# Schema Micro2

| Les | Hoofdstuk | Paragraaf |
|---|---|---|
| 1 | 7 | 7.1, 7.2, 7.3, 7.8 |
| 2 | 7 | 7.5, 7.6, 7.7 |
| 3 | 7 | 7.9, 7.10, 7.11 |
| 4 | 7 | 7.12, 7.13, 7.14, 7.15 |
| 5 | 5 | 5.1, 5.2, 5.3, 5.4, 5.5, 5.6 |
| 6 | 5 en 11 | 5.7, 5.8, 11.1, 11.2 |
| 7 | 11 | 11.6, 11.7, 11.8 (MS2 niet) |
| 8 | 11 | 11.9, 11.11, |
| 9 | 11 | 11.13, 11.15, 11.16 |
| 10 | 24 | 24.1, 24.2, 24.5 |
| 11 | 25 | 25.1, 25.2, 25.3, 25.5 |
| 12 | 25 | 25.6, 25.7, 25.8 |
| 13 | 28 en 8 | 28.10, 28.11, 28.12, 8.10 |
| 14 | Oefententamen | Alles |

NB: Hfdstnrs niet accuraat


PowerPoint® Lecture Presentations

CHAPTER 24

# Microbial Symbioses with Humans

# Microbial Symbioses with Humans

- All sites on a human that contain microorganisms are part of a *microbiome.*
- A *microbiome* is a functional collection of different microbes in a particular environmental system (*e.g.*, the human microbiome).
- Scientists use the term microbiota to describe all the microbes in a microhabitat (*e.g.*, skin microbiota).
- Different microhabitats support different microbes, so the skin will have very different microbes than the mouth.

# NB:

- Belangrijke rol Next Generation Sequencing

  => maakt het sequencen en determineren van populaties mogelijk.

# I. Structure and Function of the Healthy Adult Human Microbiome

- 24.1 Overview of the Human Microbiome
- 24.2 Gastrointestinal Microbiota
- 24.5 The Skin and Its Microbes

# 24.1 Overview of the Human Microbiome

- There are approximately $10^{13}$ microbes in the human microbiome (Figure 24.1) living in complex communities.

## Signature microbes follow you from house to house

Householders share more than habitation; they also share inhabitants. In a diverse sample of U.S. homes, Lax *et al.* found that people and animals sharing homes shared their microbial communities (microbiota) too, probably because of skin shedding and hand and foot contamination. When families moved, their microbiological "aura" followed. If one person left the home even for a few days, their contribution to the microbiome diminished. These findings have implications not only for household identity and composition, but also for indicators of the members' health and well-being.

*Science*, this issue p. **1048**



https://www.nu.nl/wetenschap/3864721/mens-verspreidt-aura-van-bacterien.html

# 24.1 Overview of the Human Microbiome

- Future Benefits of Knowing the Human Microbiome
  - development of biomarkers for predicting predisposition to diseases
  - designing targeted therapies
  - personalized drug therapies and probiotics
- These are very early studies, and they reveal that there are complex interactions between host and its microbiota.

# 24.1 Overview of the Human Microbiome

- Experimental Protocols and Body Target Sites
  - Most *Bacteria* cannot be cultured; however, advanced sequencing techniques allow for identification of different microbiota at different body sites. (Figure 24.2)
  - There have been multiple studies to determine the nature of the normal microbiota. (Table 24.1)

# 24.1 Overview of the Human Microbiome

- There are currently integrated projects underway to answer basic questions about the human microbiome.
  - Do individuals share a core human microbiome?
  - Is there a correlation between the composition of microbiota colonizing a body site and host genotype?
  - Do differences in the human microbiome correlate with differences in human health?
  - Are differences in the relative abundance of specific bacterial populations important to either health or disease?

# 24.2 Gastrointestinal Microbiota

- Humans are *monogastric* and omnivorous.
- Microbes in gut affect early development, health, and predisposition to disease.
- Colonization of gut begins at birth.

# Fewer 'good gut' bacteria in C-section infants

By Honor Whiteman | Published Thursday 8 August 2013

**Researchers have discovered that infants who are delivered by caesarean section have a lower range of good gut bacteria in their first 2 years of life, compared with infants delivered through the mother's birth canal.**



The study, published in the BMJ journal *Gut*, reveals that lower levels of beneficial gut bacteria has implications for the development of the immune system, particularly as infants delivered by C-section also showed lower levels of chemicals responsible for the prevention of allergies.

Researchers from Sweden analyzed the guts of 24 infants. Nine of these infants were delivered by C-section, while 15 were delivered vaginally.

https://www.medicalnewstoday.com/articles/264473.php

# 24.2 Gastrointestinal Microbiota

- The human gastrointestinal (GI) tract (Figure 24.3)
- Consists of stomach, small intestine, and large intestine; comprises 400 $m^2$ of surface area
- Responsible for digestion of food, absorption of nutrients, and production of nutrients by the indigenous microbial flora
- Contains $10^{13}$ to $10^{14}$ microbial cells

