Impact of antibiotherapy on growing rabbits assessed by a whole-blood transcriptomic approach

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INTRODUCTION

Reduction of antibiotic use

(societal expectations and European pressure)

Without degrading performances of rabbits (growth and health)

3 different approaches

- **Phenotypic**
- **Transcriptomic**
- **Metagenomic**

_01

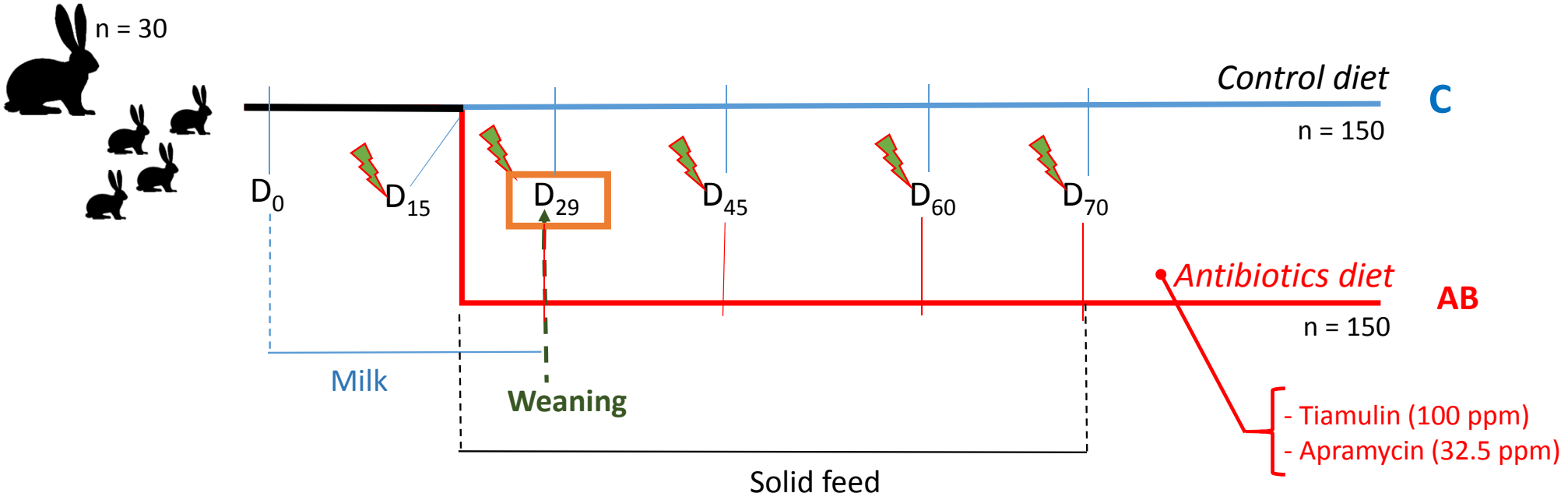
MATERIALS AND METHODS

Materials and Methods

Phenotypic study

Slaugther : sampling of blood tissues, feces, and cecal content

Checked
- daily : mortality + morbidity
- weekly : weight of rabbits + feed intake



Materials and Methods

Transcriptomic study

CRB GADIE (http://crb-gadie.inra.fr/)

Blood → D_{29}, D_{45} → RNA extraction → RT, labeling, Hybridization, and scan → Statistical analysis (R – Limma) → Ingenuity Pathway Analysis (IPA)

	2 groups
X	2 ages
X	8 animals
=	32 samples

INGENUITY SYSTEMS

_02
RESULTS

Results

Phenotypic study – Feed Intake

	Period	AB	C	*SEM*	*P-value*
Feed Intake (g/d)	D_{28-42}	104.6	97.9	*2.3*	*0.16*
	D_{42-70}	153.5	151.1	*3.0*	*0.69*
	D_{28-70}	137.2	133.3	*2.3*	*0.42*

N.S.

