



Påvirkning af tarmens metagenom gennem fodring og fæcestransplantation

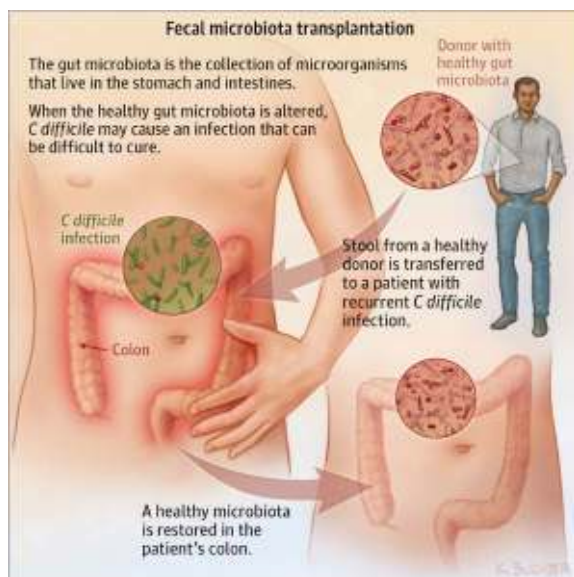
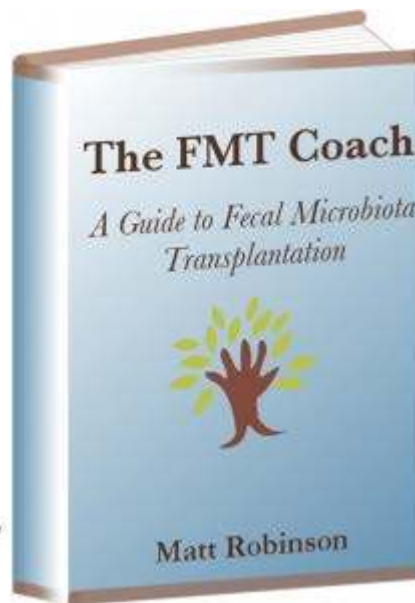
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Comparative Pediatrics and Nutrition





POO AS MEDICINE

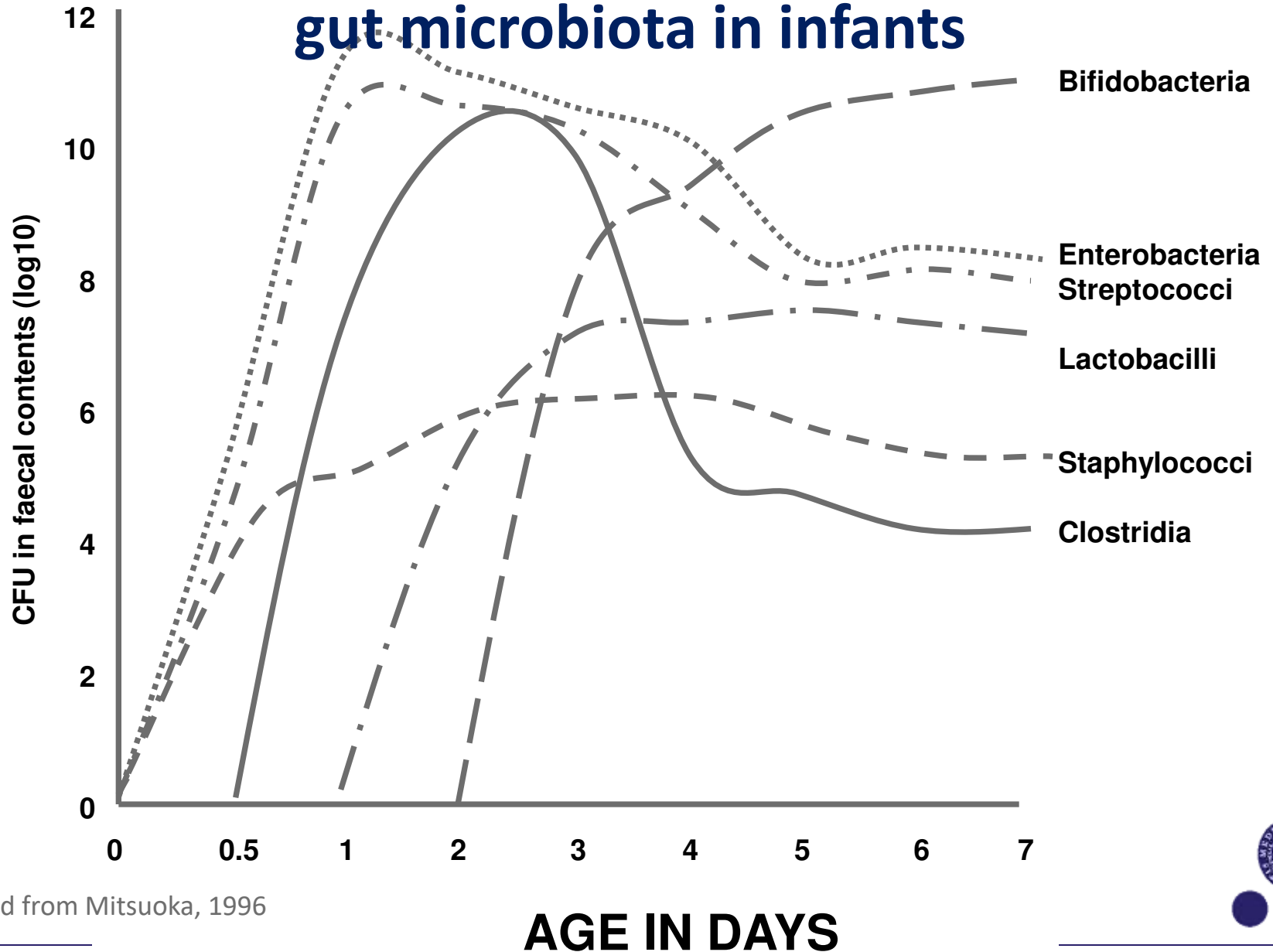
Dr. Daniel Aronov



FMT relevant for newborn infants and pigs ?



