Het microbioom en wij

S. Van Outryve
GZA-ziekenhuizen

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Het microbioom

- 10^{14} bacteriën en archaea, fungi en virussen
- ~ 1-2 kg
- Human Microbiome Project
- Sequentiebepaling 10^{6} DNA-nucleotide basen:

  2001: 10.000 $

  2011: 0.10 $
- Tussen 70-160 ≠ gekende bacteriële species/pp

  (1.500)

Table 2. Geography of the Intestinal Microbiome and Implications for Sequencing-Based Studies

Region	Microbe density, *cells/mL*	Representative microbial clades	Sequencing implications
Small intestine contents	Duodenum 10^3 Jejunum 10^4–10^5 Ileum 10^7–10^8	*Streptococcus*, *Lactobacillus*, *Escherichia*, *Corynebacterium*	Low bacterial biomass decreases DNA yields and increases difficulty of non-16S sequencing approaches
Large intestine contents and stool	10^{11}–10^{12}	Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, *Methanobrevibacter*, *Candida*	DNA and RNA in stool samples are almost completely microbial (>99%); shotgun DNA and RNA approaches are viable
Mucosa	-	Small intestine: TM7, *Enterobacteriaceae*, *Pasteurellaceae*, *Lachnospiraceae*, *Eubacterium*, *Streptococcus*, *Faecalibacterium* Large intestine: Bacteroidetes, Firmicutes, Actinobacteria, Fusobacteria, *Akkermansia*	Shotgun sequencing will yield large numbers of host reads; joint host and microbial data readily obtained

Morgan et al. Gastroenterology 2014; 146:1437-48.

Genen

- De mens: 20.000 tot 25.000 genen
- Ons microbioom: 3.300.000 genen

Functie

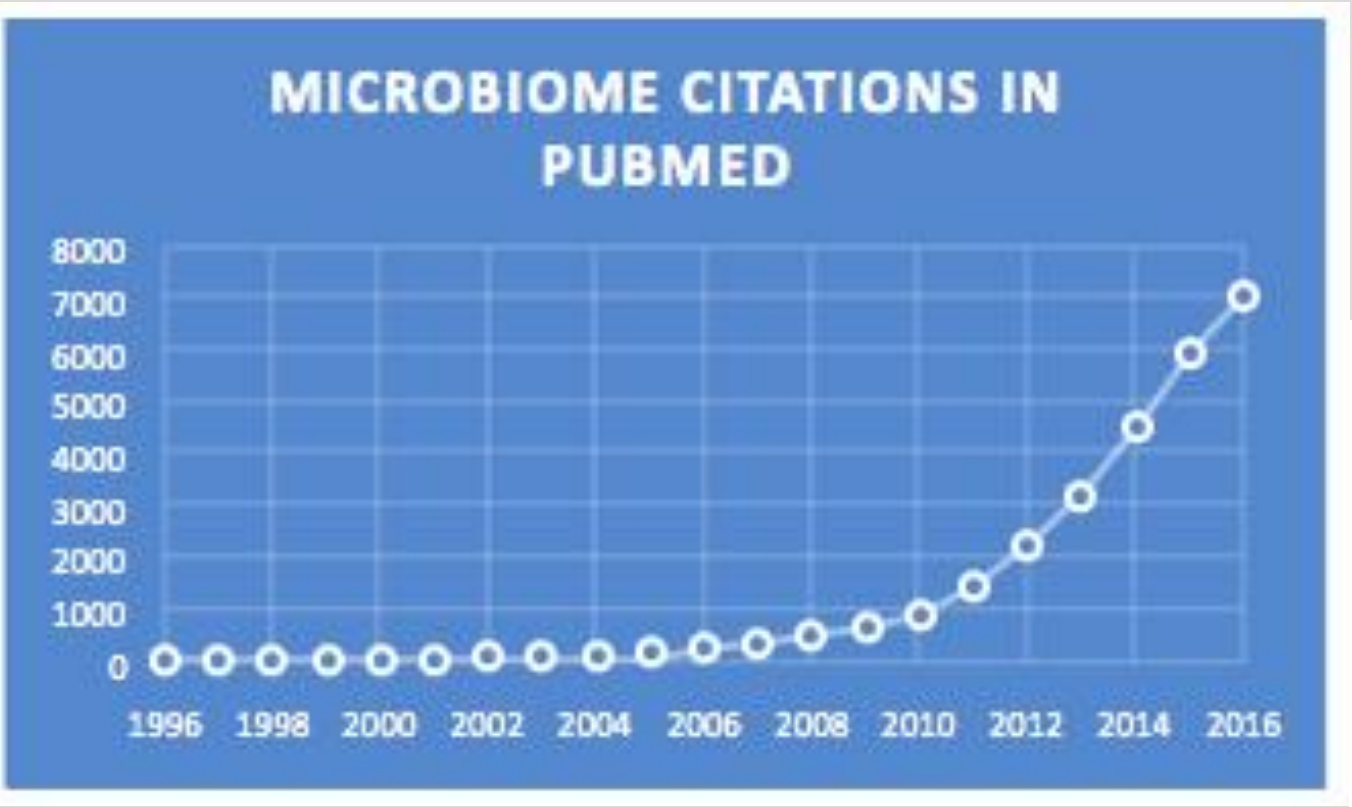
- Metabolisme van nutriënten
- Ontwikkeling van de immuniteit
- Preventie van infecties door pathogene bacteriën