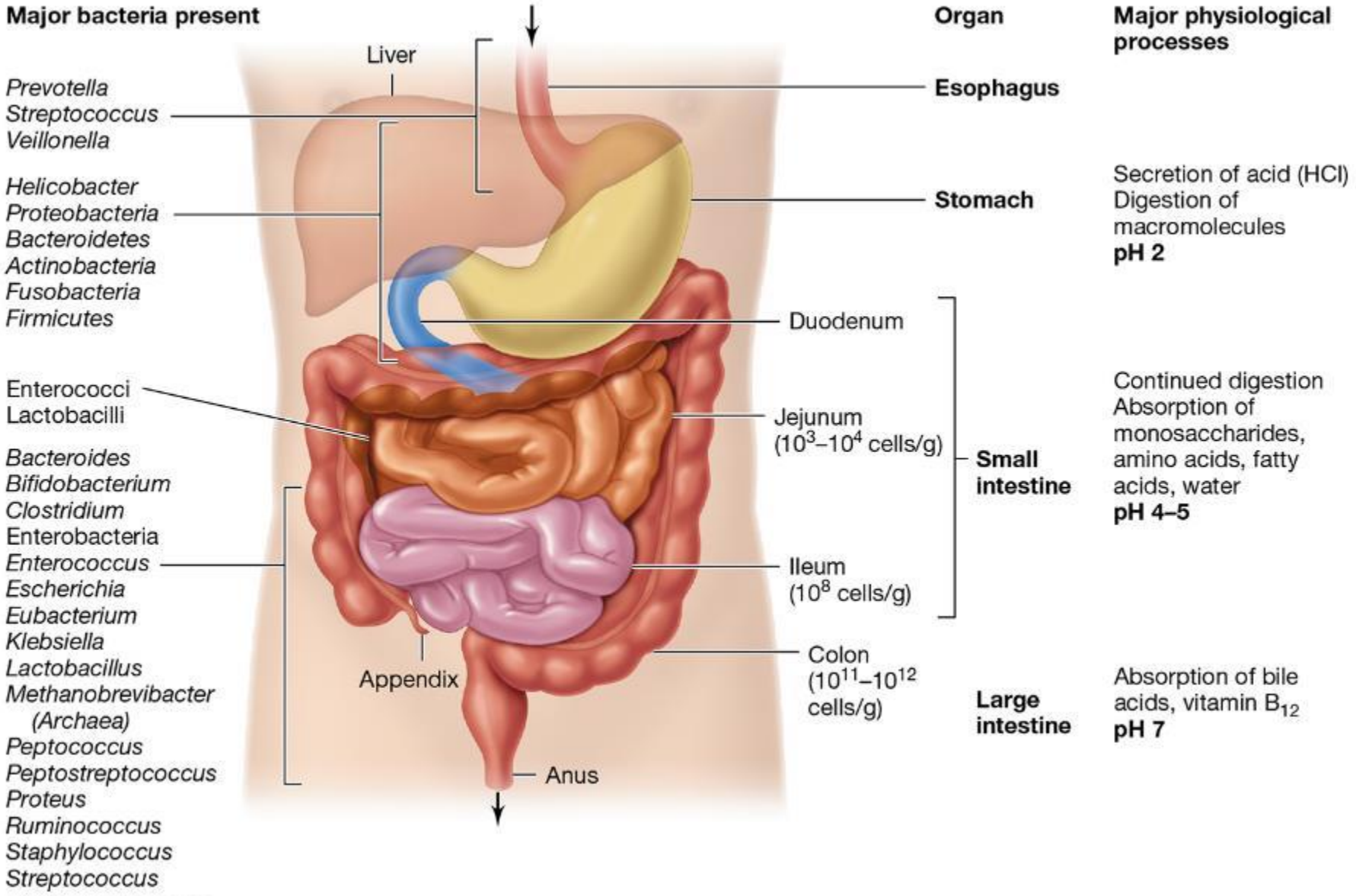



**Figure 24.3**

# 24.2 Gastrointestinal Microbiota

- The Stomach and Small Intestine
  - Microbial populations in different areas of the GI tract are influenced by diet and the physical conditions in the area.
  - The acidity of the stomach and the duodenum of the small intestine (~pH 2) prevent many organisms from colonizing the GI tract; however, there is a rich microbiome in the healthy stomach.
  - *Firmicutes*, *Bacteroidetes*, and *Actinobacteria* are common in the gastric fluid, while *Firmicutes* and *Proteobacteria* are common in the mucus layer of the stomach.
  - *Helicobacter pylori* was discovered in the 1980s and has since been found in ~50 percent of the world's population. When present, it is found in the gastric mucosa.

- Barry Marshall
- 2005 ontving hij samen met Robin Warren de Nobelprijs voor de Fysiologie of Geneeskunde .

https://nl.wikipedia.org/wiki/Barry_Marshall

# 24.2 Gastrointestinal Microbiota

- Intestinal microorganisms carry out a variety of essential metabolic reactions that produce various compounds
- The Large Intestine
  - The colon is essentially an *in vivo* fermentation vessel, with the microbiota using nutrients derived from the digestion of food.
  - Most organisms are restricted to the lumen of the large intestine, while others are in the mucosal layers. (Figure 24.5)