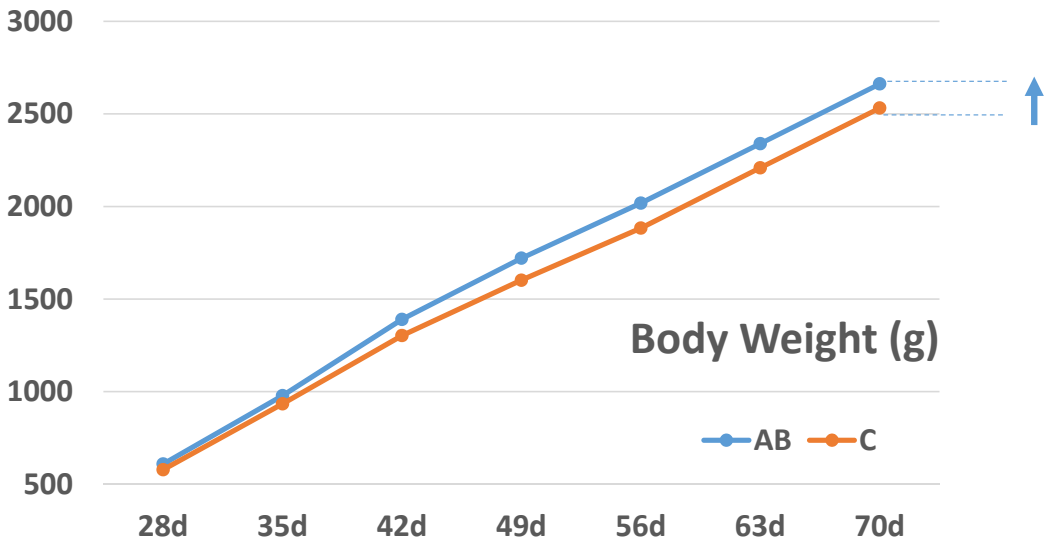
	Period	AB	C	*SEM*	*P-value*
Feed Conversion Ratio	D_{28-42}	1.85	1.88	*0.02*	*0.61*
	D_{42-70}	3.30	3.43	*0.06*	*0.32*
	D_{28-70}	2.77	2.85	*0.04*	*0.31*

N.S.

➡ No impact of antibiotherapy on the feed intake & feed conversion ratio

Results

Phenotypic study – Weight



+ 130 g / rabbit
For **AB** group

	Period	AB	C	*SEM*	*P-value*
Weight Gain (g/d)	D_{28-42}	56.5	52.3	*1.1*	*0.047*
	D_{42-70}	46.4	44.1	*0.6*	*0.075*
	D_{28-70}	49.6	46.8	*0.6*	*0.014*

And a greater weight gain

Results

Phenotypic study – Health Status

- Globally : good health status

- A post weaning **morbidity rate** lower with AB diet

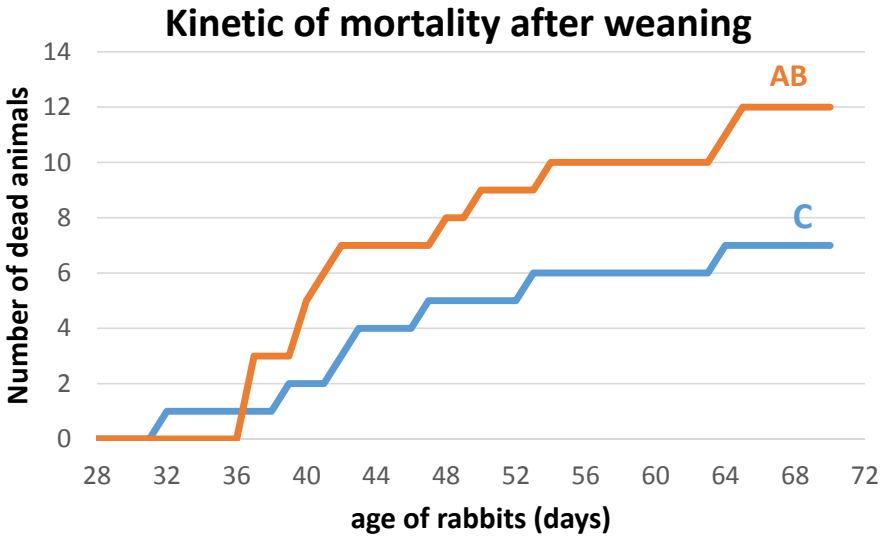
- But not between 42-70d

And…

- No significant difference in **mortality rate (P=0.32)!**

Morbidity rate (%)

Period	AB	C	*P-value*
28-42d	0.9	10.9	*0.002*
42-70d	2.6	3.0	*1*



Results

Transcriptomic study

Differential expression (DE)	Condition	Probes DE	Annotated genes DE
Group effect : **AB vs C**	29d	10	7
	45d	0	0
Age effect : **45d vs 29d**	C	2539	1698
	AB	0	0

Some higher gene expression for C group at 29d

Gene ID	logFC
SMYD3	- 0.78
SPINK4	- 1.92
PRELP	- 0.96
NCAPG2	- 0.91
DCHS1	- 1.37
ARRB1	- 1.21
IDE	- 1.18

Hypothesis : normal maturation of gene expression with age is inhibited by antibiotics through a an inhibition of the microbiota implantation