Developmental trajectory of fecal gut microbiota in infants



Modified from Mitsuoka, 1996



Mass sequencing

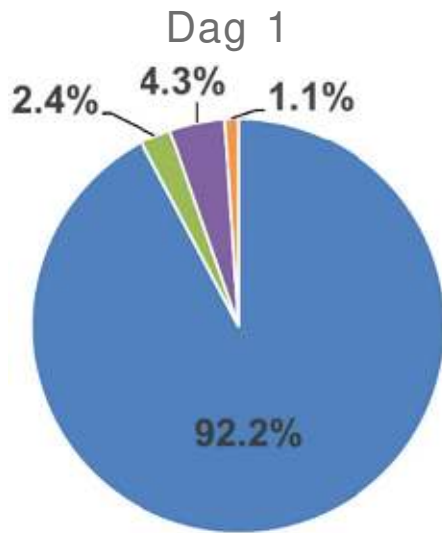
Sekventering af
genomet og
metagenomet



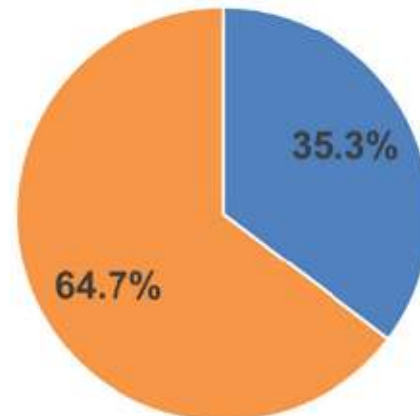
Stripped Science

by Viktor S. Poór

Hvor kommer de koloniserende mikroorganismer fra ?

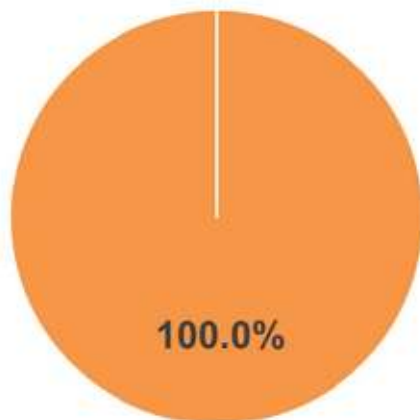


Dag 3

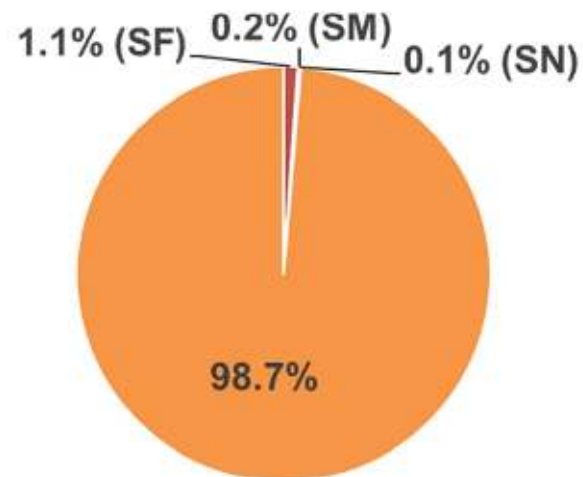


- stibund
- so fæces
- so mælk
- patte
- fødselskanal
- ukendt

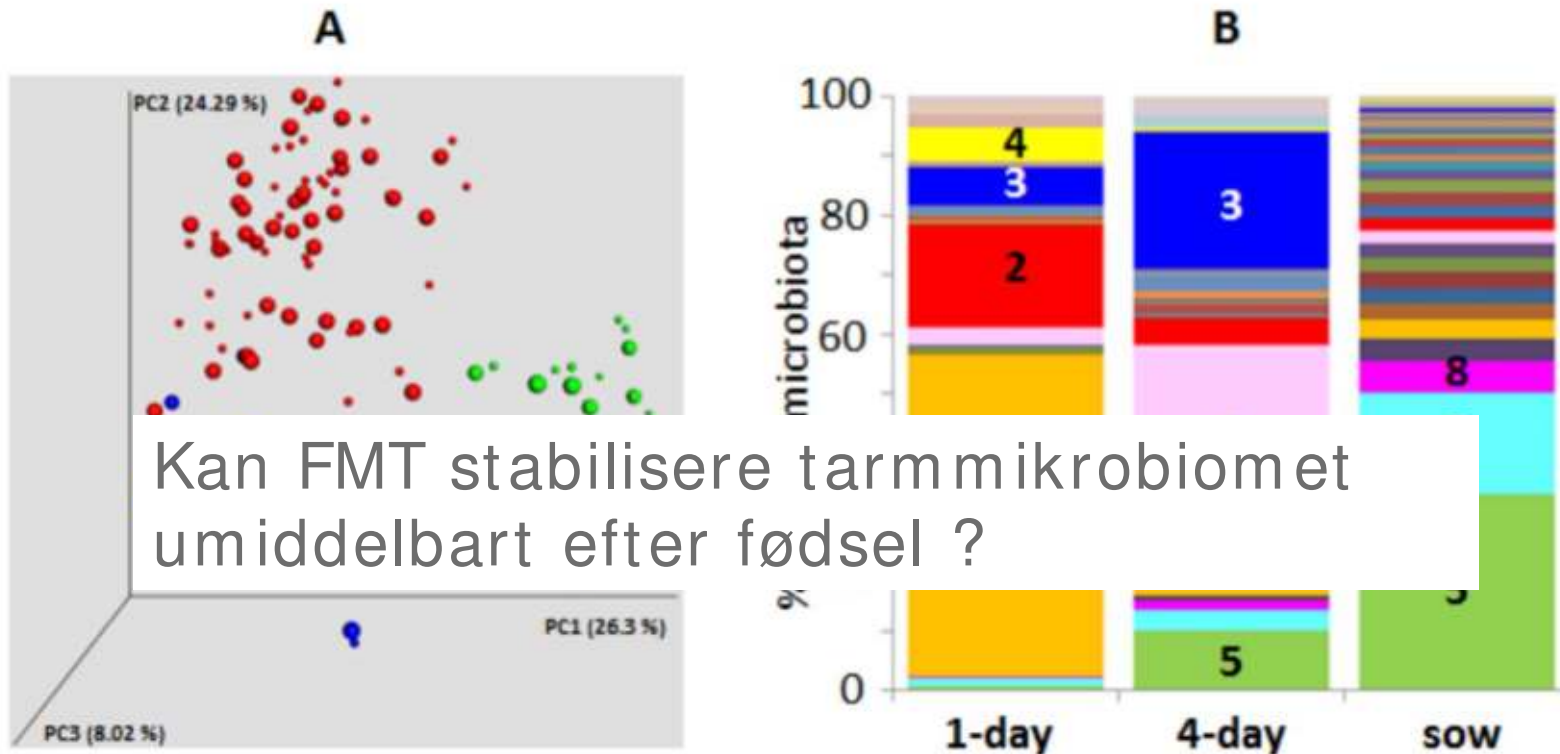
Dag 7



Dag 21



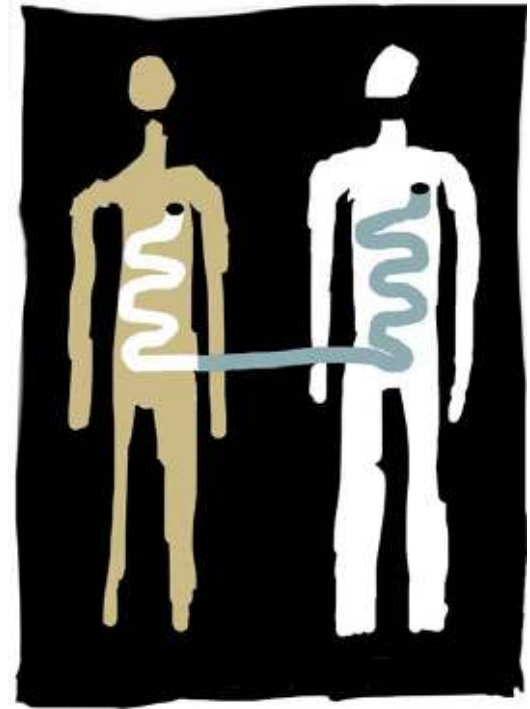
Hvordan ændrer mikrobiomet sig lige efter fødsel?