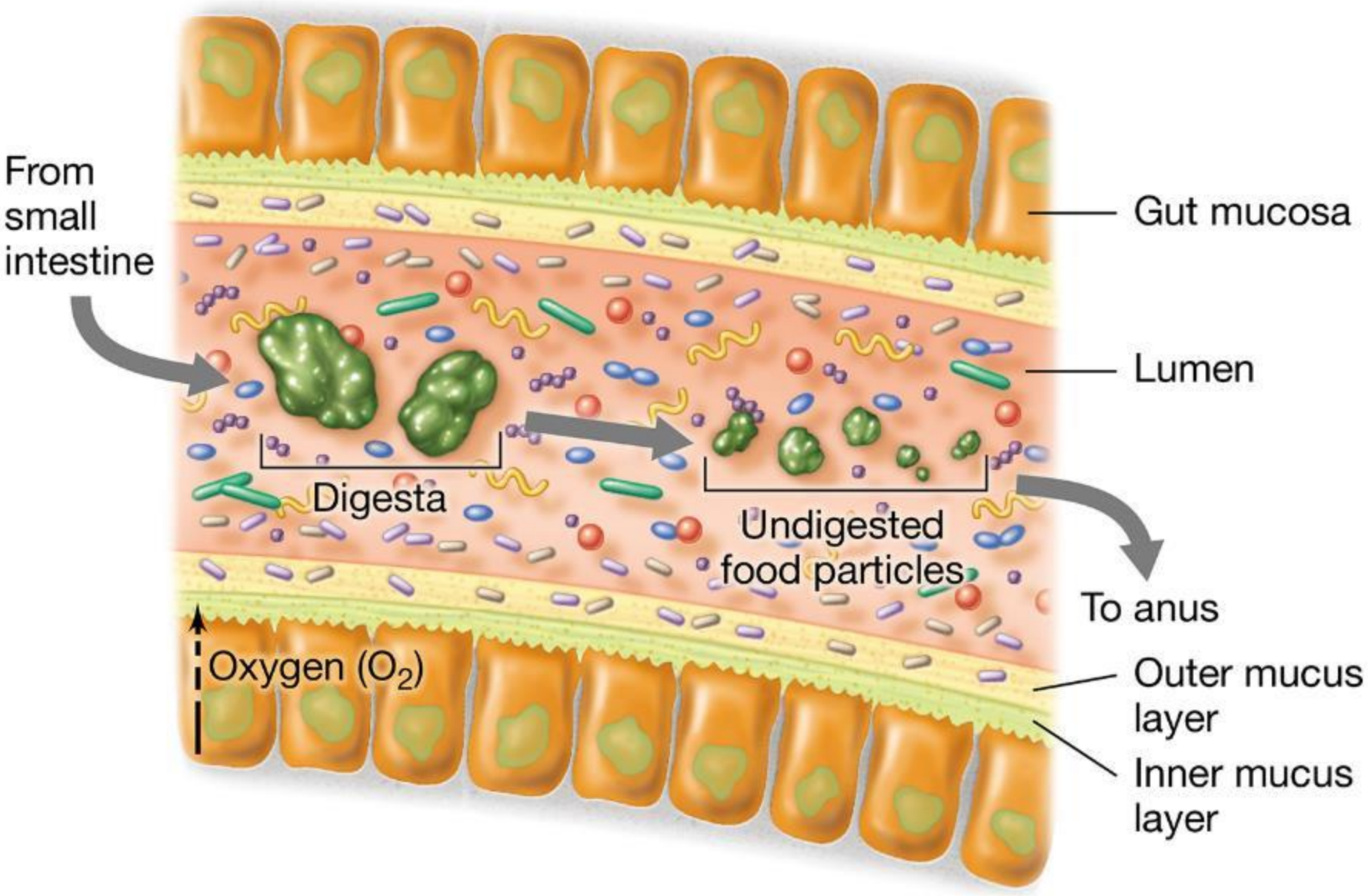



**Figure 24.5**

# 24.2 Gastrointestinal Microbiota

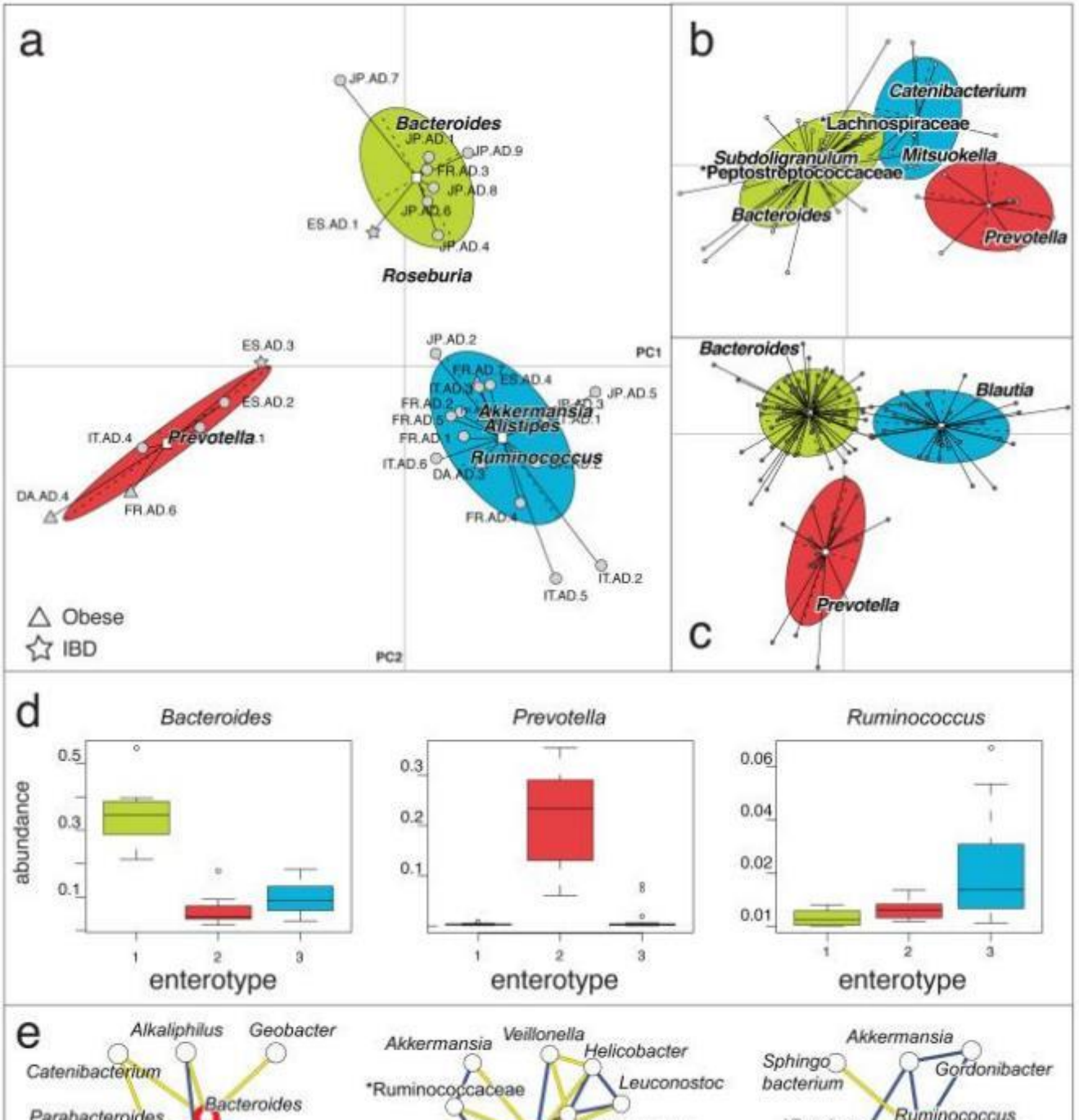
- Summary of the Gut Microbiota: The Two Major Components
- The vast majority (~98 percent) of all human gut phylotypes fall into one of three major bacterial phyla: *Firmicutes, Bacteroidetes,* and *Proteobacteria.*
  - Individuals may have mostly *Firmicutes*, mostly *Bacteriodetes*, or a mix of the two. This may regulate metabolism and the host's propensity for obesity.