Results

Transcriptomic study

INGENUITY SYSTEMS

TOP FUNCTIONS

	# Molecules
Diseases and Disorders	
Cancer	1181
Infectious Disease	280
Gastrointestinal Disease	640
Hematological Disease	256
Immunological Disease	313
Molecular and Cellular Functions	
Cell Growth and Proliferation	558
Cell Death and Survival	543
Gene Expression	362
Cellular Assembly and Organization	255
Cellular Function and Maintenance	420
Physiological System Develoment and Function	
Organismal Survival	386
Hematological System Develoment and Function	324
Tissue Morphology	315
Hematopoiesis	198
Lymphoid Tissue Structure and Development	170

Top genes up-regulated

ID	LogFC
GZMB	2.253
IRF7	2.146
CCL5	2.090
PRF1	1.871
HSP90B1	1.782

Top genes down-regulated

ID	LogFC
PKNOX2	- 2.188
DCHS1	- 2.050
METTL7A	- 1.723
ARRB1	- 1.708
PTCHD3	- 1.648

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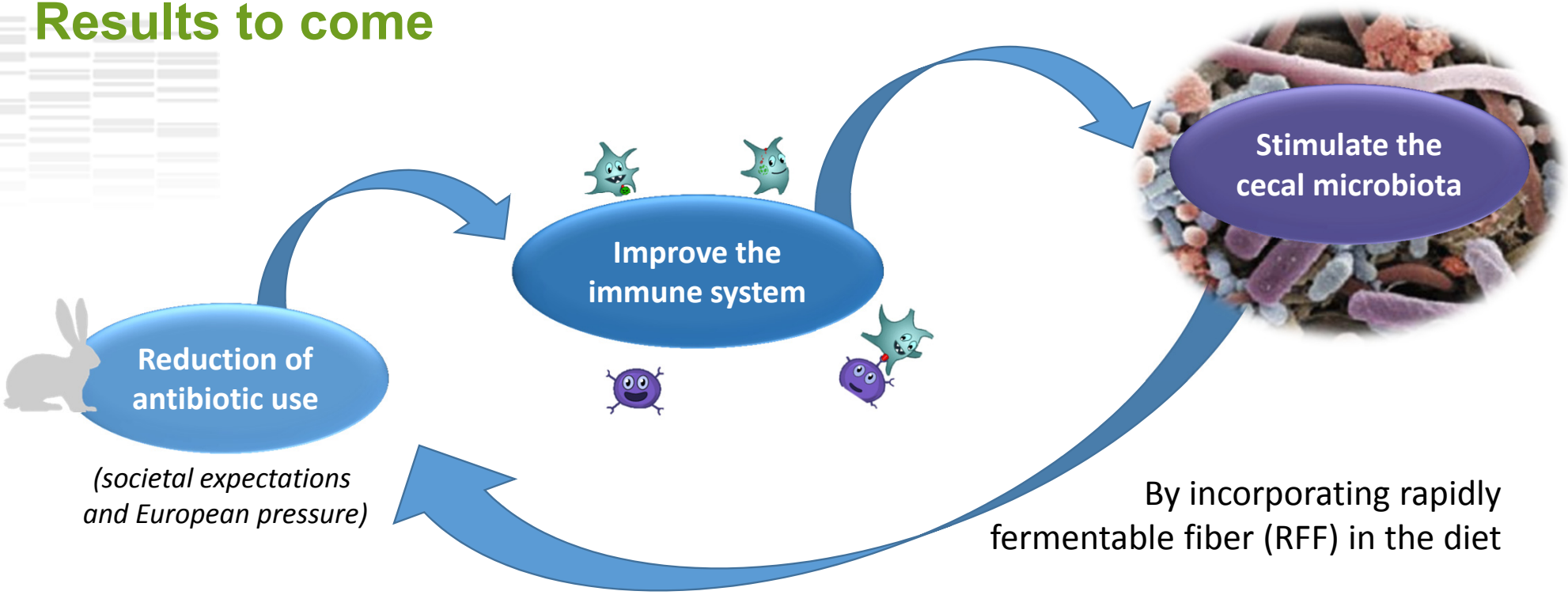
RESULTS TO COME & CONCLUSION

Results to come



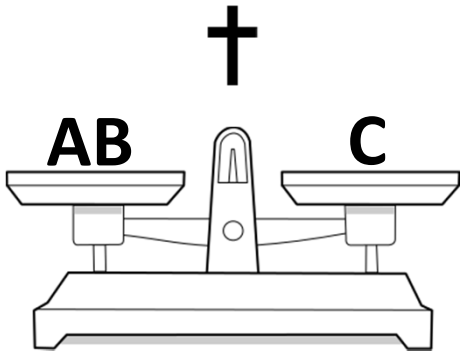
- Promising results with RFF, especially during post-weaning period.

