

# Bioactive milk components to secure growth and gut development in preterm pigs

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PIGUTNET FA1401 – STSM



LUND  
UNIVERSITY



# STSM

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Pigutnet FA1401 – STSM 03/September – 30/November/2017 (3 months)

Host: Thomas Thymann  
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# OUTLINE

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BACKGROUND

STSM – AIMS

STSM – TIMELINE

STSM – TASKS LEARNED / SKILLS ACQUIRED

STSM – OUTCOMES

# Background

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□ PhD thesis:

□ Development of the gastrointestinal tract in young mammals:

Effects of enteral provocation with **protease** or **phytohaemagglutinin (PHA)** in neonatal rats

□ Postnatal **gut maturation** precociously induced by **luminal stimuli**

□ **Switch** to an adult-type **intestinal epithelium** with changed **digestive** and **absorptive** properties, increased **barrier** properties and increased **pancreatic function**

# Background

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- Orally administered **pancreatic** and *pancreatic-like enzymes*:
  - **Proteases** provoked **precocious gut maturation**
  - Other enzymatic activities had no effects
  
- **Protease and PHA induced precocious gut maturation**
  - Mimic changes occurring naturally at weaning
  - Decreased intestinal macromolecular permeability
  - Increased leakiness temporarily
  - **Stimulation of pancreatic function**

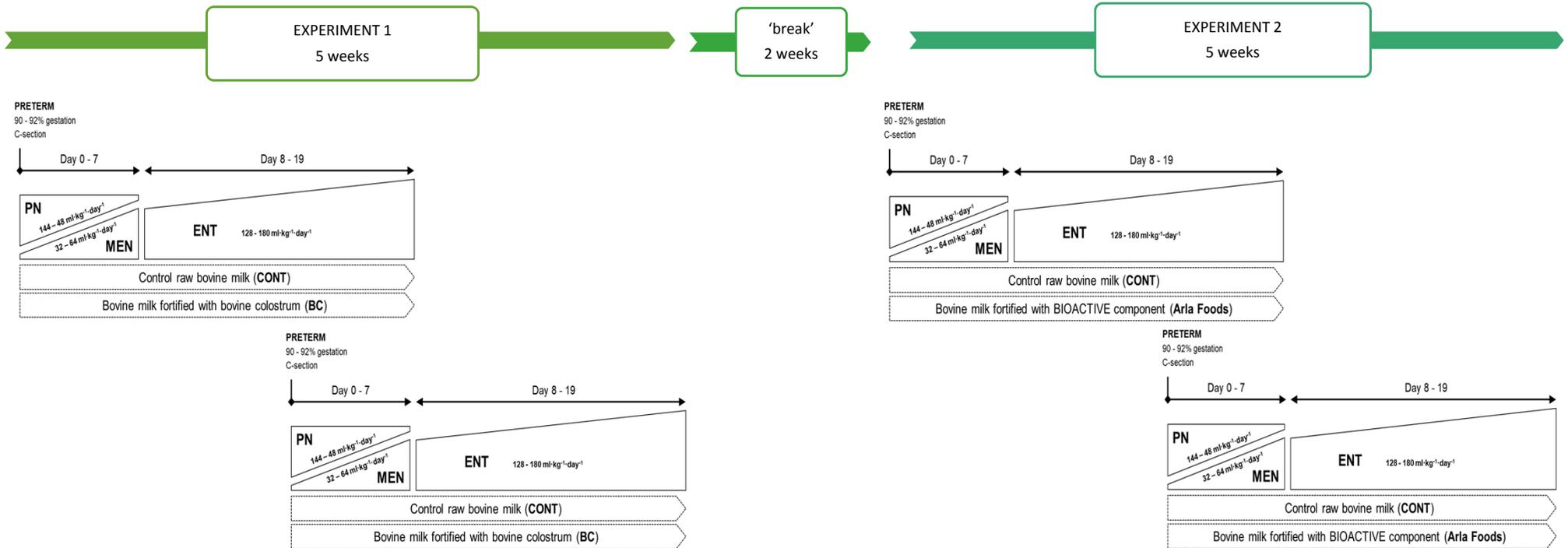
# STSM - Aims

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## □ Practical training on laboratory animal handling in experiments on pre-term pigs

