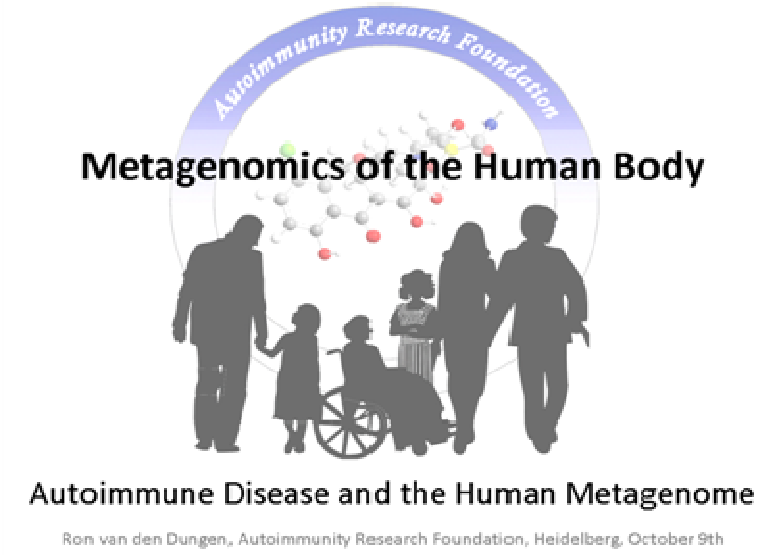


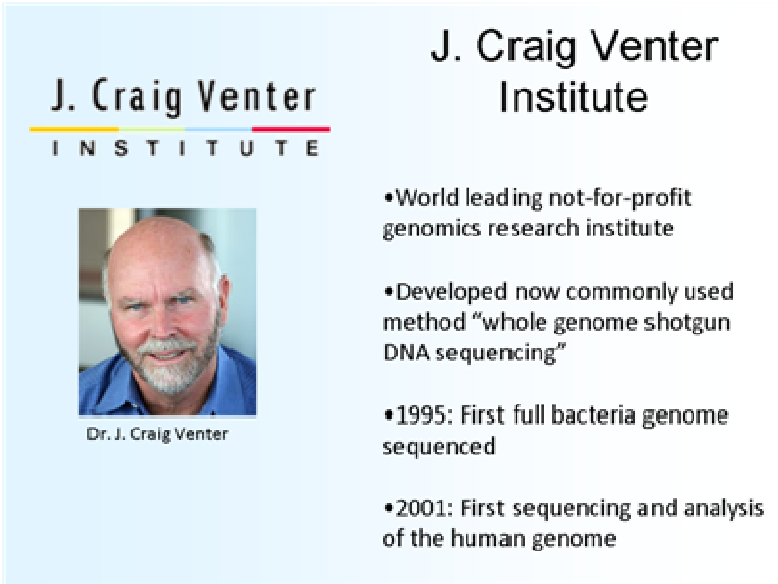
Metagenomics of the Human Body

(Introduction of the book chapter "**Autoimmune Disease and the Human Metagenome**" on 9 October in Heidelberg)

While preparing these slides, I recalled this quotation from Antoni van Leeuwenhoek, who was a Dutch scientist and is commonly known as the 'Father of Microbiology'. Van Leeuwenhoek eventually became a Fellow of the Royal Society of London. Initially his credibility was questioned when he sent the Royal Society a copy of his first observations of microscopic single-celled organisms. After his appointment to the Society, he wrote hundreds of letters to the Society. This is a quotation from one of them.

In English this would translate into something like:

"We will then hope, that the enquirers into Nature's works, who will delve deeper and deeper into mysteries that have thus far remained hidden, having placed more and more truth before their eyes, will acquire aversion of errors of former times, which all those who love the truth should endeavor."



A person who certainly strives to delve deeper and deeper is Dr. Craig Venter. Dr. Venter is founder and president of the world's leading non-profit genomics research center, the J. Craig Venter Institute.