Kan FMT stabilisere tarmmikrobiomet umiddelbart efter fødsel ?

Fig 1. Microbiota composition in sows, 1- and 4-day-old piglets. Panel A, weighted PCoA analysis of microbiota composition in sows (blue spots), 1-day-old piglets (green spots) and 4-day-old piglets (red spots). Smaller spots—microbiota of sows kept under conventional conditions with slatted floor, or of piglets delivered by these sows. Bigger spots—microbiota of sows kept in enriched pens with floor covered with straw bedding, or of piglets delivered by these sows. Panel B, composition of fecal microbiota of 1-day-old piglets, 4-day-old piglets and sows at the time of farrow 1—*Escherichia*, 2—*Clostridium*, 3—*Fusobacterium*, 4—*Actinobacillus*, 5—*Prevotella*, 6—*Bacteroides*, 7—*Oscillospira*, 8—*Ruminococcus*. For all genera, see S1 Table.

Hvem er den bedste donor ?
Hvornår skal det gives ?
Hvor meget ?
Hvilken vej ?
Hvor ofte ?
Intakt fæces eller filtrat ?



Nekrotiserende enterocolitis (NEC)

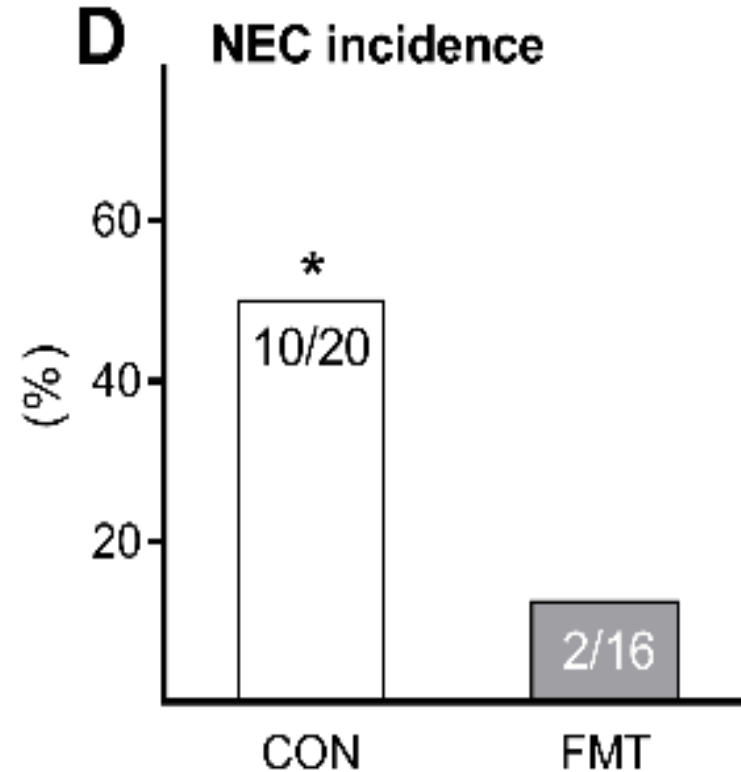
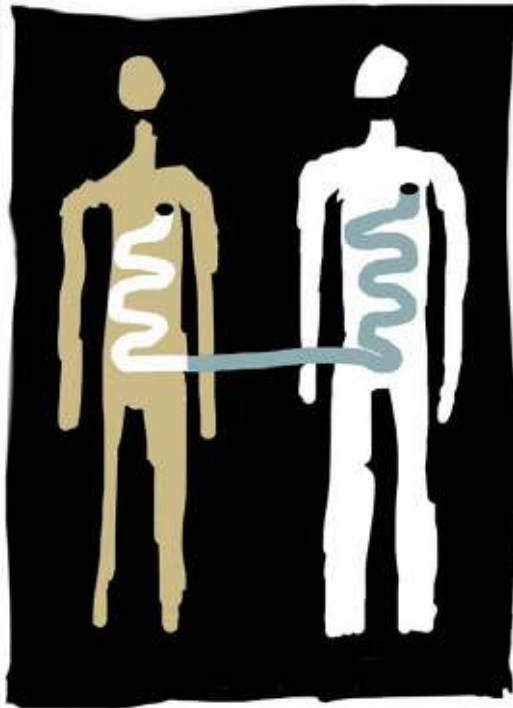


NEC i præmature grise
benyttes en følsom
sygdoms-model

Fecal transplant to preterm pigs



25 incubators
Respiratory support
Temp./moisture control
Parenteral/enteral nutrition
24 hour camera surveillance



Fecal microbial transplantation (FMT) from 10-day old healthy pigs reduces NEC in preterm piglet recipients.

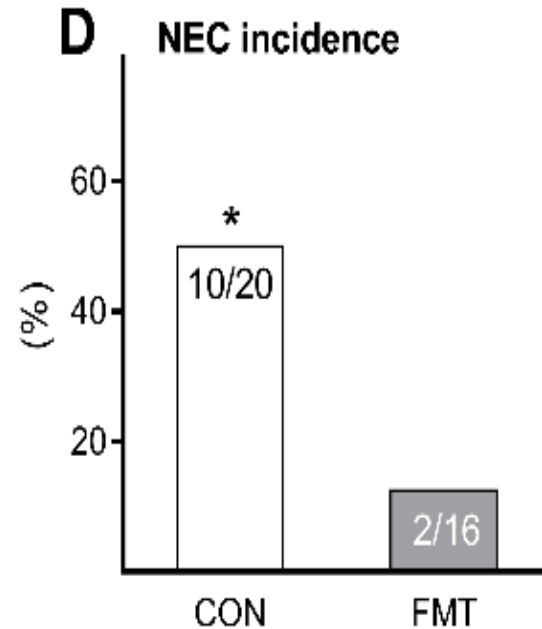
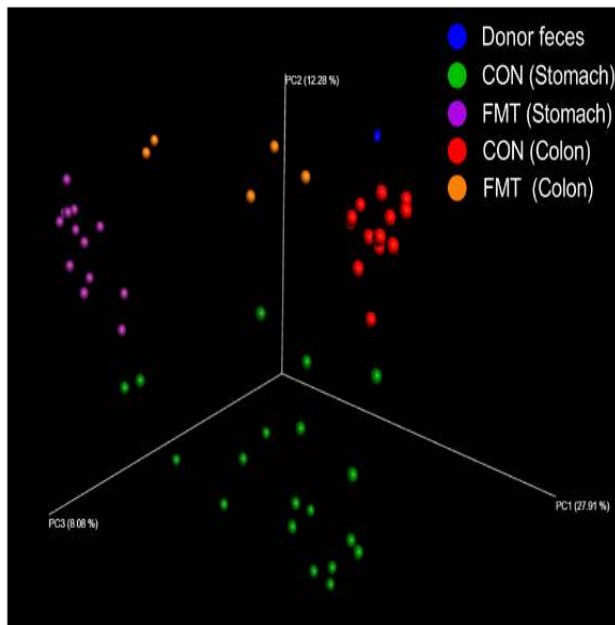
Brunse & Martin et al. 2018, ISME