- Become an active member of the team participating in the two big experiments:
  1. Protein fortification (bovine colostrum) of a base diet for preterm pigs
    - Evaluation of bovine colostrum protein fortification of a base diet for pre-terms. It has been found out that donor's milk has low protein content. Even though there is a commercially available human protein fortifier, the costs are very high. Thus, a bovine origin fortifier could be used in replacement and make it commercially accessible.
  2. Testing of a bioactive component from the company Arla Foods Ingredients
    - To monitor gastrointestinal function status for the potential health benefits of the dietary factor

# STSM - Timeline



# STSM – Tasks learned / skills acquired

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- During caesarean sections: bring newborn piglets to NICU, monitor breathing and temperature until stabilisation
- Daily routines: body weight, dosage, data recording, enteral feeding (every 2/3 hours), PN lines, administering i.v. boluses when needed
- CLINICAL and 'faeces' **scoring** to assess gut and general **health status**
- *In vivo Tests Assistance*: galactose absorption test and Behaviour tests: trough drinking training, room and handling habituation, assisting during behaviour tests
- Sampling organs: gut, other internal organs, brain, etc. as well as blood collection from the jugular vein

# STSM Outcome

51<sup>st</sup> annual meeting  
ESPGHAN 2018  
Geneve, Switzerland

Abstract

Poster presentation

## Pancreatic enzyme maturation is delayed and not affected by the first enteral nutrition in preterm pigs

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**Objectives:** Preterm infants have an immature digestive system, predisposing them to short- and long-term complications, including food intolerance and necrotizing enterocolitis (NEC). Pancreatic enzymes are important for digestion but little is known about the postnatal development of the exocrine pancreas, and how it responds to enteral nutrition. Using a piglet model, our objective was to compare the exocrine pancreas of preterm and term pigs, fed either minimal enteral nutrition (MEN) or total parenteral nutrition (TPN) for the first 5 days after birth.

**Hypothesis:** - Postnatal development of the exocrine pancreas is delayed after preterm birth.

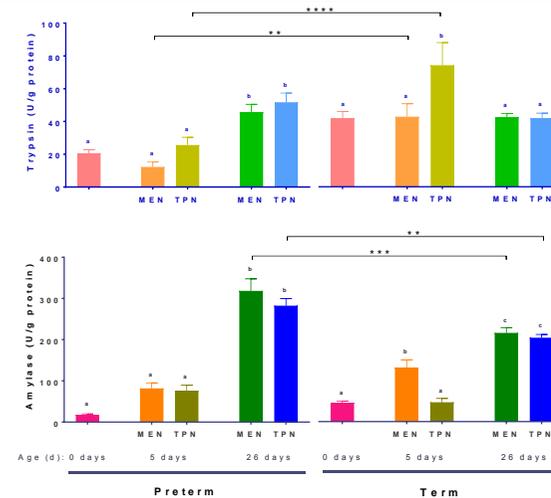
- Minimal enteral nutrition during the first days of life provides better stimulation of the exocrine pancreas function relative to total parenteral nutrition.

### Conclusions:

- Pancreatic trypsin and amylase relative activities increased with age in preterm piglets, and by day 26 the enzyme levels converged to those of term piglets.
- TPN or MEN nutrition for the first 5 days only had transient effects on enzyme levels in term piglets, indicating that the effect of enteral nutrition is age-dependent.
- Increased trypsin activity in term, 5 d-old TPN-fed piglets may be explained by lack of enteral stimuli to stimulate pancreatic secretion.
- Conversely, amylase activity level was very low at birth and increased with age.
- Lower amylase activity in term, 5 d-old TPN-fed piglets may be explained by lack of enteral stimuli to increase enzyme production.

**Pancreatic trypsin and amylase activities depend on both gestational age at birth and postnatal age and have different sensitivities to the first feeding.**

**Methods:** Pigs were delivered by caesarean section preterm (90% gestation) or at full term, and were nurtured during the first 5 days with total parenteral nutrition (TPN) or with parenteral nutrition plus minimal enteral nutrition (MEN) with bovine colostrum. From day 6, all pigs were fed full enteral nutrition with bovine milk until postnatal day 26. Pancreatic samples were collected on days 1, 5 or 26 from both preterm and term pigs (n=116). Trypsin and amylase activities were analyzed in tissue homogenates. Protein content was measured and used to calculate the relative amount of the enzymes. Data were analyzed for the same gestational age between treatments (e.g. MEN vs TPN, Tukey's post-hoc test,  $P < 0.05$  indicated with different letters) and within treatments between different gestational ages (e.g. Preterm vs Term, Sidak's post-hoc test,  $P < 0.05$  indicated with \*).



