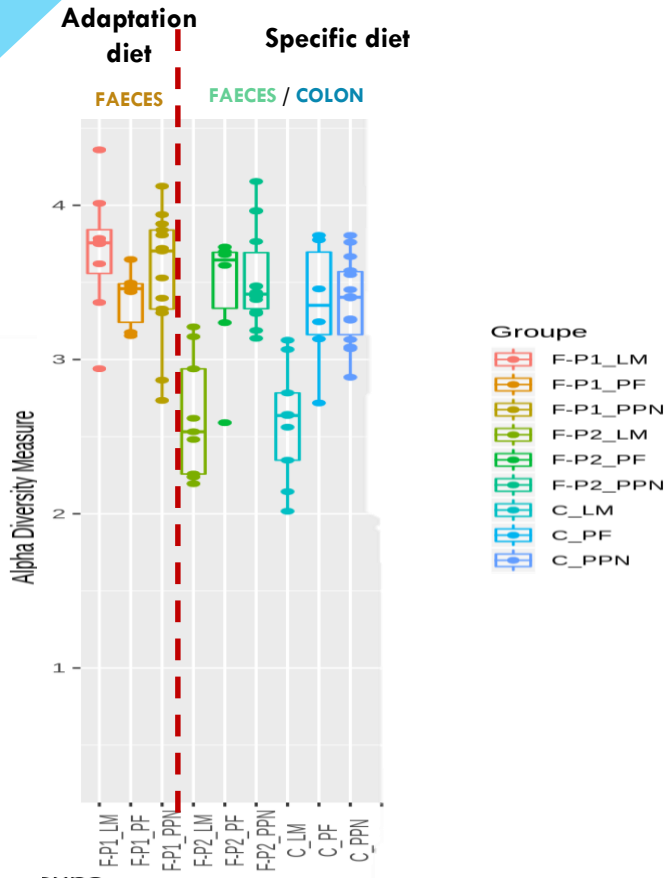
AFTER ADAPTATION DIET : in faeces, no differences between piglets

AFTER SPECIFIC DIET :

- In faeces (green):
  - **Reduction of** α-diversity for **HM diet → decrease of OTU number**
  - **Similar** alpha-diversity for **IF and PF diets**

03 – Results : Microbiota



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AFTER ADAPTATION DIET : in faeces, no differences between piglets

AFTER SPECIFIC DIET :

- In faeces (green):
  - **Reduction of** α-diversity for **HM diet → decrease of OTU number**
  - **Similar** alpha-diversity for **IF and PF diets**
- In colon (blue):
  - Colon microbiota is similar to faecal microbiota

→ Alpha-diversity decreases in breastfed infants and reduced at 6 age of month

(Ho *et al.*, 2018 ; Ma *et al.*, 2020)

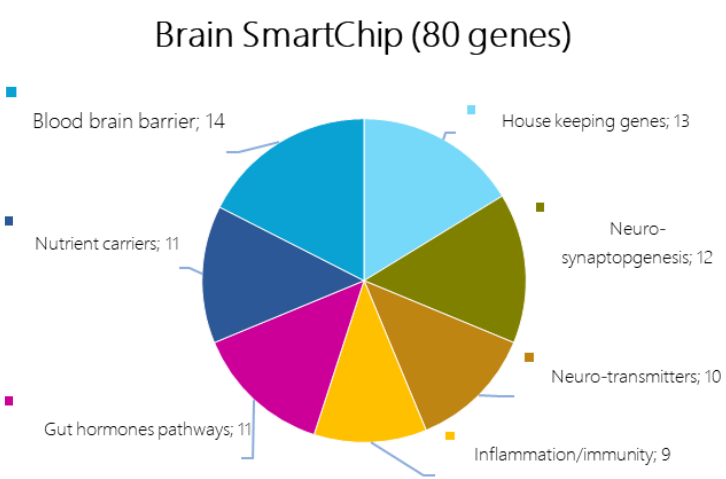
04 – Perspective : Gut-Brain axis

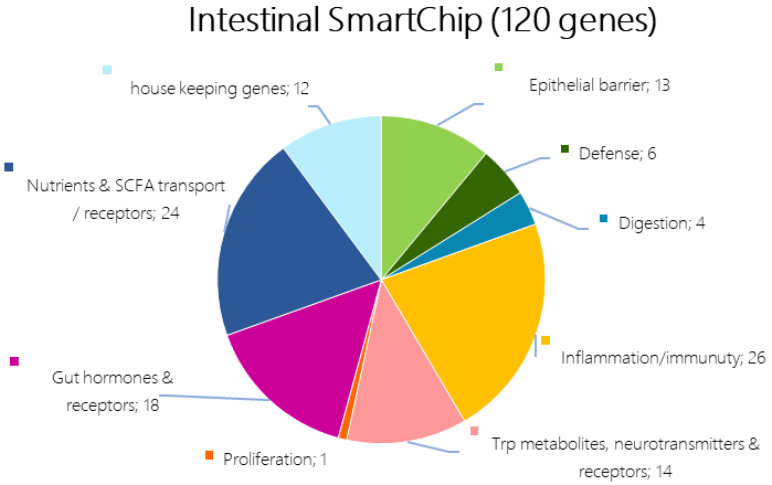
Metabolomic analysis : Tryptophan metabolites analysis in the Riddet Institute (New-Zealand)

Transcriptomic analysis : SmartChip analysis on brain and on intestine

Study of the effect of the diet on gut-brain axis with Alexandre's help (Master 2 trainee)

- Both are designed
- Intestinal SmartChip is ongoing





Conclusion

Diet affect apparent digestibility

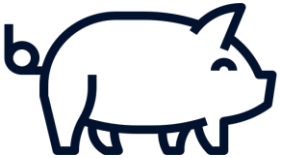
Differences in Ntot and Trp Apparent digestibility

Effect of diet on microbiota

Effect on intestine/brain development?

Study of gut-brain axis in process…

More research to do



Thanks

Do you have any questions?

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