He and his team developed a method called "whole genome shotgun sequencing" which greatly reduced the time needed to determine genomes. Their work led to the first full bacteria genome to be published in 1995 and in 2001, the first human genome. This was not the complete hereditary information of a single individual, but rather a consensus assembly from five individuals.


news.de

Artikel vom 21.05.2010

KÜNSTLICHES ERBGUT

Craig Venter baut Bakterien

Craig Venter kontrolliert die Biologie immer mehr: Der US-Genetiker hat ein Bakterium mit künstlichem Erbgut geschaffen. Damit will sein einmal Forscherteam Biokraftstoffe schaffen, CO_2 absorbieren oder Impfstoffe kreieren.

Die Forscher bauten die Gene eines Bakteriums mit Hilfe einzelner Erbgutstückchen nach und setzten dieses Kunstgenom dann in eine andere Bakterienart ein. Folge: Die so vom künstlichen Erbgut gekaperte Zelle produzierte nur noch Stoffe, die auf diesem gespeichert waren. Das Original-Erbgut der Zelle wurde herausgekickt.

Die Forscher schufen damit eine Zelle, die von einem fremden Genom kontrolliert wird. Sie sprechen von einer «synthetischen Zelle», obwohl sie nur das Erbgut künstlich geschaffen haben.

Dies werde ein sehr schlagkräftiges Werkzeug, beim Versuch die Biologie dazu zu bringen, «das zu tun, was wir wollen», sagte Venter. «Wir haben eine große Spanne von Anwendungen [im Kopf].» Das Team vom Craig Venter Institute in Rockville berichtet im Fachjournal «Science» vom Freitag von der Herstellung dieser Zellen.

J. Craig Venter Institute (cont'd)

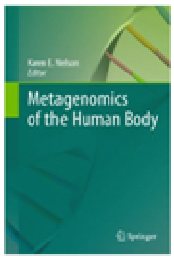
- 2007: Most complete sequencing of diploid human genome (his own)
- 2009: Awarded U.S. National Medal of Science
- 2010: World's first synthetic life form

The JVCI team then went on to compile the first individual human genome and published Craig Venter's own diploid genome, covering both of his chromosome pairs, one set being inherited from each of his parents. Last year October Craig received the U.S. National Medal of Science out of the hands of president Obama. And if all that is not enough yet Craig Venter was in the news last May because he and his team of scientists had managed to create the socalled First Self-Replicating Synthetic Life. More precisely it was the first cell with a synthetic genome that was created.

Listed as one of the scientific leaders of the Craig Venter Institute is Dr. Karen Nelson. She is a director of the institute and has memberships in important U.S. national comittees. She is also editor in chief of Microbial Ecology, the high-quality scientific journal was founded more than 50 years ago. And now she has released this important new book titled "Metagenomics of the Human Body" that will be available by the end of next month.

Contents

This is a unique book because it brings together findings from different genomic studies. It combines the major findings from the human genome project and that from studies into its metagenome, the genomics of the microbes that live in and on the human body. Furthermore, this book discusses the effects these microbes have on the host's immune system and the enormous implications for health and disease.

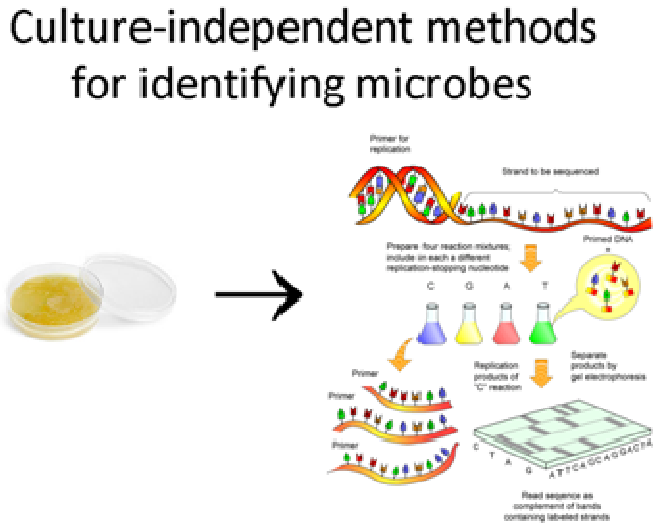


Autoimmune disease and the human metagenome

Amy D. Proal, Murdoch University
Paul J. Albert, Weill Cornell Medical College
Trevor G. Marshall, Murdoch University