**Results:** Trypsin and amylase activity increased with age in preterm piglets, especially by 26 days ( $P < 0.05$ ), with no differences between the diet regimens (TPN vs MEN) (see Figure). Term piglets showed higher trypsin activity levels at birth and these were largely maintained with advancing age, except for higher levels in TPN-fed relative to MEN on day 5 ( $P < 0.05$ ). Amylase activity was low at birth in term piglets and increased with age ( $P < 0.05$ ). At 5 days, term TPN-fed piglets had lower amylase activity relative to MEN. Trypsin activity was lower in preterm than in term piglets at 5 days after birth ( $P < 0.05$ ) whereas amylase was higher in preterm than in term piglets at day 26 ( $P < 0.05$ ).

# STSM - Outcomes

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## *Manuscript in preparation*

**‘Development of exocrine pancreatic function in early life in pigs and how it can be influenced by diet.’**

- Pancreatic tissue collected at Copenhagen, Denmark
- Analysis of pancreatic tissue for **peptidase**, **amylase** and **lipase** activity in Lund, Sweden
- Additional data to be included on expression of PLRP-2 analysed in St. Louis, USA

# STSM – Outcomes

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*Manuscript in preparation*

## □ EXPERIMENT 1

- Postconception vs. postnatal age  
(PRETERM – TERM)

## □ EXPERIMENT 2

- Parenteral Nutrition vs. Minimal Enteral Nutrition  
(TPN) (MEN)
- PRETERM vs. TERM

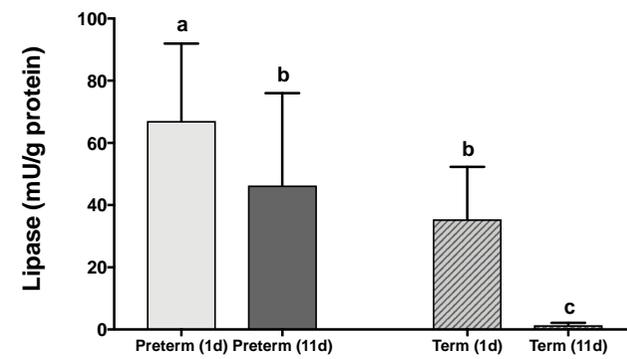
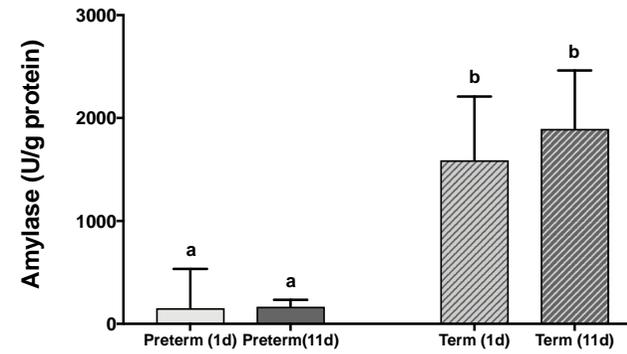
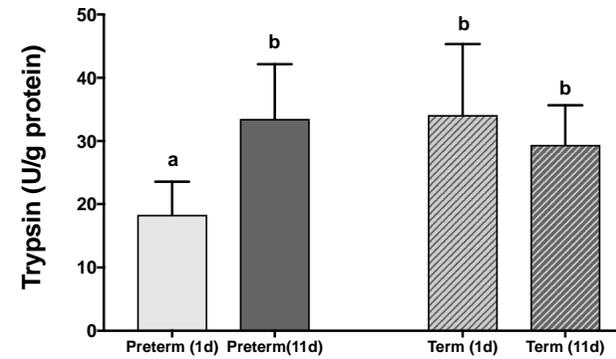
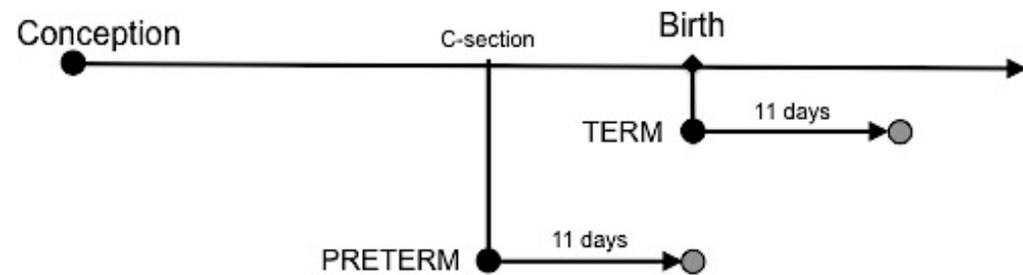
## □ EXPERIMENT 3

