



### Controlling the Rabbit Digestive Ecosystem to Improve Digestive Health and Efficacy

Sylvie Combes, Laurence FORTUN-LAMOTHE, Laurent CAUQUIL, Thierry GIDENNE

INRA Toulouse, UMR TANDEM



ASIC, Forli, 11 avril 2013



**Rabbit digestive ecosystem :** 



#### vast and rich community of microorganisms



10<sup>10</sup> - 10<sup>12</sup> Bacteria



10<sup>7</sup> - 10<sup>8</sup> Archaea





(Gouet and Fonty, 1973; Bennegadi et al 2003; Kimse et al 2008; Combes et al 2011)



(Suau et al., 1999)

#### **Dominant microbiota**



0%

### New evaluation using molecular microbiology techniques



### Molecular tools used to investigate rabbit digestive microbiota



#### 'omic' molecular tools



### Who is there?

#### Adult rabbit



80-90 % of the identified sequences → new uncultivated bacterial species

half of the sequences described in each study
are phylogenetically close to each other
→ uniqueness of the rabbit caecal microbiota



■ Bacteroidetes → 4 %

- Beta-gammaproteobacteria
- Firmicutes

Chuster IV (Firmicutes)

Cluster V (Firmicutes)



(Abecia et al., 2005 ; Monteils et al, 2007 )



### Qui est là?



### Controlling the Rabbit Digestive Ecosystem

# Roles of the microbiota and the benefits for the host

9



Why?

Microbiota implantation and ecological succession of species

How?

Potential ways to engineer the rabbit digestive ecosystem

#### Hydrolysis and fermentation of nutriments



#### **Implication in feed efficiency (evidence 1/3)**

#### **Inoculation of germ-free mice**



#### Implication in feed efficiency (evidence 2/3)



<sup>(</sup>Turnbaugh et al., 2006)

#### Implication in feed efficiency (evidence 3/3)

#### microbiota Particularity ?





(Ley et al. 2006)

### Role in defence against infectious agents and in the intestinal immune system (1/4)



### Role in defence against infectious agents and in the intestinal immune system (2/4)



(Stappenbeck et al., 2002)

### Role in defence against infectious agents and in the intestinal immune system (3/4)

#### **Diversification of the primary repertoire of antibodies** Stimulation by exogenous Ag **Microbiota** No exogenous stimulation Specific immune response Fetal liver, bone marrow GALT 2<sup>nd</sup> lymphoïdes organs Neonatal repertoire **Primary Repertoire** Secondary Repertoire -2 10 12 weeks 2 8 0 4 6 Birth Weaning Very low diversification **Diverse repertoire Highly diverse repertoire**

(Mage et al., 2006; Hanson and Lanning, 2008; Lanning et al., 2000; Fortun-Lamothe et Boullier, 2007)

### Role in defence against infectious agents and in the intestinal immune system (4/4)

#### Hygiene hypothesis:

• **the lack of stimulation or exposure** to pathogens and symbiotic microorganisms (microbiota) or frequent use of antibiotics in young children increases the susceptibility of patients to develop allergic disorders and autoimmune diseases



#### "dirty pig" experiment

- Microbiota alteration
- Higher expression of genes involved
- in inflammatory immune response

### Controlling the Rabbit Digestive Ecosystem



### Controlling the Rabbit Digestive Ecosystem

# Roles of the microbiota and the benefits for the host

19



Why?

# Microbiota implantation and ecological succession of species



Potential ways to engineer the rabbit digestive ecosystem

• Microbial colonization really begins at birth in contact with the mother and the immediate environment















<sup>(</sup>Combes et al. 2011)

Graphical representation of distances between bacterial communities



nMDS



#### Controlling the Rabbit Digestive Ecosystem



### Controlling the Rabbit Digestive Ecosystem

Roles of the microbiota and the benefits for the host

25



Why?

Microbiota implantation and ecological succession of species

How?

Potential ways to engineer the rabbit digestive ecosystem

### Potential ways to engineer the rabbit digestive <sup>26</sup> ecosystem



Immediate environment



#### Nutrition

Quantity et quality of fibres, proteins ... Prebiotics Probiotics

### Potential ways to engineer the rabbit digestive <sup>27</sup> ecosystem



#### Immediate environment

Initial colonisation is a subset of a wider meta-community including all species capable of living in the digestive tract (Curtis et Sloan, 2004)

✓ Does: genital and digestive tract, fur, maternal feces
✓ Breeding condition: nest box, beding, hygiene, farmer

28



### Immediate environment

✓ nursing mother *vs* the biological mother





#### Immediate environment

✓ during nursing, the doe leaves some faecal pellets in the nest that are eaten by the pups (Moncomble et al., 2004; Kovacs et al .2006)





29

(Combes et al., Submitted JAS).



#### Immediate environment

✓ during nursing, the doe leaves some faecal pellets in the nest that are eaten by the pups (Moncomble et al., 2004; Kovacs et al .2006)

• Does this behaviour contribute to mother microbiota transmission ?

The prevention of ingestion of maternal faeces by the pups delayed the implantation of *Bacteroides*. (Kovacs et al., 2006).



29

The prevention of ingestion delayed implantation dynamics

- Delayed the *Ruminococcaceae* age related increase
- Delayed the *Bacteroides* age related decrease (*Combes et al., Submitted JAS*).

30



(Michelland et al., 2011)



(Rodriguez-Romero et al., 2013)

### Potential ways to engineer the rabbit digestive <sup>31</sup> ecosystem



### Potential ways to engineer the rabbit digestive <sup>32</sup> ecosystem

Living microorganisms used as feed additives for animals and humans that can modulate the activities of the digestive microbiota in order to improve the health or performance of the host.



### Potential ways to engineer the rabbit digestive <sup>32</sup> ecosystem





(Motta et al. 2012)



(Kimse et al. 2012 ; Gidenne et al. 2006)

### Conclusion





#### **Thanks for your attention**

#### Merci pour votre attention

#### Thanks to all my team members



Laurent Cauguil





Carole Bannelier



Muriel Segura

Véronique Tartie





Katia Massip



Béatrice Gabinaud



Viviane Batailler



PhD students : Christelle Knudsen, Vincent Jacquier, Yapi Yapo Magloire, Muhammad Kaleem, Mickeal Rey, Asma Zened, Mélanie Martignon, Moussa Kimsé, Rory Michelland, Mélanie Gallois, Alexandre Feugier, Nadia Bennegadi, Laurence Debray...





ALIMENTATION AGRICULTURE ENVIRONNEMENT