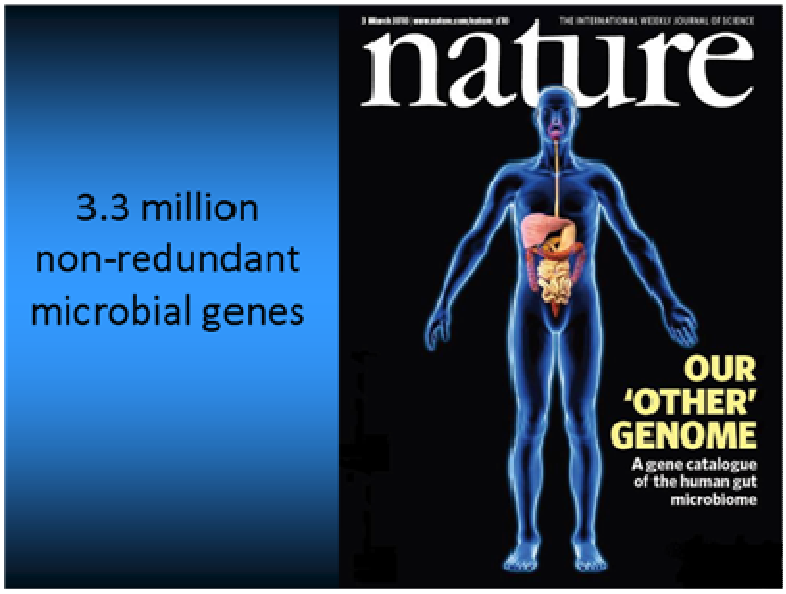
In particular, it is Chapter 11 that focuses on this area. “Autoimmune Disease and the Human Metagenome” is the title of that chapter and it is a joined effort of Professor Marshall and two colleagues in the Autoimmunity Research Foundation, Amy Proal and Paul Albert. It’s about thirty pages and I will not give away everything but I would like to highlight some important subjects.

In 2007 NASA announced that the so-called Clean Rooms, where technicians assemble spacecrafts and which are supposed to be sterile, were in fact full of bacteria. They found about a hundred different species. In fact, they had been there all the time and that came as a shock to NASA. All of a sudden it became apparent that we probably have been shipping microbes around space for decades. They simply had not been detected before and now new methods were revealing them.

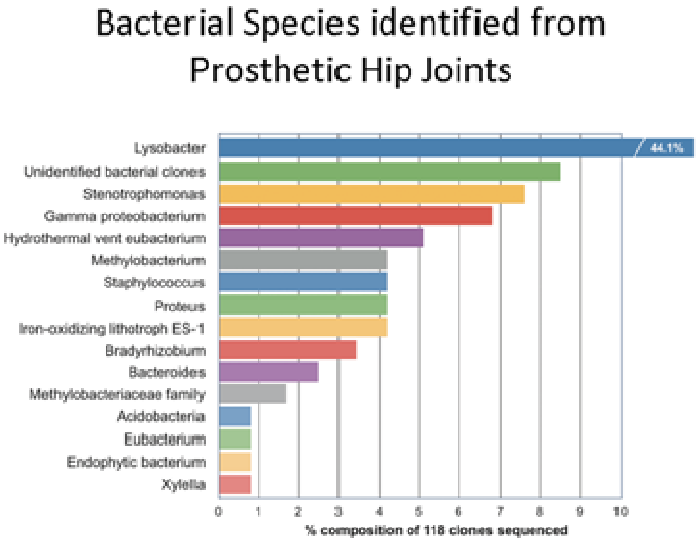


With the development of new techniques it is becoming clear that only a very limited number of microbes will grow on the medium of a Petri dish. Instead, new methods use detection of genetic material to identify microbes.