Fecal microbial transplantation (FMT) to preterm pigs.

Donor: 10 day old pigs

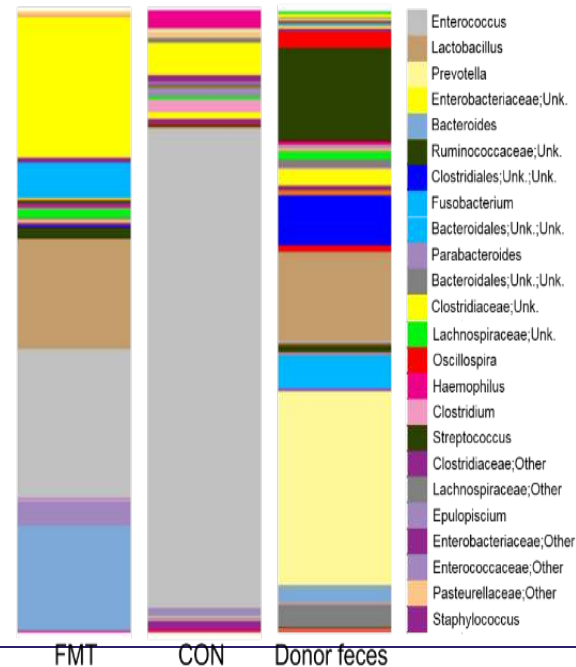
Brunse & Martin et al. ISME 2018

A

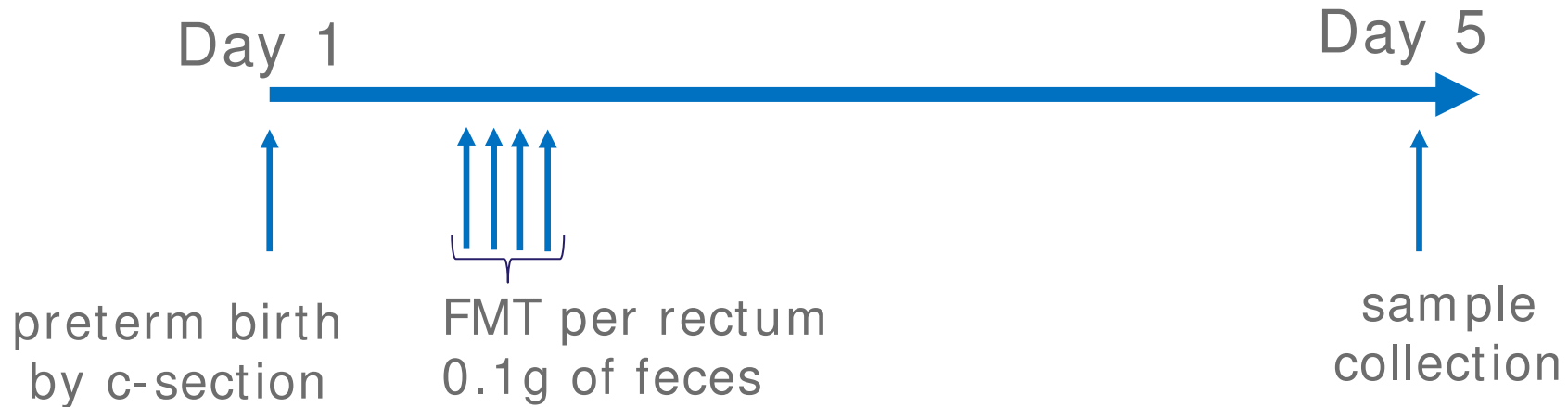


Do all donors provide the same effect ?