# 24.2 Gastrointestinal Microbiota

- Gut Enterotypes
  - While individuals vary in their gut microbiota, each individual has a relatively stable gut microbiota.
  - There are three basic enterotypes currently being studied: #1 is enriched in *Bacteroides*, #2 in *Prevotella*, and #3 is enriched in *Ruminococcus*.
    - Early studies indicate that each enterotype is functionally as well as phylogenetically distinct.

# Enterotypen

https://www.ncbi.nlm.nih.gov/pubmed/21508958/



# 24.2 Gastrointestinal Microbiota

- Products of Intestinal Microbiota and “Educating” the Immune System
  - Many microbial metabolites or transformation products that can be generated in the gut have significant influence on host physiology. (Table 24.2)
    - vitamin production
    - modification of steroids
    - amino acid biosynthesis

nature
International journal of science

Letter | Published: 11 December 2013

# Diet rapidly and reproducibly alters the human gut microbiome

Lawrence A. David, Corinne F. Maurice, Rachel N. Carmody, David B. Gootenberg, Julie E. Button, Benjamin E. Wolfe, Alisha V. Ling, A. Sloan Devlin, Yug Varma, Michael A. Fischbach, Sudha B. Biddinger, Rachel J. Dutton & Peter J. Turnbaugh

*Nature* **505**, 559–563 (23 January 2014) | Download Citation

## Abstract

Long-term dietary intake influences the structure and activity of the trillions of microorganisms residing in the human gut[1,2,3,4,5], but it remains unclear how rapidly and reproducibly the human gut microbiome responds to short-term macronutrient change. Here we show that the short-term consumption of diets composed entirely of

Am J Gastroenterol. 2016 Feb;111(2):163-9. doi: 10.1038/ajg.2015.301. Epub 2015 Sep 29.

# The Link between the Appendix and Ulcerative Colitis: Clinical Relevance and Potential Immunological Mechanisms.

Sahami S[1], Kooij IA[2], Meijer SL[3], Van den Brink GR[2,4], Buskens CJ[1], Te Velde AA[2].

Author information

## Abstract

The human appendix has long been considered as a vestigial organ, an organ that has lost its function during evolution. In recent years, however, reports have emerged that link the appendix to numerous immunological functions in humans. Evidence has been presented for an important role of the appendix in maintaining intestinal health. This theory suggests that the appendix may be a reservoir or 'safe house' from which the commensal gut flora can rapidly be reestablished if it is eradicated from the colon. However, the appendix may also have a role in the development of inflammatory bowel disease (IBD). Several large epidemiological cohort studies have demonstrated the preventive effect of appendectomy on the development of ulcerative colitis, a finding that has been confirmed in murine colitis models. In addition, current studies are examining the possible therapeutic effect of an appendectomy to modulate disease course in patients with ulcerative colitis. This literature review assesses the current knowledge about the clinical and immunological aspects of the vermiform appendix in IBD and suggests that the idea of the appendix as a vestigial remnant should be discarded.

deVolkskrant

NIEUWS WETENSCHAPPELIJK ONDERZOEK

# Zonder blindedarm minder parkinson: onderzoek bevestigt vermoeden dat ziekte in de darmen begint

Wie op jonge leeftijd zijn blindedarm is kwijtgeraakt, lijkt 19 procent minder kans te hebben om later de ziekte van Parkinson te krijgen. Als parkinson toch toeslaat, is dat gemiddeld 3,6 jaar later dan bij patiënten die nog wel hun blindedarm hebben.