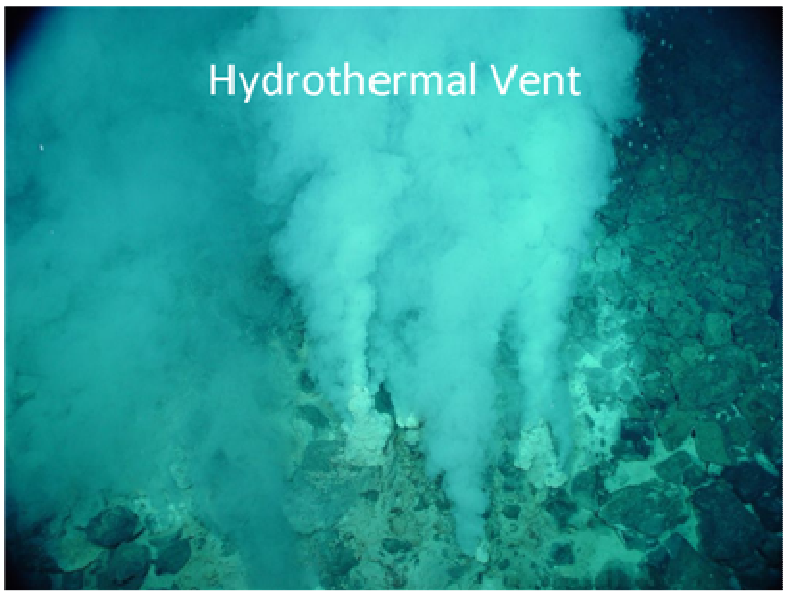
Today, the National Institutes of Health (NIH) estimates that a mere 10% of the cells that comprise Homo sapiens are human cells. The remeining 90% are microbial in origin.



The European initiative, called Metagenomics of the Human Intestinal Tract (MetaHIT), focuses on the microbial inhabitants of the gut. The MetaHIT project too, found overwhelming evidence that these microbes are indeed there. The team recently reported to have characterized 3.3 million non-redundant microbial genes.

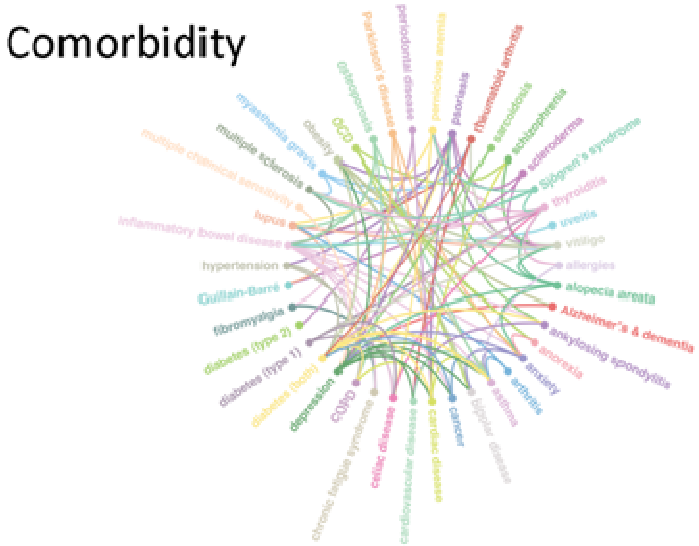


Analysis using gene sequencing detected these types of bacteria on prosthetic hip joints. The prevalence of hydrothermal vent eubacteria was higher than the prevalence of Staphylococcus aureus, which is a common species.



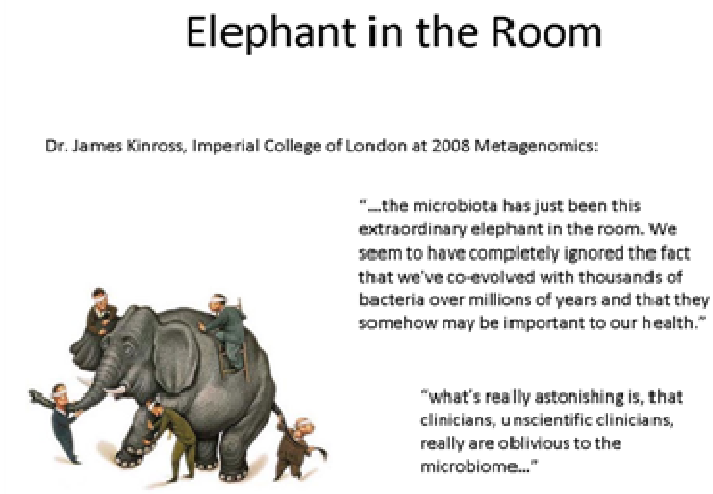
Hydrothermal vent eubacteria were previously thought to persist only in the depths of the ocean in hydrothermal vents like this one. Well, they appear to also live inside us.