- Bovine colostrum fortification vs. raw bovine milk  
in preterm piglets

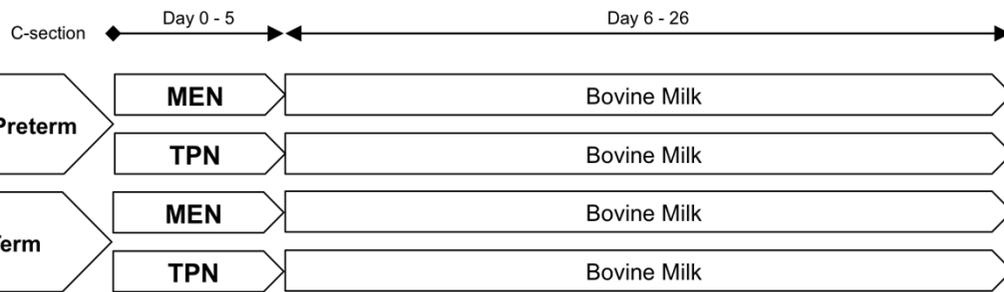
## HYPOTHESIS

- Postnatal development of the exocrine pancreas is delayed after preterm birth
- Minimal enteral nutrition during the first days of life provides better stimulation of the exocrine pancreas function relative to total parenteral nutrition
- Bovine colostrum fortification stimulates exocrine pancreas function

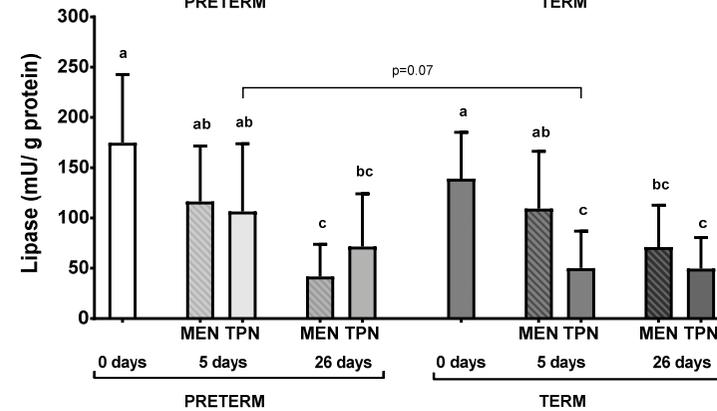
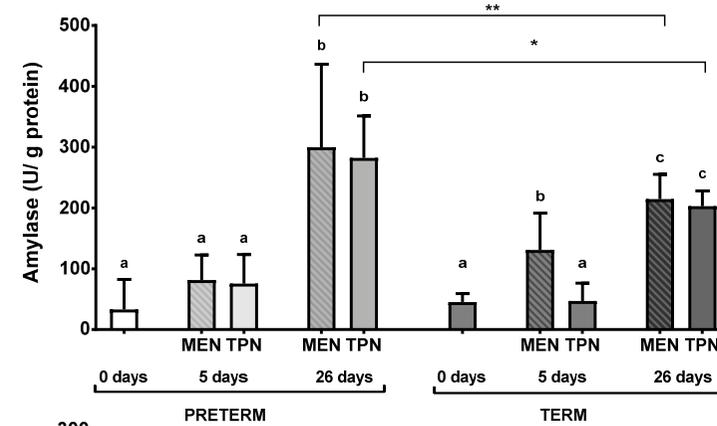
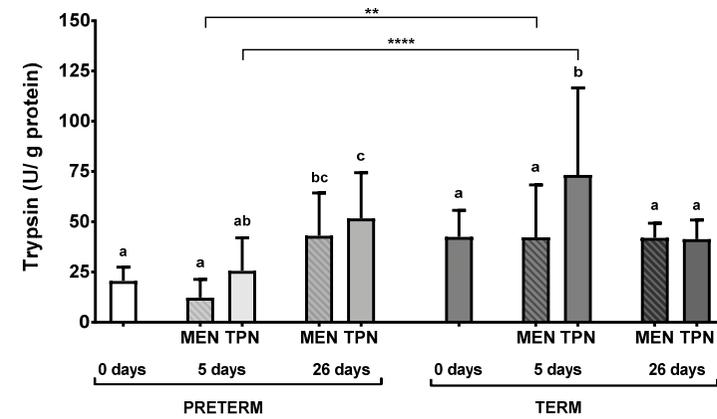
# Post-conception vs. Postnatal age