**Margreet Vermeulen** 1 november 2018, 19:17

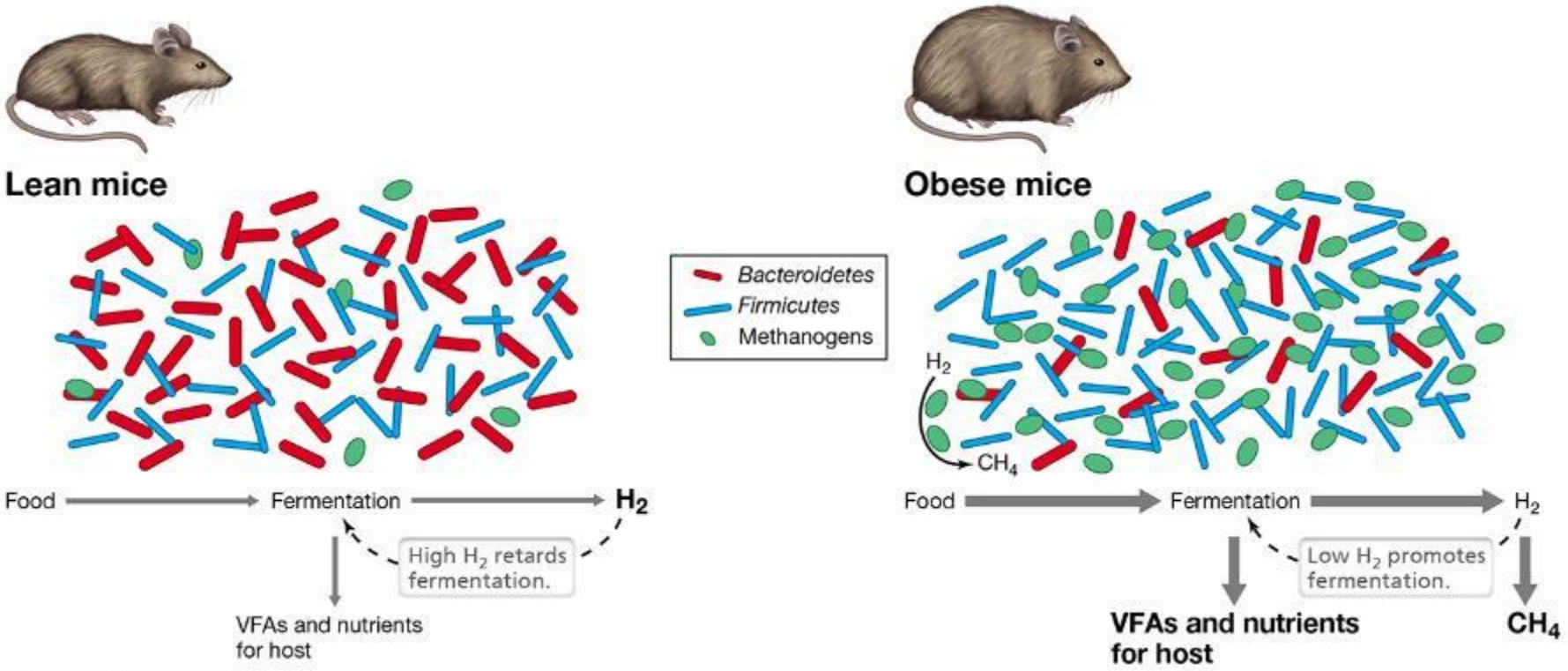



Figure 24.19

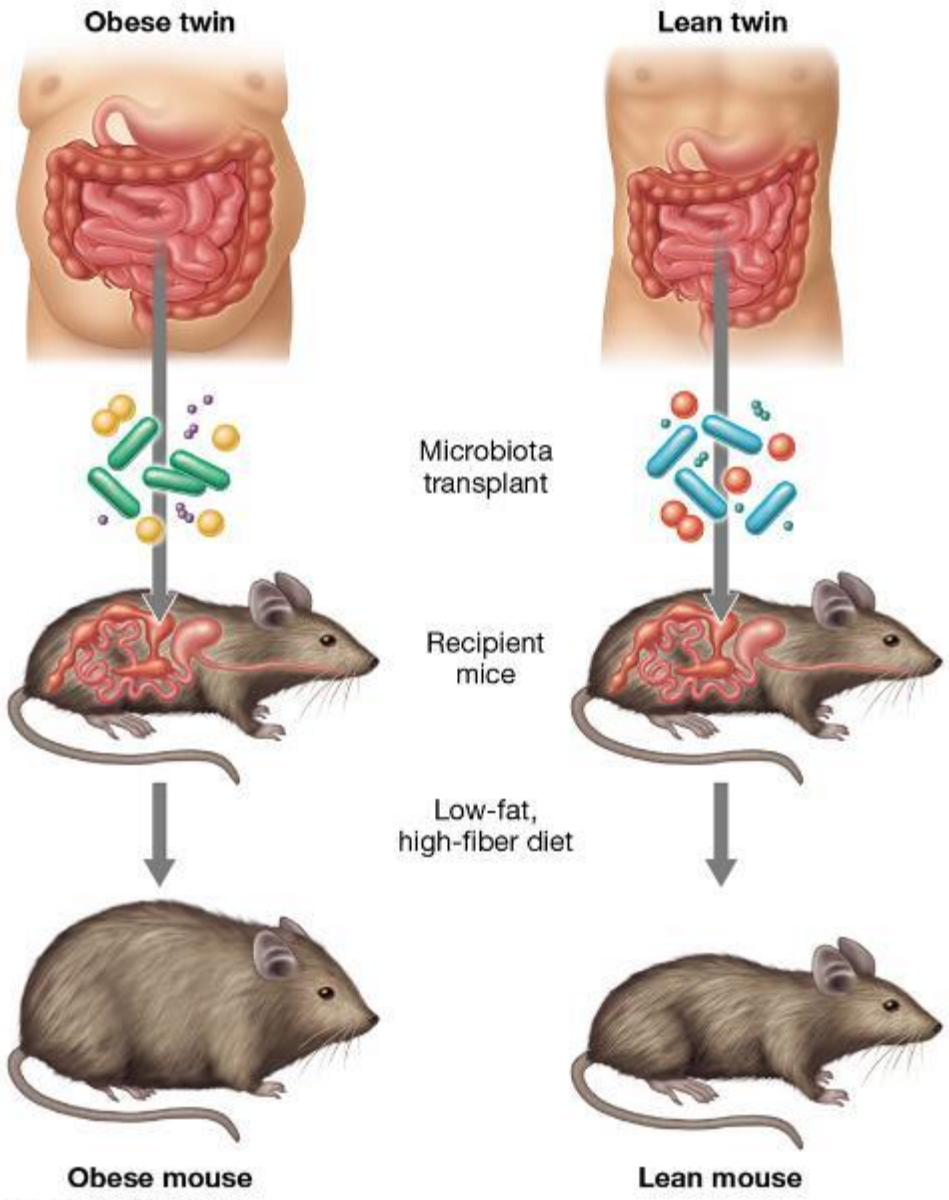



**Figure 24.20**

- Poeptransplantaties! (Willem de Vos)

**Persbericht**

## Kans op succes van poeptransplantatie groter bij matching donor en patiënt

28 april 2016

Onderzoekers van fecestransplantatie zijn erin geslaagd te traceren welke bacteriestammen van een donor na transplantatie aanslaan in de darmen van een patiënt. Een team onder leiding van het European Molecular Biology Laboratory, met medewerkers van Universiteit Wageningen , het Academisch Medisch Centrum (AMC) in Amsterdam en de Universiteit van Helsinki, ontdekte dat overeenkomst tussen donor en patiënt een grotere rol speelt bij deze transplantaties dan voorheen werd gedacht. Het onderzoek, dat vandaag wordt

Contactpersoon

prof.dr. WM (Willem) de Vos

Contactformulier