So the new insights force us to reconsider common beliefs. In the same vein, it is also commonly believed that one disease or condition causes the other. For example, it is commonly believed that obesity is a causative factor in the development of diabetes. In fact, patients with type 2 diabetes are so likely to become morbidly obese that the two conditions are sometimes collectively referred to as "diabesity."

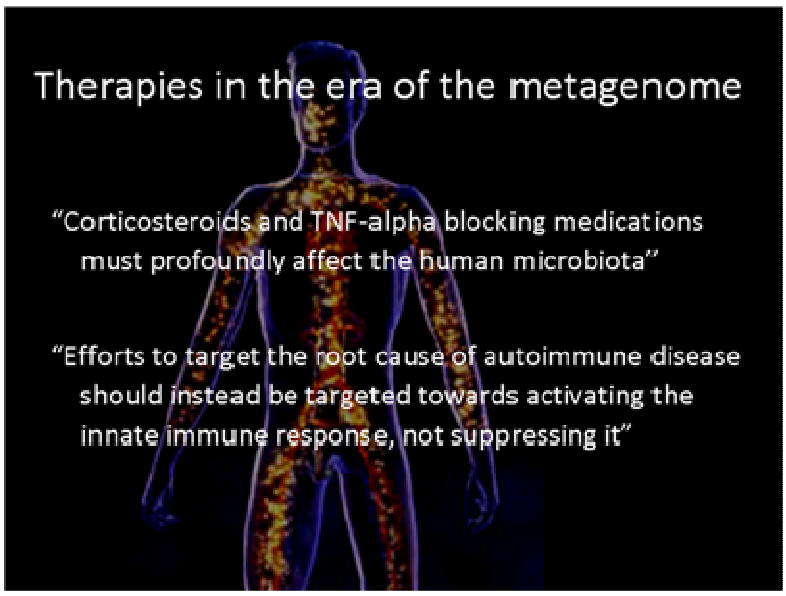


The same goes for other sets of parallel conditions such as tooth decay and dementia, rheumatoid arthritis and uveitis, high cholesterol and heart disease, and others. But now understand more about the microbes it is far more likely that these conditions have the microbiota as a common cause rather than one condition being causal for the other.

This is another picture from the book chapter and shows comorbidities among common inflammatory diseases.

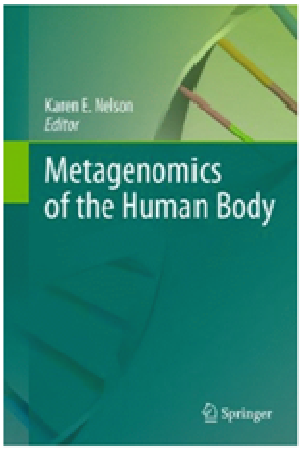


At the 2008 Metagenomics Conference, James Kinross of the Imperial College of London began his speech with the following statement: *"We surgeons have been operating on the gut for literally thousands of years and the microbiota has just been this extraordinary elephant in the room. We seem to have*
completely ignored the fact that we've co-evolved with thousands of bacteria over millions of years and that they somehow may be important to our health. As doctors, we routinely do terrible things to the microbiota and I'm sure this has implications for our health."



Indeed, many doctors still believe that most parts of the body are sterile and that bacteria and other pathogens are not driving factors in the autoimmune disease. Instead, the standard of care for patients with autoimmune disease continues to be corticosteroids and TNF-alpha blocking medications.

These are two quotes from the book chapter: "Corticosteroids and TNF-alpha blocking medications must profoundly affect the human microbiota". Suppressing the immune system encourages chronic disease. And "Efforts to target the root cause of autoimmune disease should instead be targeted towards activating the innate immune response, not suppressing it"



Nelson, Karen E. (Ed.)
1st Edition., 2011, 350 p. 40 illus., 20 in color.,
Hardcover
ISBN: 978-1-4419-7088-6
Not yet published.
Available: December 26, 2010

That is all I will give away for now. The rest can be read in the book, that will be available by December this year. Thank you.