

Winter School 2008-09:

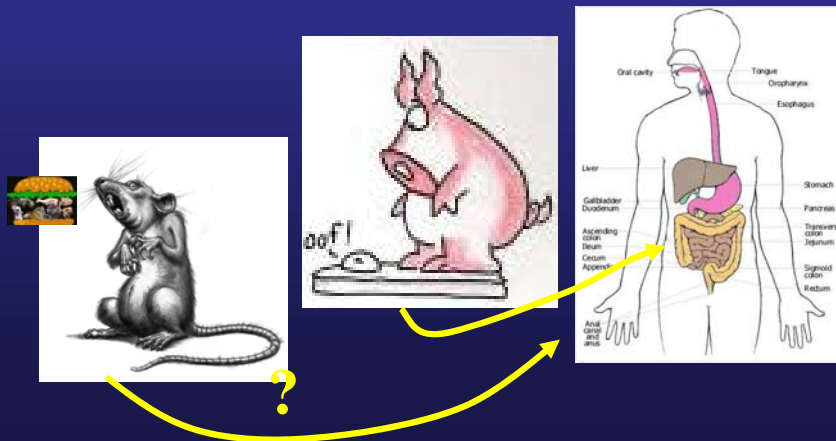
## **Gastrointestinal tract in development of allergy and obesity Pre- and probiotics?**

- 1) What is state-of-the-art within the field in question?
  - Intense studies on time/dose/strains. A deep soup!
- 2) What are the hypotheses?
  - That pre- and probiotics will positively affect gut flora
- 3) Which results have been achieved?
  - A great pile of highly diverse, mainly clinical, results
- 4) What are the most important areas to focus on?
  - The biological mechanisms of pre- and probiotic action
- 5) What is the best way to use the results for prevention of allergy and/or obesity?
  - Make more combined cell, animal and human studies

## **Main conclusions from early LIFE work:**

- 1) Initial colonization in at birth plays a major role for gut health  
(Gastroenterology, 2006)
- 2) Gut colonization depends on birth mode (caesarean/vaginal)  
(Am.J.Physiol. 2008)
- 3) Antibiotics at weaning greatly alters gut colonization/immunity  
(Br. J. Nutr. 2007)
- 4) Enteral versus parenteral nutrition greatly affects colonization  
(Am. J. Physiol. 2009)
- 5) Immunomodulatory diets affect immunity and colonization  
(J. Nutr., Gastroenterology 2009, submitted)
- 6) Milk lactose is a pre-biotic, nutritional fermentation is crucial  
(Am. J. Physiol. to be submitted)
- 7) Probiotics decrease inflammation via mucosal protection  
(J. Nutr., 2008)
- 8) Probiotics may be harmful for hypersensitive subjects  
(J. Ped. Gastr. Nutr., 2008)

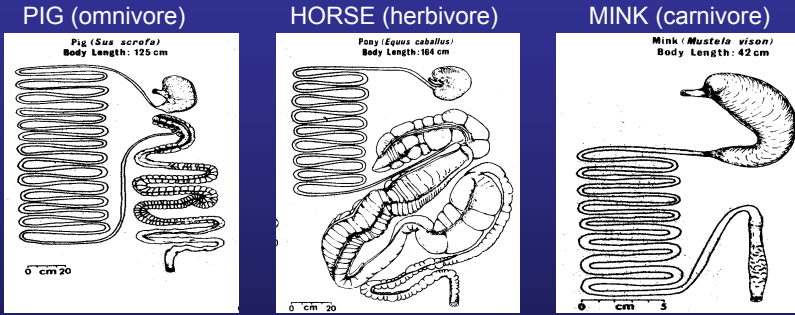
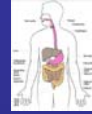
## Animal models in pre – and probiotic research?



## What is a good model for gut-nutrition-microflora?

- 1) **Similarity in key nutrition-relevant organs/tissues?**  
(gastrointestinal tract, liver, metabolism.....)
- 2) **Similarity in natural dietary habits?**  
(herbivore, omnivore, carnivore, meal pattern, seasonal changes....)
- 3) **Spontaneous nutrition-related diseases**  
(e.g. type-2, CHD, obesity, allergy, malabsorption, atherosclerosis...?)
- 4) **Life cycle development & body composition**  
(maturity at birth, life span, nutritional transitions.....)