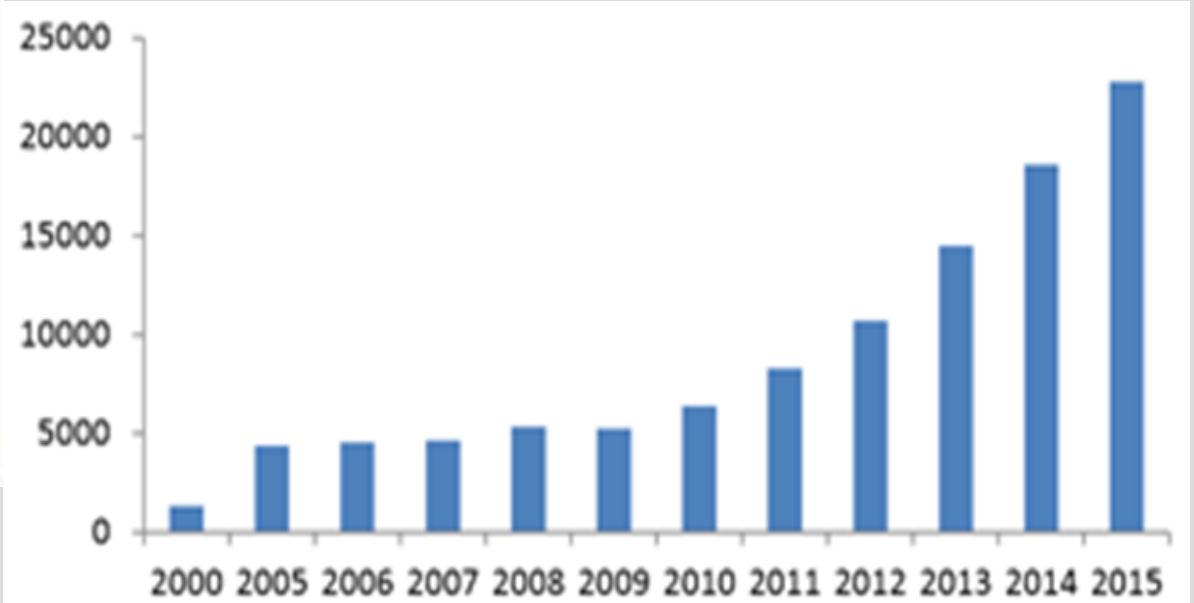
Samenstelling microbioom

Beïnvloed door:

- type bevalling
- genetica
- hygiëne
- voeding
- leeftijd
- roken
- medicatie
- .....

Het microbioom gaat ‘viraal’





Microbiome publications by year

Dysbiose en ziekte: IBD

- ***Inflammatoire darmziekten:***
  - reductie in biodiversiteit
  - ↓ Firmicutes
  - ↑ Gammaproteobacteria
  - ↑ Fusobacteria (coloncarcinoom!)
  - interactie genetica ⇔ microbioom

Dysbiose en ziekte: auto-immune ziekten

- Omgekeerde relatie tussen prevalentie van worminfecties en prevalentie van Auto-immuunziekten