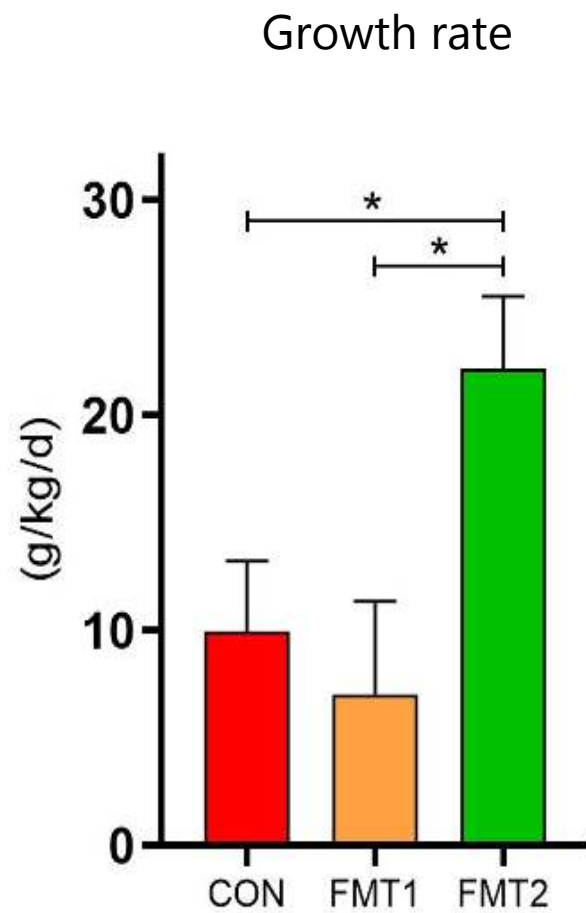
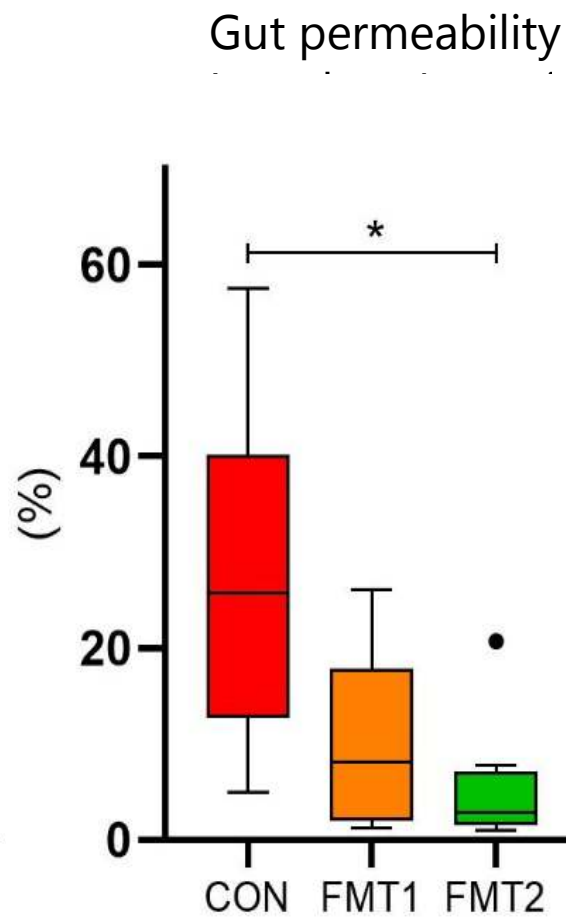
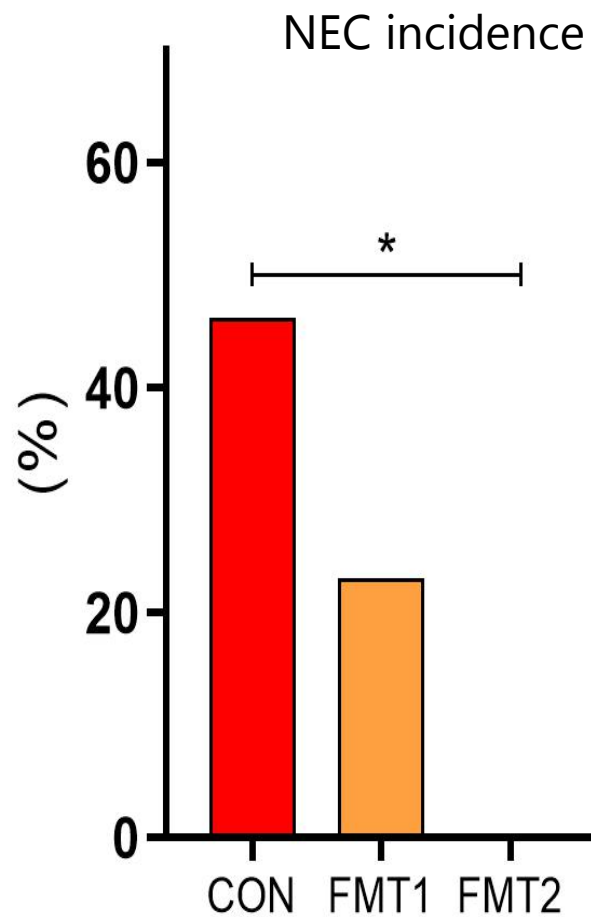
B



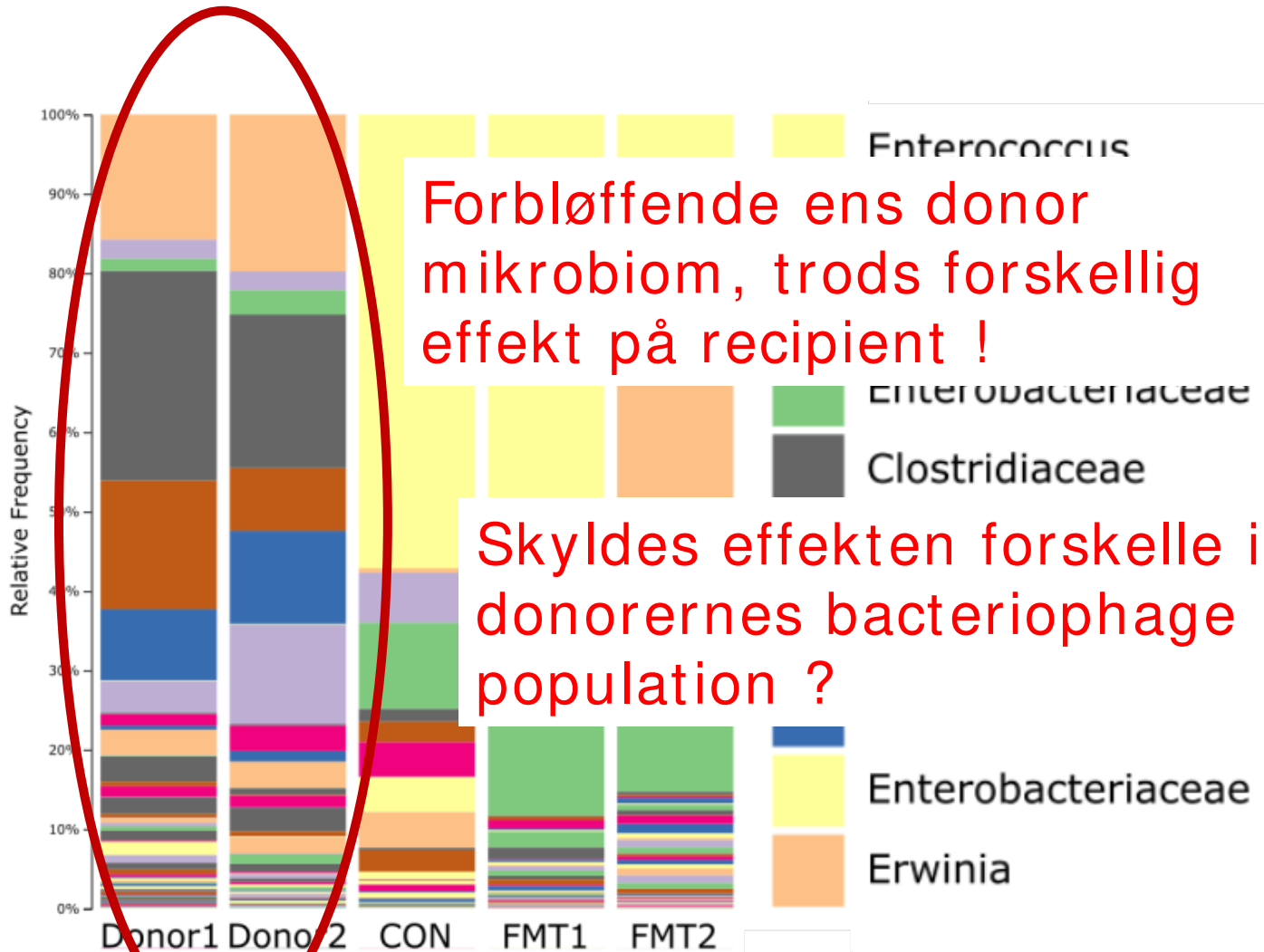
Donor feces from two 10-day old pigs from different locations FMT1 & FMT2 (n= 13-14)