# Bij voldoende tijd:

- https://www.youtube.com/watch?v=i6RBfoITbls

## TABLE 24.2 Biochemical/metabolic contributions of intestinal microorganisms

| *Process* | *Product or enzyme* |
|---|---|
| Vitamin synthesis | Thiamine, riboflavin, pyridoxine, $B_{12}$, K |
| Amino acid synthesis[a] | Asparagine, glutamate, methionine, tryptophan, lysine, and others |
| Gas production | $CO_2$, $CH_4$, $H_2$ |
| Odor production | $H_2S$, $NH_3$, amines, indole, skatole, butyric acid |
| Organic acid production | Acetic, propionic, butyric acids |
| Glycosidase reactions | β-Glucuronidase, β-galactosidase, β-glucosidase, α-glucosidase, α-galactosidase |
| Steroid metabolism (bile acids) | Esterified, dehydroxylated, oxidized, or reduced steroids |

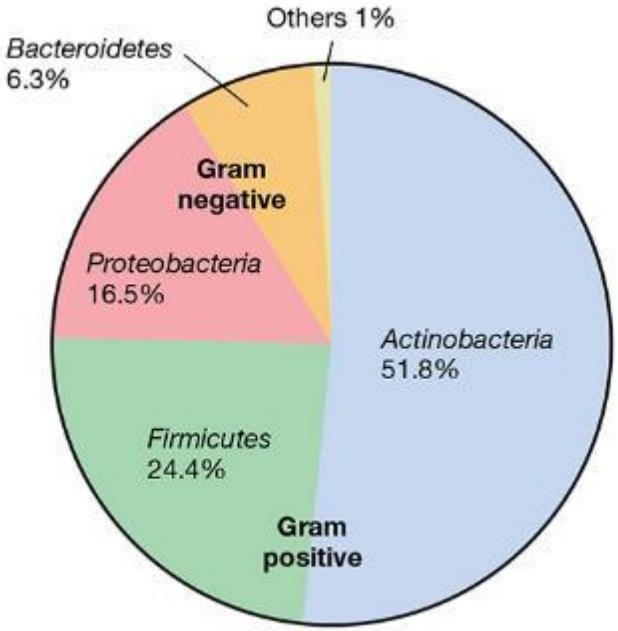
[a]Capacity for amino acid biosynthesis inferred from the identification of biochemical pathways encoded in gut metagenomic sequences (↔ Sections 9.8 and 19.8).



