Food & Nutrition – Systems Approaches

Celebrating 93 Years of Wageningen University

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Professor of Microbiology
Professor of Molecular Microbiology
Finland Distinguished Professor

NWO
Netherlands Organisation for Scientific Research

European Research Council
Scientific Council
erc

SUOMEN AKATEMIA
FINLANDS AKADEMI • ACADEMY OF FINLAND

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Celebrating 10 Years of the Human Genome

F S Collins Science 331 (2011) 546-546

We Now Are Finalizing Our Other Genome !

Qin et al MetaHit Consortium (2010) A human gut microbial gene catalogue established by metagenomic sequencing.
Nature 464: 59-65

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Human GI Tract: Microbes Dominate Our Body

Karyome

~10^{13} human cells
single genome
3 Gbase sequence
~ 30 k proteins

Mitochondriome

~ 10^{14} mitochondria
single genome
17 Kbase sequence
13 proteins

Intestinal Microbiome

~ 10^{14} microbial cells ~ 10^{3} – 10^{4} genomes → 3-30 Gbase sequence
now reference genome of 3 Gbase for 3 M genes/proteins

Qin et al MetaHit Consortium Nature 2010

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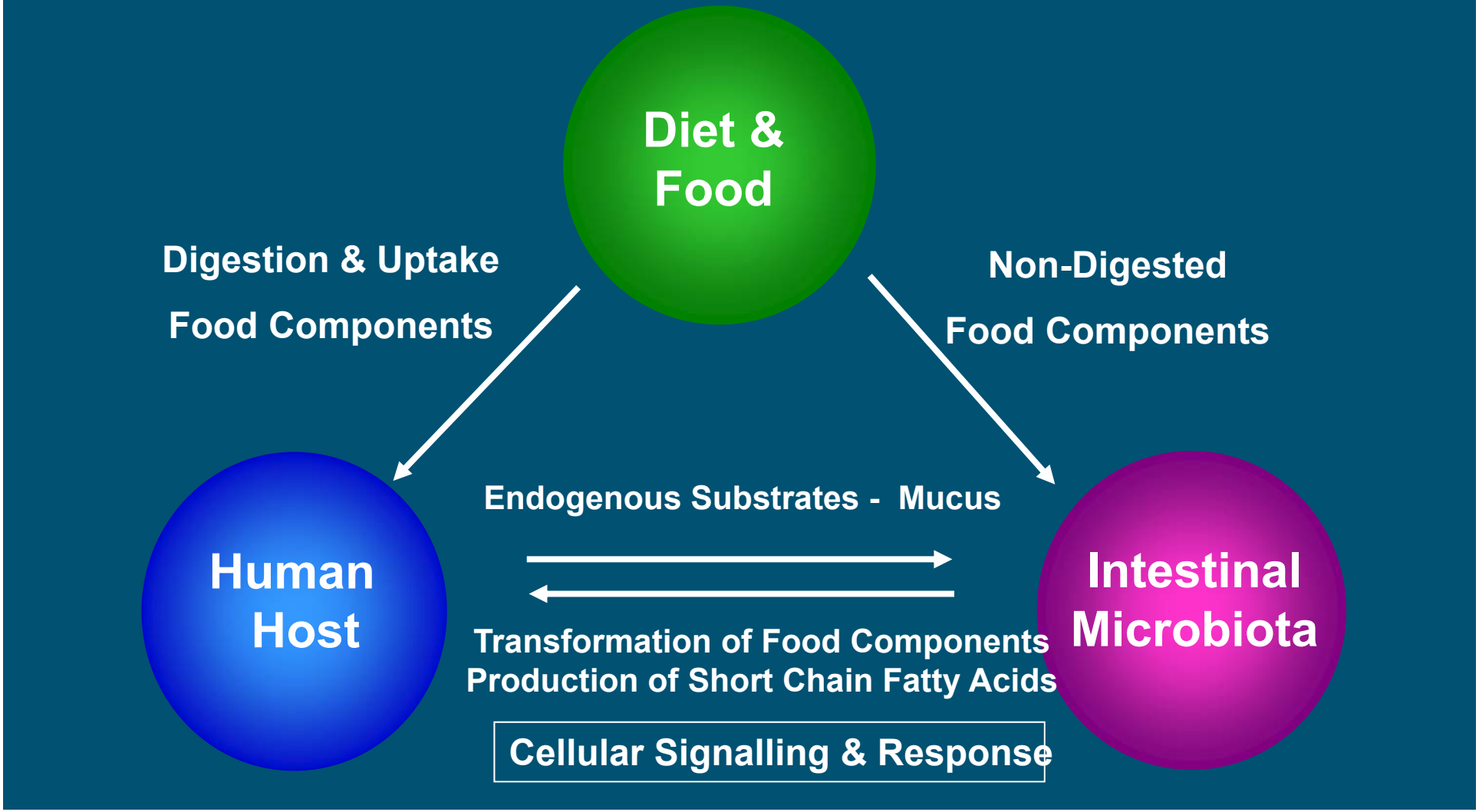
Food & Nutrition: Interplay of Host & Microbes