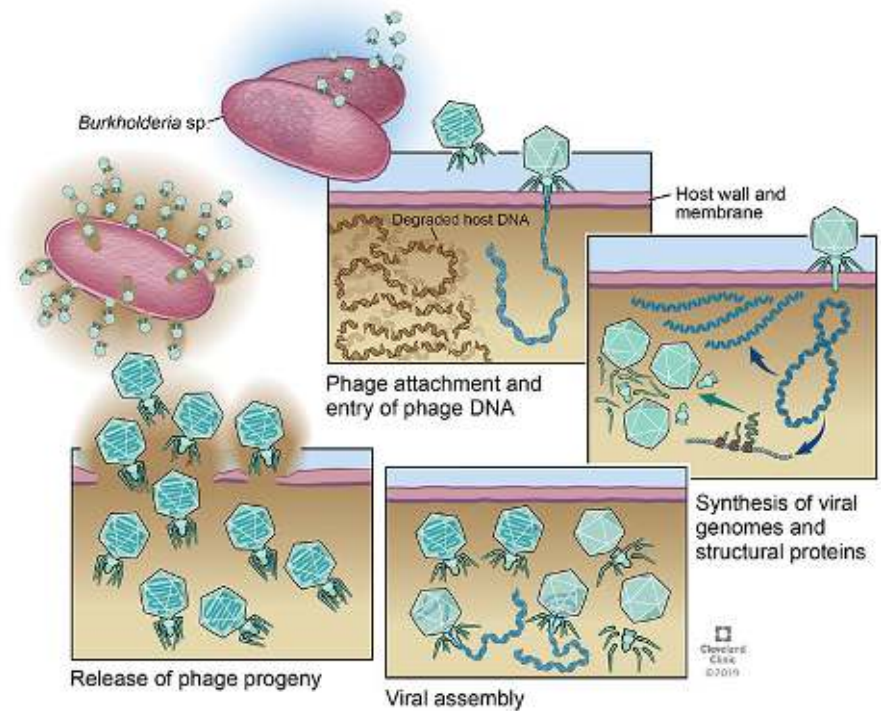
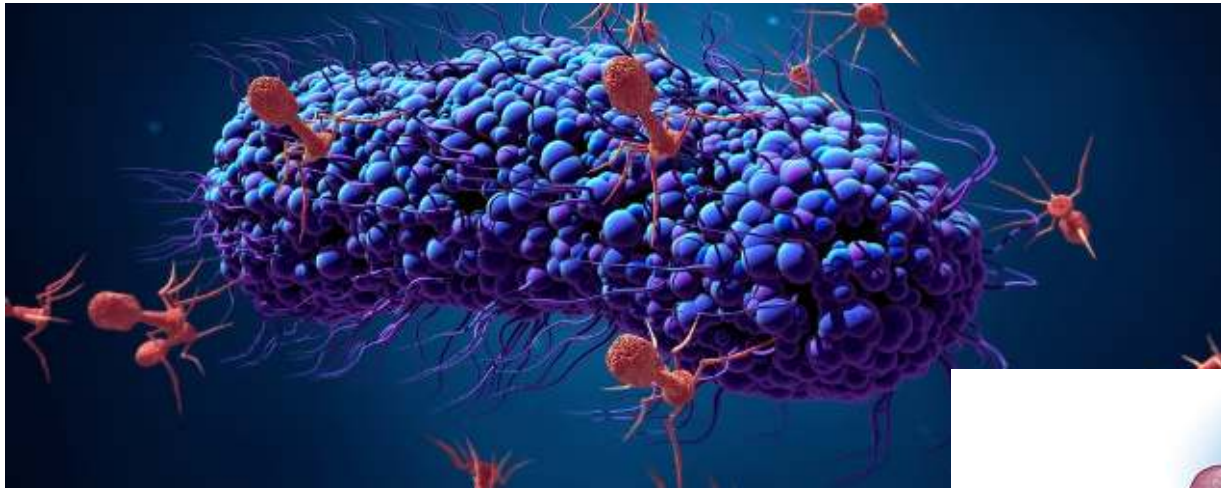
Results:



Gut bacterial composition (genus level)



Har et filtrat af fæces profylaktisk effekt i nyfødte grise ?



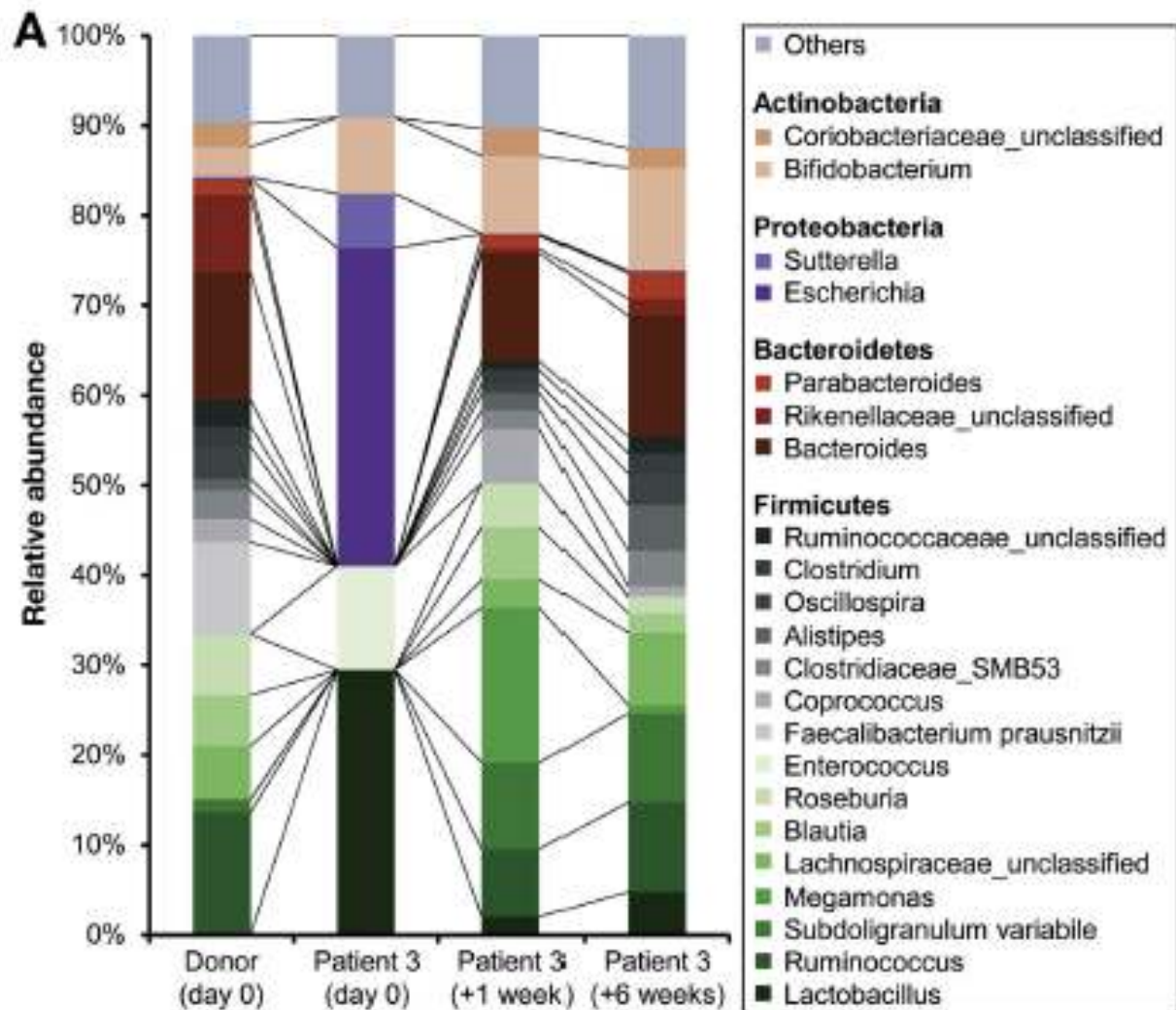
- in a filtrate all bacterial (and larger) cells are filtered away
- contains mainly bacteriophages
- but (in principle) also metabolites, bacteriocins etc.