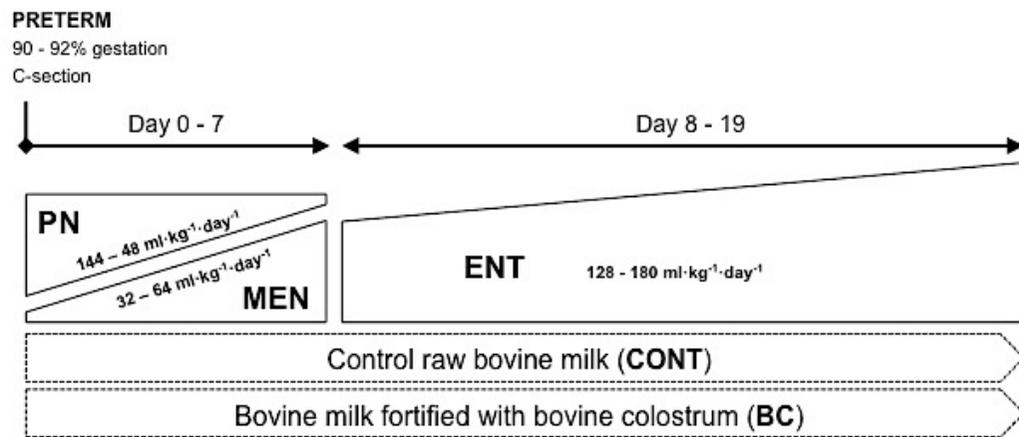
# Parenteral Nutrition (TPN) VS. Minimal Enteral Nutrition (MEN)



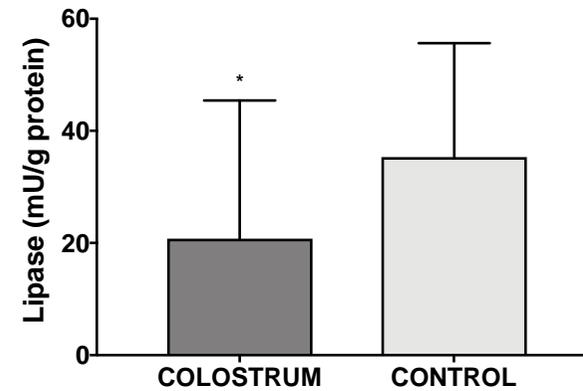
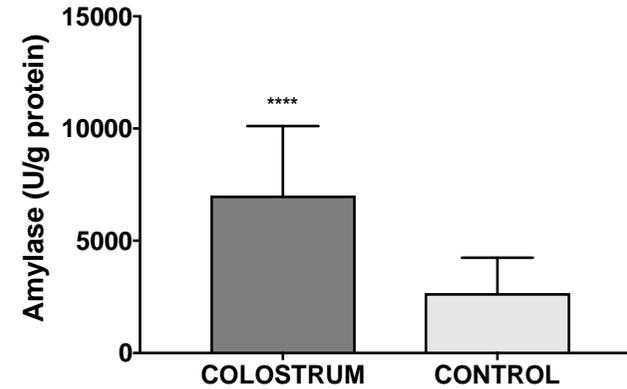
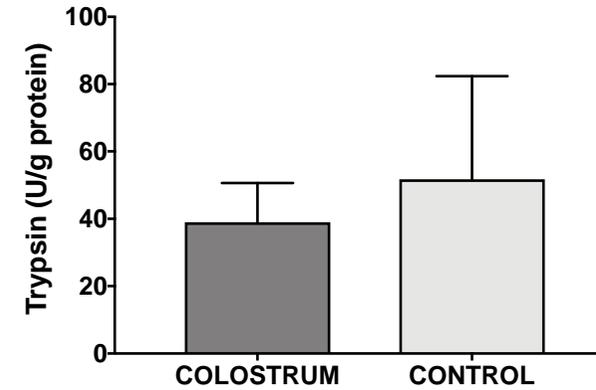
MEN: Minimal Enteral Nutrition  
 TPN: Total Parenteral Nutrition