# Gut anatomy - a key factor for species-specific nutrition & gut microflora



Similar tissue/cell metabolism

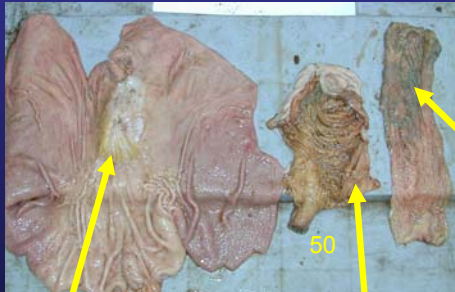
## Nutrition/microbiota-related gut disease:

**DP Burkitt (1975):**

Big faeces → Small hospitals  
Small faeces → Big hospitals



High fat – low fiber:



Low fat – high fiber:

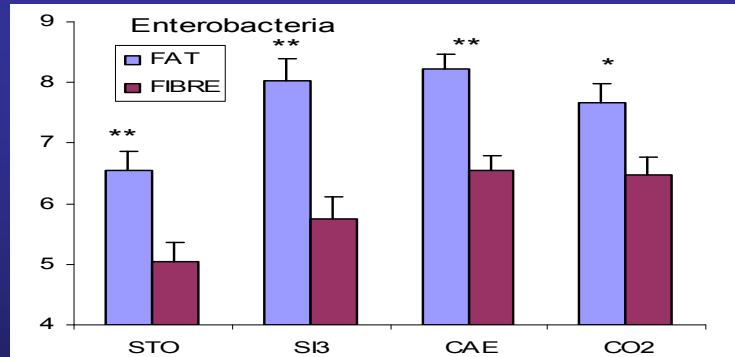


Stomach: Keratinization and mild erosive damage (early ulcer)

Caecum: Red/brown/yellow inflamed mucosal surface

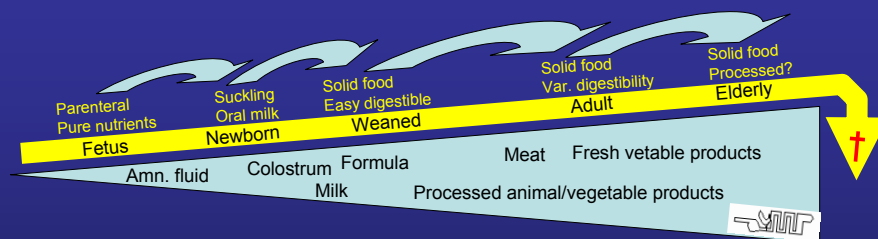
Colon: Sticky food material with much epithelial contact

## Nutrition-induced gut microflora change?

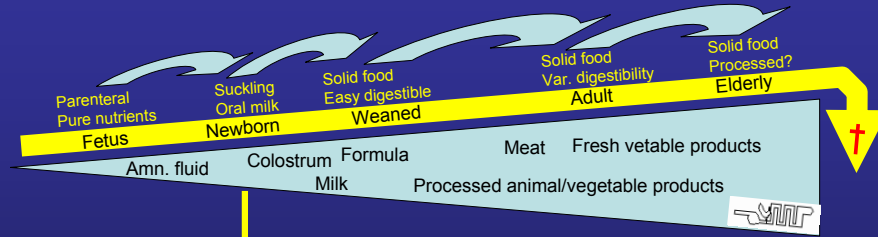


- ☹️ Microbiology (more pathogens, sub-optimal fermentation)
- ☹️ Patology/histology (inflammation, histology OK)
- ☹️ Organ anatomy (smaller stomach, colon)
- ☹️ Gene expression (reduc. C1Ca-1 mRNA, 90 others OK)
- 😊 Mucosa physiology (OK digestive enzymes)

## Developmental Nutrition & Microbiology



# Developmental Nutrition & Microbiology



**Preterm birth + milk + flora → NEC**

Probiotic diet?

Immunosuppressives?

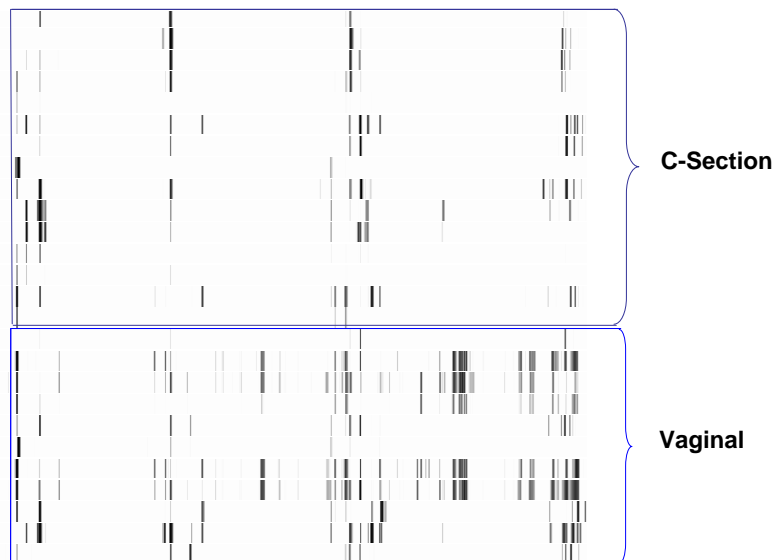
Prebiotic diet?