Gastroenterology 2017;152:799-811

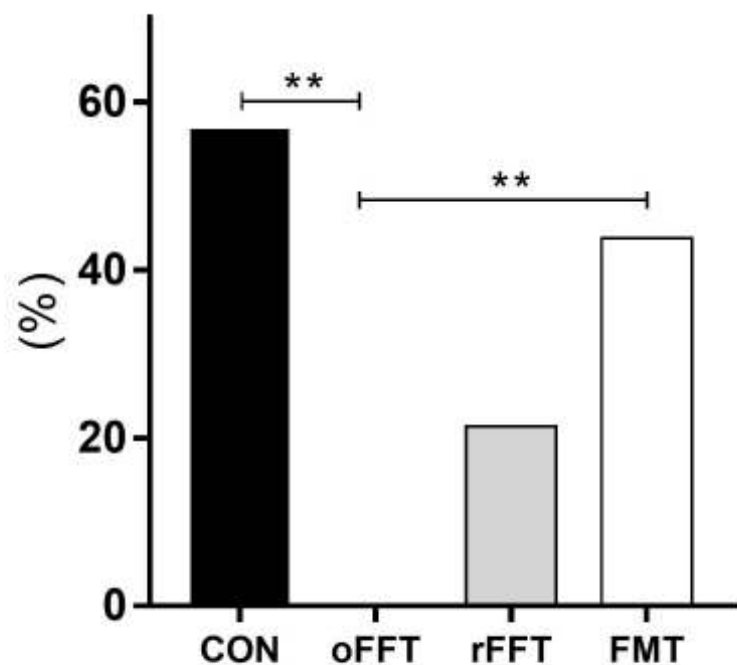
Efficacy of Sterile Fecal Filtrate Transfer for Treating Patients With *Clostridium difficile* Infection

Stephan J. Ott,^{1,2} Georg H. Waetzig,^{2,3} Ateequr Rehman,^{3,4} Jacqueline Moitzau-Anderson,^{3,4} Richa Bharti,³ Juris A. Grasis,⁵ Liam Cassidy,⁵ Andreas Tholey,⁶ Helmut Fickenscher,⁷ Dirk Seeger,² Philip Rosenstiel,^{3,6} and Stefan Schreiber^{1,3,6}

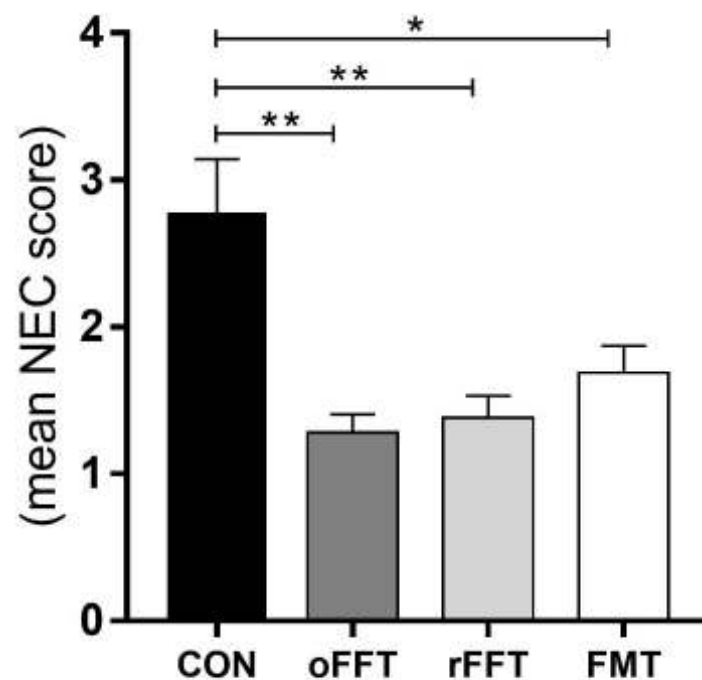


Fækal Filtrat transplantation (FFT) Fækal microbiota transplantation (FMT)

NEC incidence



Pathological severity



Brunse et al. work in progress



Bedste foreløbige bud på hvorledes fækal transplantation kan benyttes i praksis

Hvem er den bedste donor ?

Bedste foreløbige bud er 10-14 dage gamle grise

Hvornår skal det gives ?

Så tidligt som praktisk muligt efter fødsel

Hvor meget ?

Testet 5×10^9 CFU. Andre doser formentlig også ok

Hvilken vej ?