Dysbiose en ziekte: GI-tractus

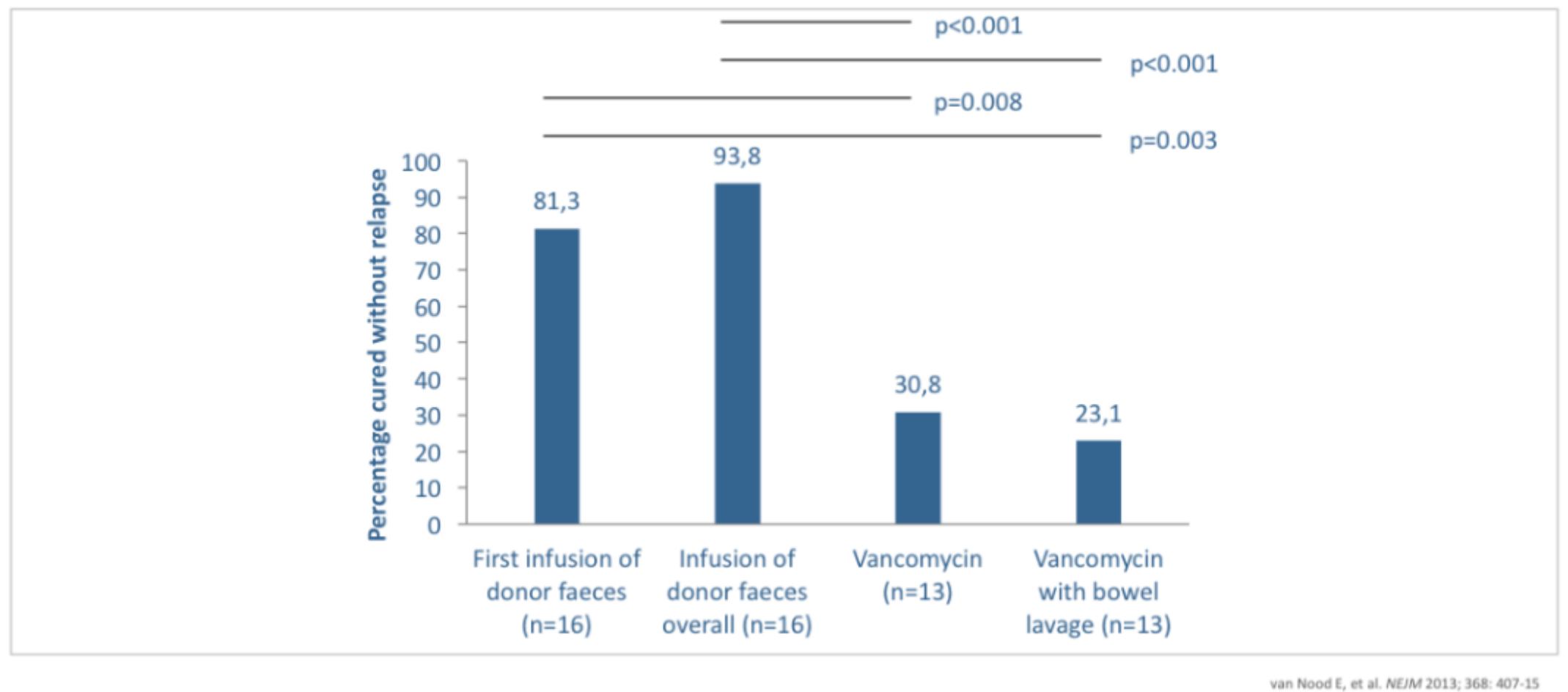
- ***Leverziekten*** (NASH, NAFLD, PSC,….)
- ***Diabetes type 2***
- ***Obesitas***
- ***Gastro-intestinale maligniteiten*** (H. Pylori,…)
- **Clostridium difficile**
- ….

Dysbiose en ziekte: Clostridium difficile

- Verdubbeling hospitalisaties in 2010 tov 2000[1,2]
- In VS: belangrijkste oorzaak van gastro-enteritis geassocieerd overlijden (in 2007 14.000 doden door C. Difficile[3])
- Zeer grote kost voor gezondheidszorg[4,5,6]
- Toenemende mortaliteit[7,8,9]

1. Gould CV, et al. *Clin Infect Dis.* 2013; 57: 1304-7; 2. Longtin Y, et al. *Clin Infect Dis.* 2013; 56: 67-73; 3. Hall AJ, et al. *Clin Infect Dis.* 2012; 55: 216-23; 4. Miller BA, et al. *Hosp Epidemiol.* 2011; 32: 387-90; 5. Magill SS, et al. *NEJM.* 2014; 370: 1198-208; 6. Dubberke ER, et al. *Clin Infect Dis.* 2012; 55: S88-S92; 7. Lessa FC, et al. *NEJM.* 2015 ;372: 825-34; 8. Varier RU, et al. *Infect Control Hosp Epidemiol.* 2015; 36: 438-44; 9. McGlone SM, et al. *Clin Microbiol Infect.* 2012; 18: 282-9

Clostridium difficile: stoelgangstransplantatie



van Nood E, et al. *NEJM* 2013; 368: 407-15

Vooral bij recurrente CDI, minder bij refractaire CDI !