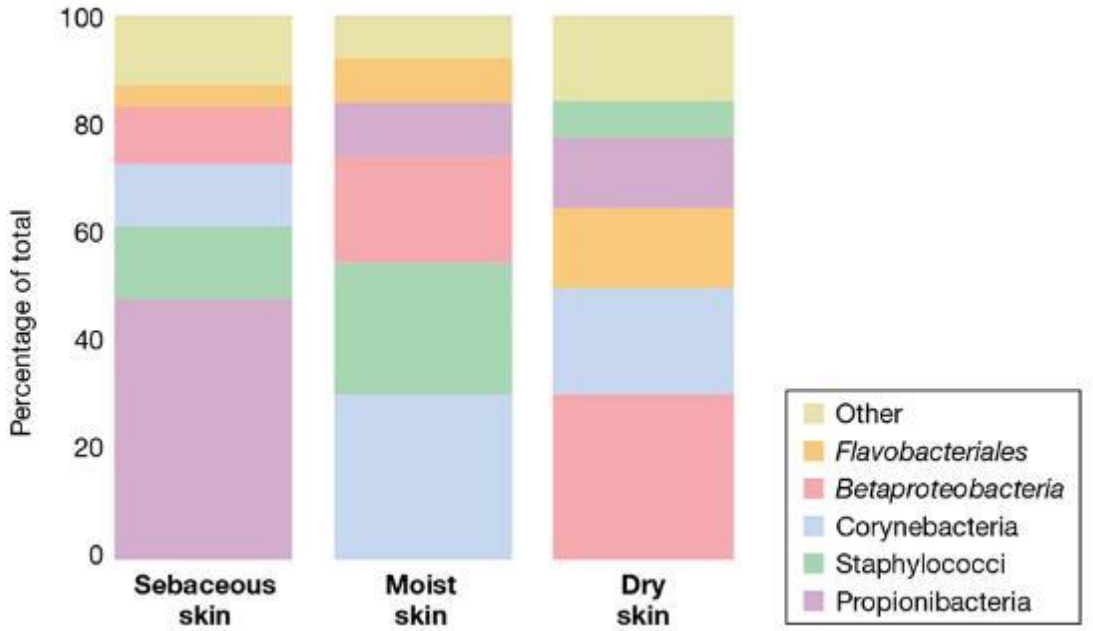
Table 24.2

# 24.5 The Skin and Its Microbes

- There are approximately 1 million resident bacteria per square centimeter of skin for a total of about $10^{10}$ skin microorganisms covering the average adult.
- The skin surface varies greatly in chemical composition and moisture content
  - three microenvironments (Figure 24.15)
    - dry skin
    - moist skin
    - sebaceous skin




(a)




(b)



**Figure 24.15**

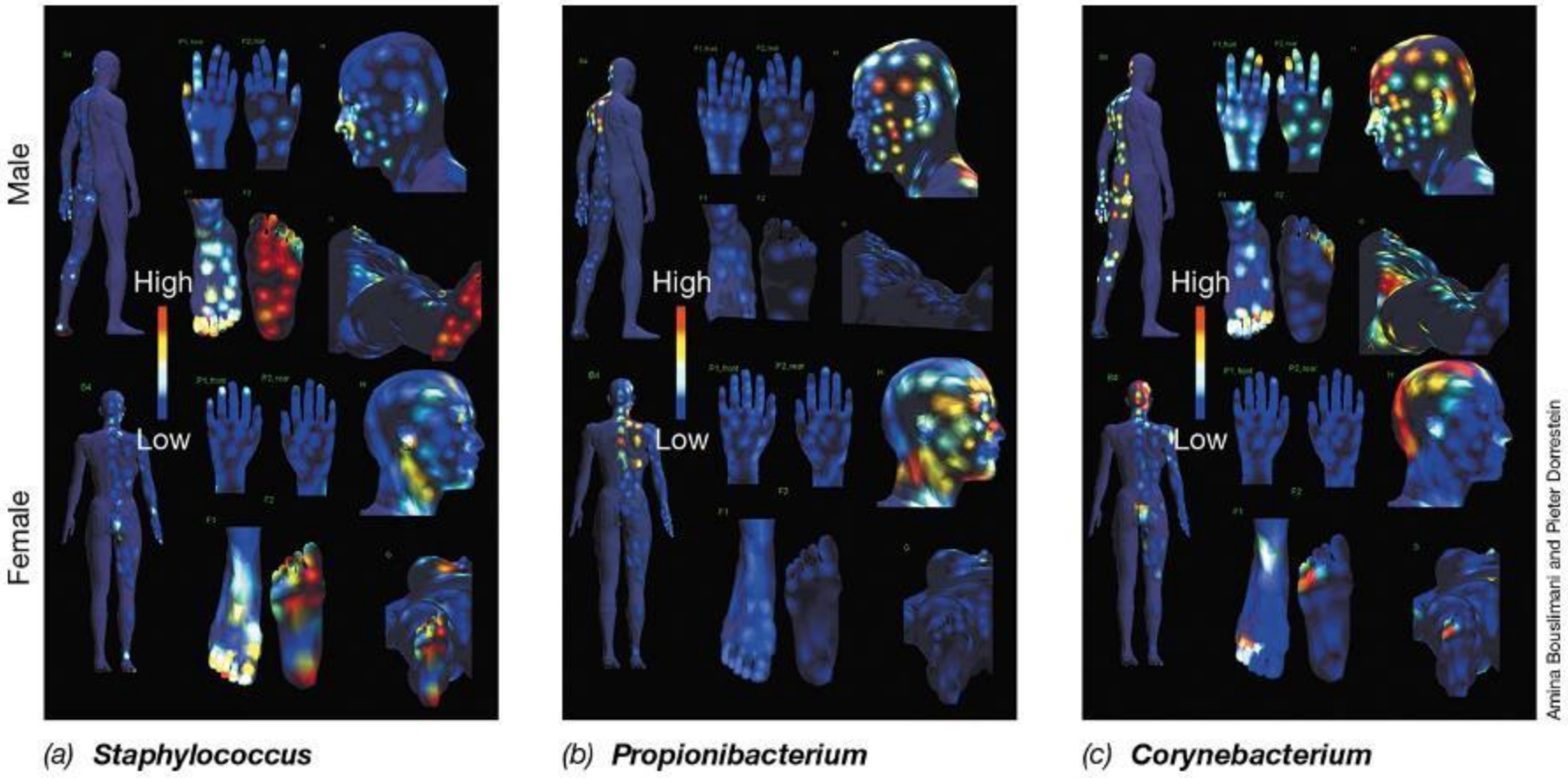
# Sebaceous

- Sebum = talg
- Vetachtige substantie die een beschermende werking heeft tegen uitdroging van de huid en het haar en tegen infectie door bacteriën en schimmels.

Voor meer info: Dr. Pimple Popper op TLC….