Rektal. Dog kan FFT gives oralt

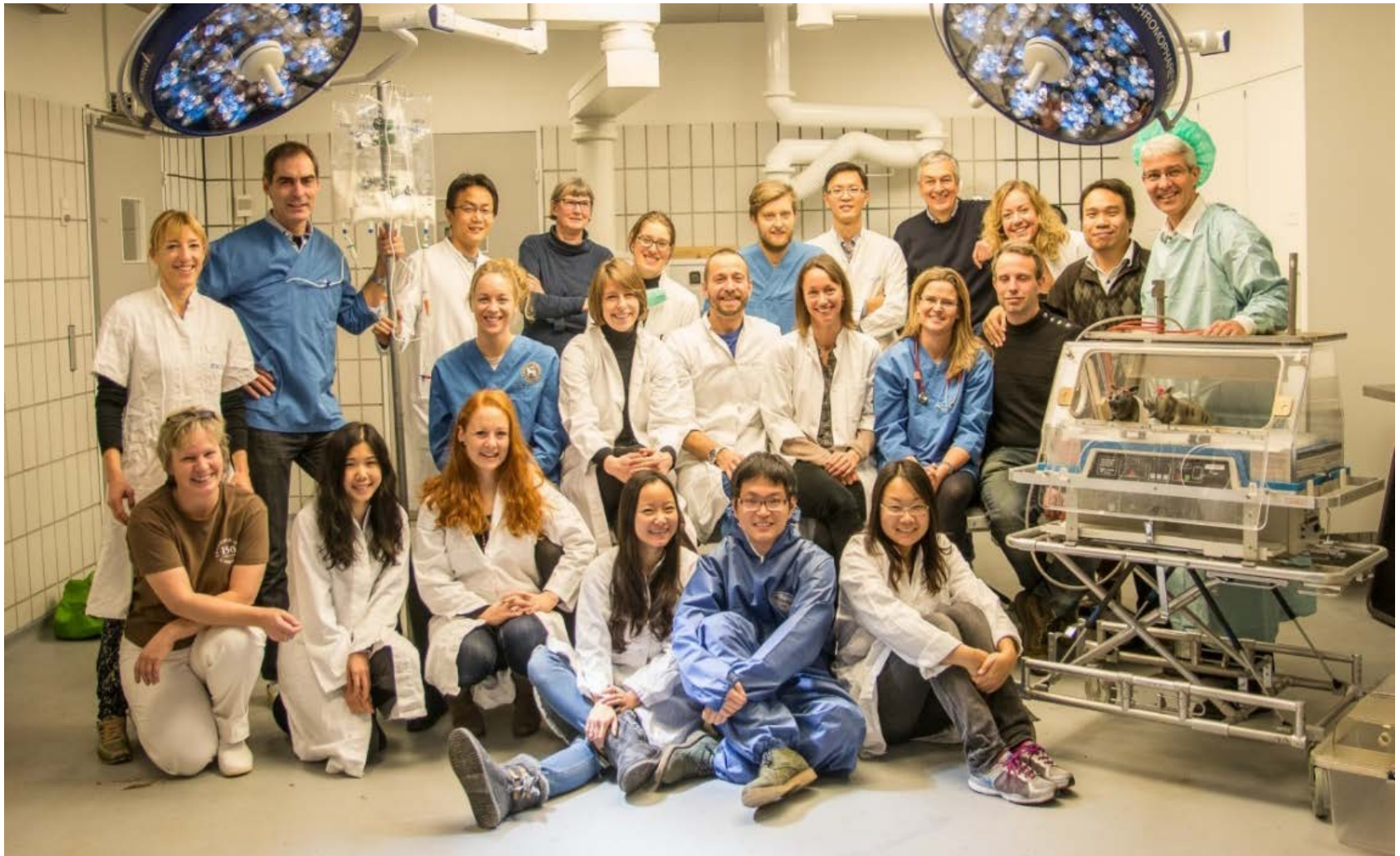
Hvor ofte ?

Få inokuleringer formentlig tilstrækkeligt

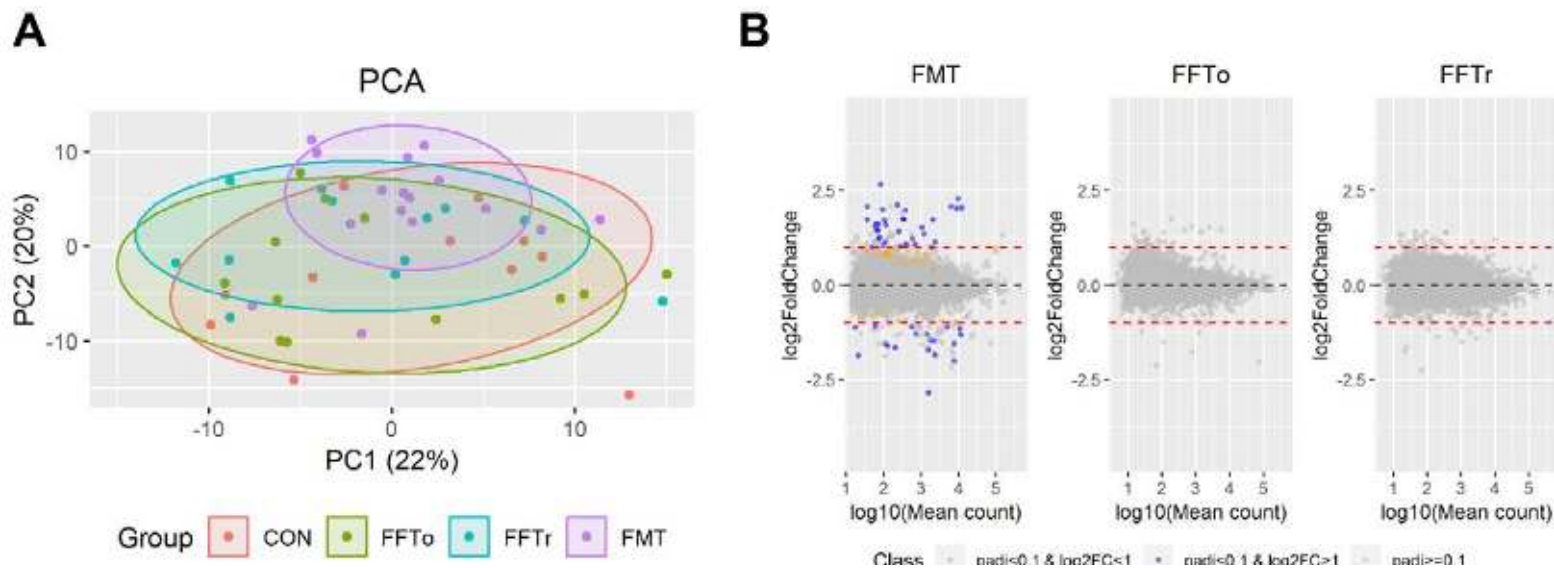
Intakt fæces eller filtrat ?

Filtrat





Tak for opmærksomheden



TLR4 pathway, complement system (C5AR1)
neutrophil/macrophage function (NCF2, CSF1R)
suggesting FMT stimulated innate immune response
in the mucosa.