# Bovine colostrum fortification vs. raw bovine milk in preterm piglets



MEN: Minimal Enteral Nutrition  
PN: Parenteral Nutrition  
ENT: Enteral Nutrition



# STSM – Outcomes

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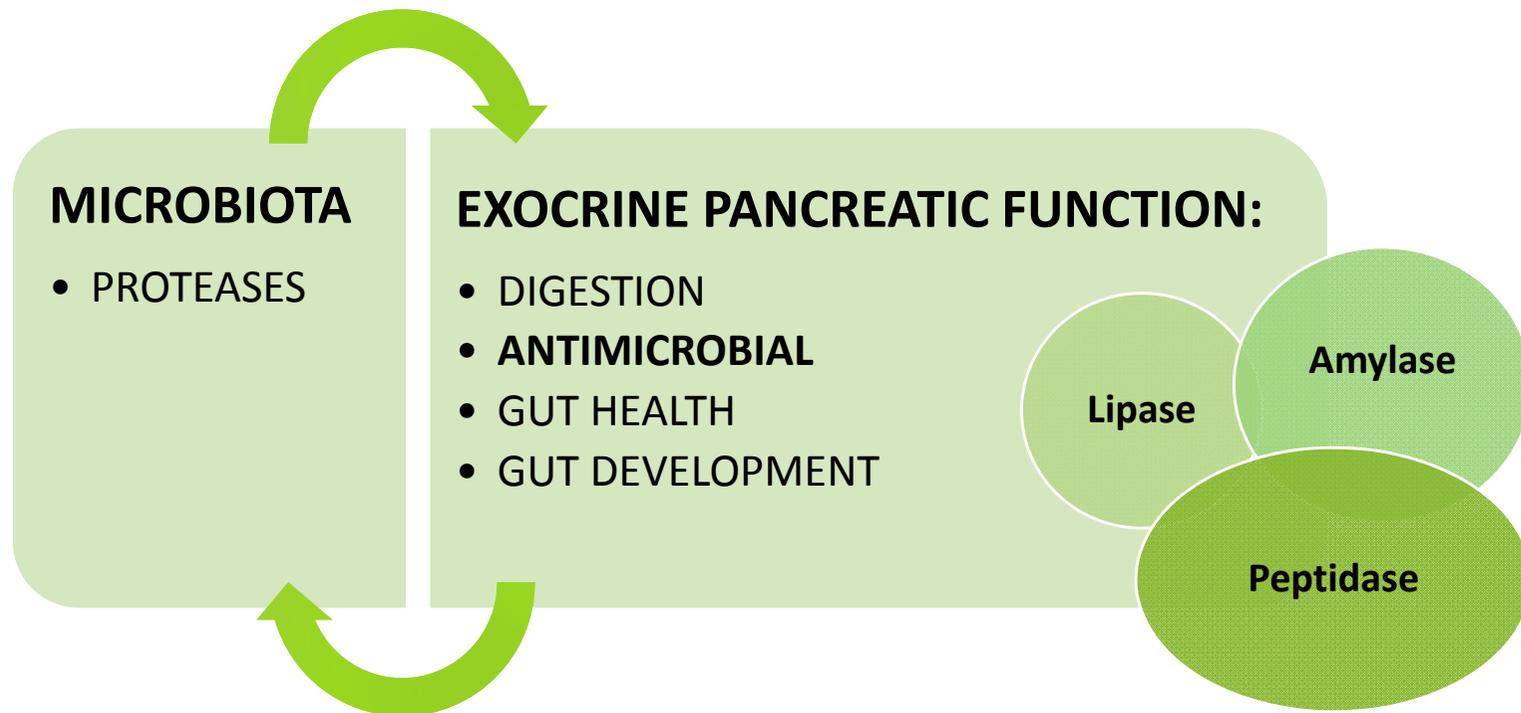
*Manuscript in preparation*

## CONCLUSIONS

- Pancreatic enzymes activities depend on both gestational age at birth and postnatal age
  
- Effect of enteral nutrition is age-dependent
  - TPN or MEN nutrition for the first 5 days only had transient effects on enzyme levels in term piglets
  - TPN – lack of enteral stimuli – has different effects on different pancreatic enzyme activities
  
- Pancreatic enzyme activities have different sensitivities to the first feeding

# DIETARY MODULATION

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# THANKS FOR YOUR ATTENTION

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