Stoelgangstransplantatie

Practical considerations – donor selection

Preliminary interview

INFECTIOUS DISEASES

- History of, or known exposure to, HIV, HBV or HCV, syphilis, human T-lymphotropic virus I & II, malaria, trypanosomiasis, tuberculosis
- Known systemic infection not controlled at the time of donation
- Use of illegal drugs
- Risky sexual behaviour (anonymous sexual contact; sexual contacts with prostitutes, drug addicts, individuals with HIV, viral hepatitis, syphilis; work as a prostitute; history of sexually transmittable disease)
- Previous reception of tissue/organ transplant
- Previous (<12 months) reception of blood products
- Recent (<6 months) needle stick accident
- Recent (<6 months) body tattoo, piercing, earring, acupuncture
- Recent medical treatment in poor hygienic conditions
- Risk of transmission of diseases caused by prions
- Recent parasitosis or infection from rotavirus, *Giardia lamblia* and other microbes with GI involvement
- Recent (<6 months) travel in tropical countries, countries at high risk of communicable diseases or traveller's diarrhoea
- Recent (<6 months) history of vaccination with a live attenuated virus, if there is a possible risk of transmission
- Healthcare workers (to exclude the risk of transmission of multidrug-resistant organisms)
- Individual working with animals (to exclude the risk of transmission of zoonotic infections)

GI, METABOLIC AND NEUROLOGICAL DISORDERS

- History of IBS, IBD, functional chronic constipation, coeliac disease, other chronic GI disorders
- History or chronic, systemic autoimmune disorders with GI involvement
- History of, or high risk for, GI cancer or polyposis
- Recent appearance of diarrhoea, hematochezia
- History of neurological/neurodegenerative disorders
- History of psychiatric conditions
- Overweight and obesity (body mass index >25)

DRUGS THAT CAN IMPAIR GUT MICROBIOTA COMPOSITION

- Recent (<3 months) exposure to antibiotics, immunosuppressants, chemotherapy
- Chronic therapy with proton pump inhibitors

Cammarota G, et al. *Gut*. 2017; 66: 569-580

Stoelgangstransplantatie

Practical considerations – donor selection

Blood and stool testing

GENERAL BLOOD TESTING

- Cytomegalovirus
- Epstein-Barr virus
- Hepatitis A
- HBV
- HCV
- Hepatitis E virus
- Syphilis
- HIV-1 & HIV-2
- *Entamoeba histolytica*
- Complete blood cell count with differential
- C-reactive protein and erythrocyte sedimentation rate
- Albumin
- Creatinine and electrolytes
- Aminotransferases, bilirubin, gamma-glutamyltransferase, alkaline phosphatase

GENERAL STOOL TESTING

- Detection of *Clostridium difficile*
- Detection of enteric pathogens, including *Salmonella, Shigella*
- *Campylobacter, Escherichia coli O157 H7, Yersinia*, vancomycin-resistant enterococci, methicillin-resistant *Staphylococcus aureus*, gram-negative multidrug-resistant bacteria
- Norovirus
- Antigens and/or acid fast staining for *Giardia lamblia* and *Criptosporidium parvum*
- Protozoa (including *Blastocystis hominis)* and helminths
- Faecal occult blood testing

BLOOD TESTING IN SPECIFIC SITUATIONS

- Human T-lymphotropic virus types I & II antibodies
- *Strongyloides stercoralis*

STOOL TESTING IN SPECIFIC SITUATIONS

- Detection of *Vibrio cholera* and *Listeria monocytogenes*
- Antigens and/or acid fast staining for *Isospora* and *Microsporidia*
- Calprotectin
- *Helicobacter pylori* faecal antigen
- Rotavirus

Cammarota G, et al. *Gut.* 2017; 66: 569-580

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The Gut Microbiome Modulates Colon Tumorigenesis

Joseph P. Zackular,[a] Nielson T. Baxter,[a] Kathryn D. Iverson,[a] William D. Sadler,[b] Joseph F. Petrosino,[c] Grace Y. Chen,[b] Patrick D. Schloss[a]

Department of Microbiology and Immunology, University of Michigan, Ann Arbor, Michigan, USA[a]; Department of Internal Medicine, Division of Hematology and Oncology, University of Michigan, Ann Arbor, Michigan, USA[b]; Human Genome Sequencing Center and Department of Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas, USA[c]

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