Immunostimulants?

Birth colonization?

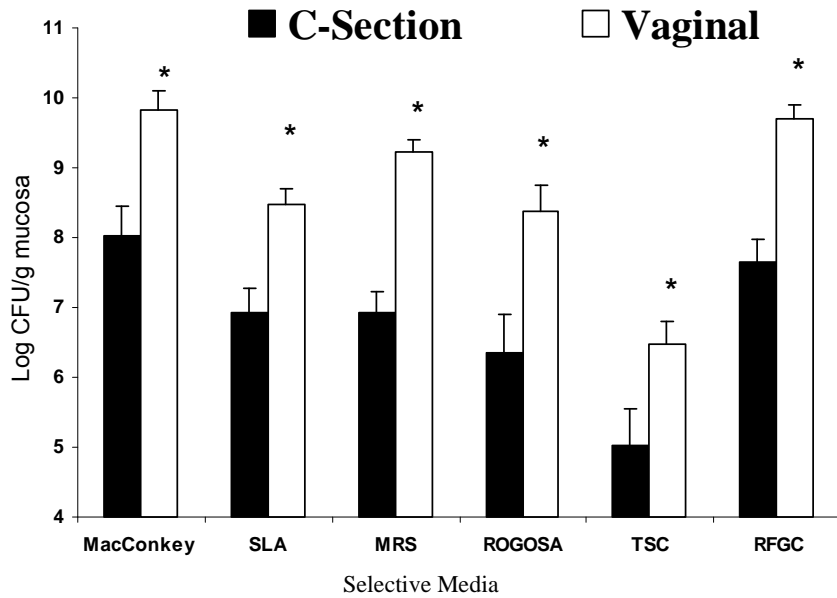
Milk bioactives?

## T-RFLP Bacterial Identification



**Vaginal Delivery = Significant Increase in Bacterial Diversity**

## Microbial load in colonic mucosa of preterm pigs



## Is gut microflora crucial?

Vaginal or Caesarean - Conventional

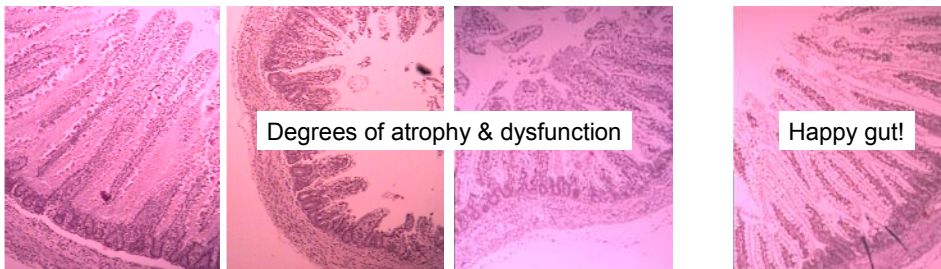
Colostrum

Formula

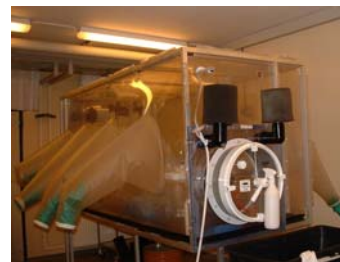
Formula

Germ free (sterile)

Formula

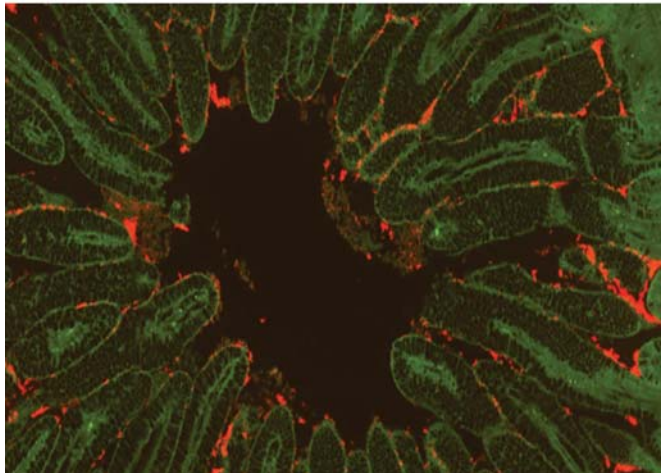


Pig NICU



Gastroenterology 130, 2006

Am. J. Physiol. 294, 2008



Probiotics in the prevention of necrotizing enterocolitis in preterm piglets

*Bifidobacterium animalis*  
*Lactobacillus acidophilus*  
*Lactobacillus casei*  
*Lactobacillus pentosus*  
*Lactobacillus plantarum*

$10^{10}/d$  during TPN/formula

NEC score ↓  
Structure ↑  
Function ↑  
Fermentation ↓  
Clostridium ↓  
Commensals ↑



### Conclusions:

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