# 24.5 The Skin and Its Microbes

- Composition is influenced by
  - environmental factors (*e.g.*, weather)
  - host factors (*e.g.*, age (puberty), personal hygiene)
  - Each microenvironment shows a unique microbiota. (Figure 24.17)




(a) ***Staphylococcus*** (b) ***Propionibacterium*** (c) ***Corynebacterium***

**Figure 24.17**

# Fluorescence detection and diagnosis of non-Melanoma skin cancer at an early stage

*Lasers in Surgery and Medicine , Volume 41 - Issue 2 p. 96- 103*

Background: The occurrence of non-melanoma skin cancer (NMSC), including actinic keratosis (AK) is increasing all over the world. The detection and diagnosis of NMSC is not optimal in clinical practice. Complementary methods for detection and accurate demarcation of NMSC at an early stage are needed in order to limit the damage caused by tumours. Objective: The purpose of the present study was to use a large area skin fluorescence detection system to detect early NMSCs (clinical visible as well as non-visible lesions) in the face, neck, chest, back and hands of patients treated with UV and outdoor workers. Methods: Fluorescence detection with a purpose-made digital camera and software (Dyaderm®) combined with 5-aminolevulinic acid (5-ALA) encapsulated in liposomes. Results: In 93 consecutively referred patients positive skin fluorescence was detected in 61 patients. After histological examination the positive fluorescence patients (sebaceous gland hyperplasia in 22 patients) and to (pre-) malignant lesions in 33 patients (actinic keratosis in 29, BCC in 3 and SCC in 1 patient). False negative fluorescence was found in only one lesion. In five patients the FD technique used in this study appeared to be more sensitive for the identification of (pre-) malignant lesions than the clinical examination. This is in contrast with FD techniques used in previous studies. Conclusion: Diagnostic skin fluorescence using liposomal encapsulated 5-ALA and a specialised computerised detection and visualisation system offers the possibility for detection of NMSC at an early, pre-clinical stage. The technique is well suited to examine large areas of skin. It also identifies areas of most interest for performing confirmatory skin biopsies, as well as pre-operative assessment of boundaries of skin malignancies, and finally, the technique is applicable in the control and follow-up of skin cancer treatment



Maar niet bij teveel *Propionibacterium* op de huid (propionzuur ‘stoort’ de detectie)

# A Propos Metagenomics

Bacteriën zijn wijdverspreid aanwezig in kankercellen

## TUMOREN HERBERGEN BACTERIEEL LEVEN

DOOR STEIJN VAN SCHIE _Bacteriën blijken zich te verschuilen in de kanker- en immuuncellen van tumoren van mogelijk alle vormen van kanker. Zelfs in tumoren die groeien op nagenoeg steriele locaties.

Humane tumoren hebben mogelijk een eigen uniek microbioom; in de kanker- en immuuncellen van de tumoren leven bacteriën. De specifieke samenstelling van de bacteriële gemeenschap is afhankelijk van het type kanker. Dat concludeert een internationaal team, waaronder drie onderzoekers van het Nederlands Kanker Instituut, 29 mei in *Science* na analyses aan 1.526 tumorsamples. Mogelijk biedt de ontdekking aanknopingspunten voor behandeling. Het is echter nog onduidelijk hoe de bacteriën in de tumoren terechtkomen en of ze een noemenswaardig effect hebben op het verloop en de verspreiding van kanker.

Het is al ruim honderd jaar bekend dat er zoiets bestaat als tumorbacteriën. Ook weet men inmiddels dat bijvoorbeeld het darmmicrobioom verschillende belangrijke effecten heeft op de biologie van daar aanwezige tumoren, zoals progressie en respons op immunotherapie. Toch zijn bacteriepopulaties in tumoren nooit uitvoerig gekarakteriseerd. En zeker niet bij kankertypes die voorkomen op plekken waar doorgaans nauwelijks bacteriën te vinden zijn, zoals in de hersenen of botten.

De onderzoekers gaan daarom op zoek naar bacterieel dna, rna en bacteriële celwandcomponenten in zeven veelvoorkomende kankers: huid-, eierstok-, long-, bot-, alvleesklier-, hersen- en borstkanker. Ook nemen ze het omringende weefsel onder de loep. Bij alle vormen van kanker kwamen ze intracellulaire bacteriën op het spoor, maar het verschilde sterk per tumortype hoe vaak: in slechts 14,3 procent van de melanomen tegenover 60 procent in borst-, bot- en alvleesklierkanker. Het gaat met name om bacteriën uit de stammen Proteobacteria en Firmicutes. Verder blijken specifieke bacteriën gelinkt aan tumortype, of iemand wel of niet rookt, en aan de respons op immunotherapie.

Hoewel het bij de meeste kankers gaat om een lage bacteriediversiteit, noemen de onderzoekers vooral de bacteriële rijkdom en diversiteit bij borstkanker opmerkelijk. Gemiddeld kwamen ze per borstkankersample 16,4 bacteriesoorten tegen, terwijl dat bij alle andere kankersoorten minder dan 9 was. Ook in bacteriële biomassa spanden de borstkankersamples de kroon. Om er zeker van te zijn dat het om levende bacteriën gaat, plaatsten de onderzoekers onder meer borstkankerweefsel op 35 verschillende soorten agar-agar-voedingsbodems. Uit vier van die tumoren kwamen meer dan duizend bacteriekolonies voort, uit de laatste slechts 37.

'Een uitgebreid begrip van het micromilieu van tumoren is een uitdagende maar cruciale stap om te komen tot een mechanistisch model van kankerprogressie', schrijven de twee Amerikaanse kankeronderzoekers Chloe Atreya en Peter Turnbaugh met lof in een begeleidend perspective. 'Indien succesvol, betekent dat mogelijk het begin van een nieuwe golf aan kankerdiagnostiek en -therapieën.' ■

# EINDE LES 10