- Waiting for metagenomics results.

Conclusion

Phenotypic study

- With antibiotics : only + 130g in BW at 70d (vs. C) and a lower morbidity rate.
- ***BUT …*** no difference between AB and C for parameters of feed intake, weight gain, and feed conversion ratio.
- Moreover, **no difference was found between groups for mortality**



Conclusion

Transcriptomic study

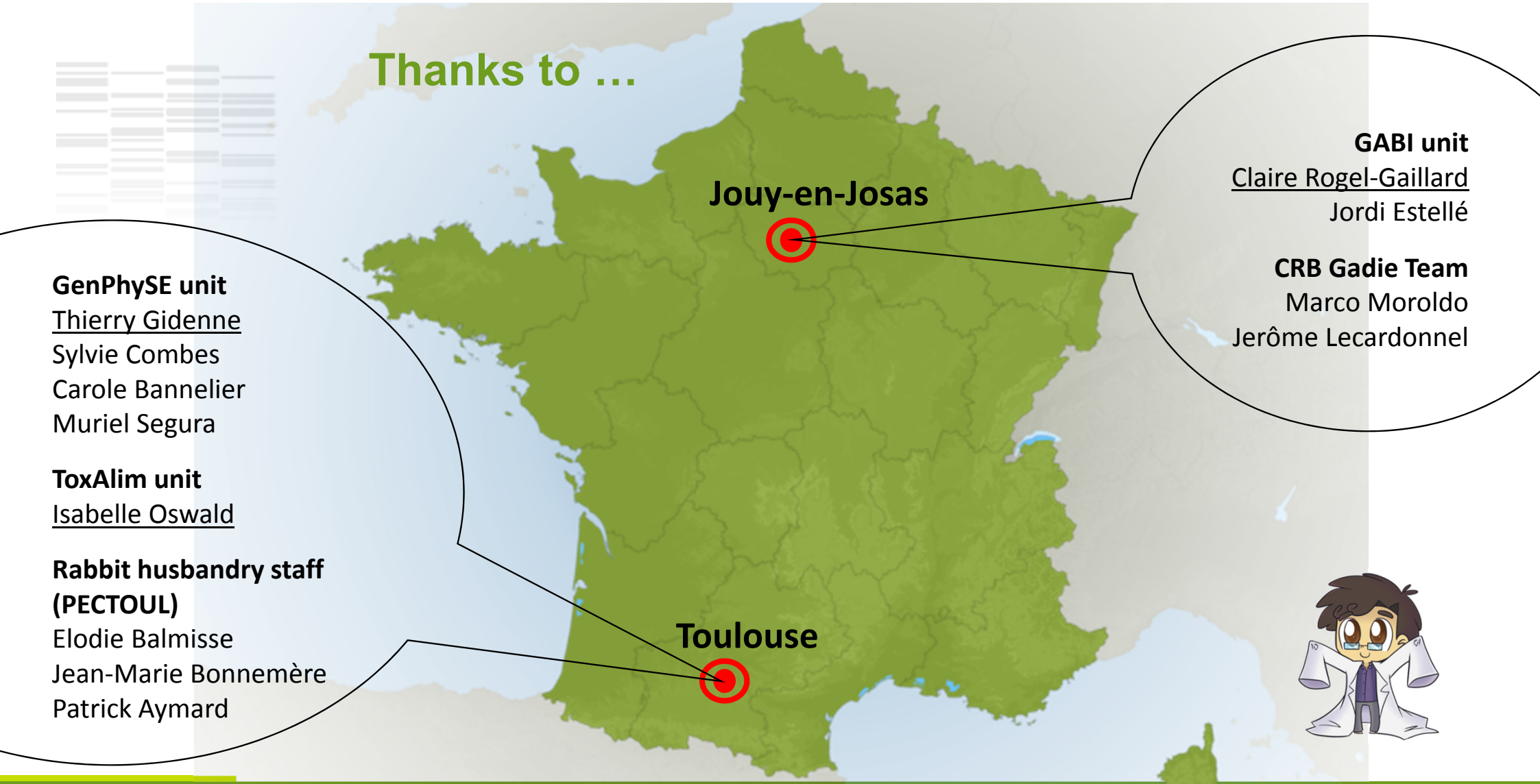
- Differential expression quite similar between AB and C for each age in blood.
- **Significantly changes** of the gene expression profile between 29 and 45 days for **C group**.
- But **no difference** in gene expression was observed for **AB group**.

→ ***Leveling of the gene expression in blood by AB***

→ ***Alternative to antibiotics in diet : rapidly fermentable fiber***

→ ***What impacts on cecal microbial ecosystem ?***

Thanks to …



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