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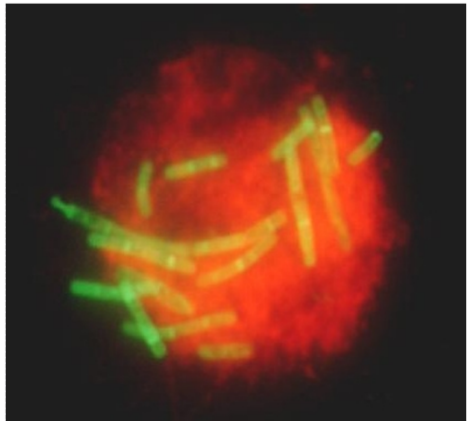
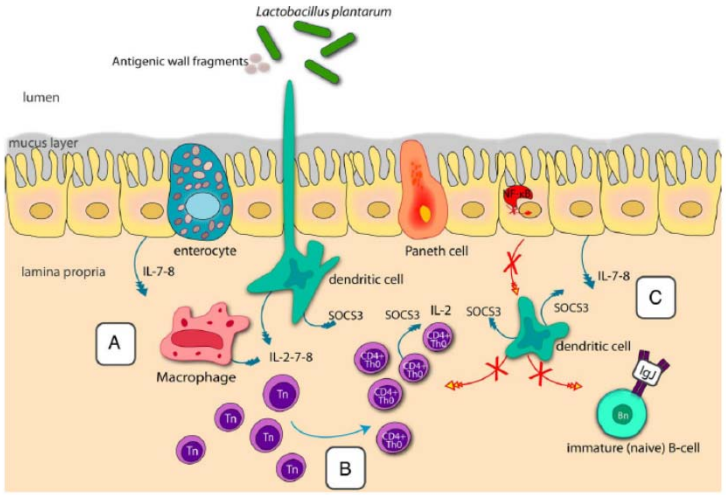
Probiotic Lactobacilli Interact in Small Intestine

S layer protein A of *Lactobacillus acidophilus* NCFM regulates immature dendritic cell and T cell functions



L.acidophilus

Sergey Konstantinov et al
PNAS 105 (2008) 19474



Differential NF-κB pathways induction by *Lactobacillus plantarum* in the duodenum of healthy humans correlating with immune tolerance

Peter van Baarlen et al PNAS 106 (2009) 2371
Peter van Baarlen et al PNAS 107 (2010) sept

Comparative genomic analysis of *Lactobacillus rhamnosus* GG reveals pili containing a human-mucus binding protein

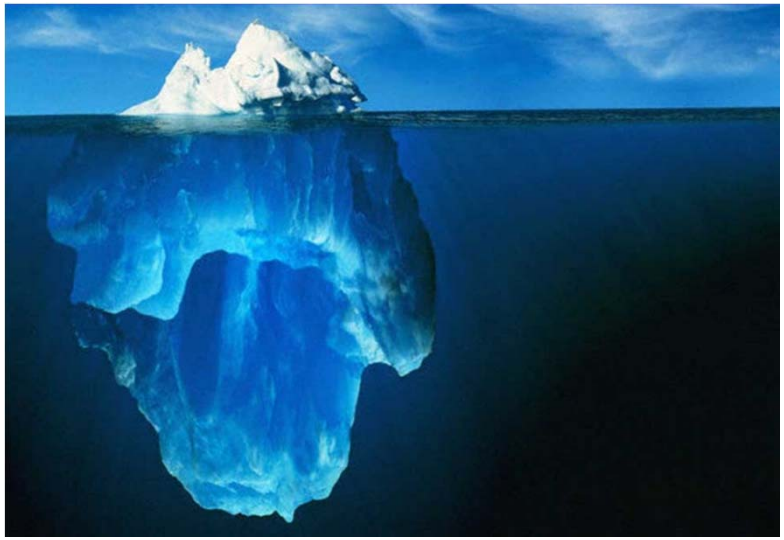
L.rhamnosus GC

Matti Kankainen et al
PNAS 106 (2009) 17193

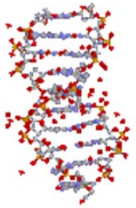
TI FOOD NUTRITION

Most Intestinal Microbes Have Not Been Culture

Cell Culturing ←



→ Not Yet Cultured

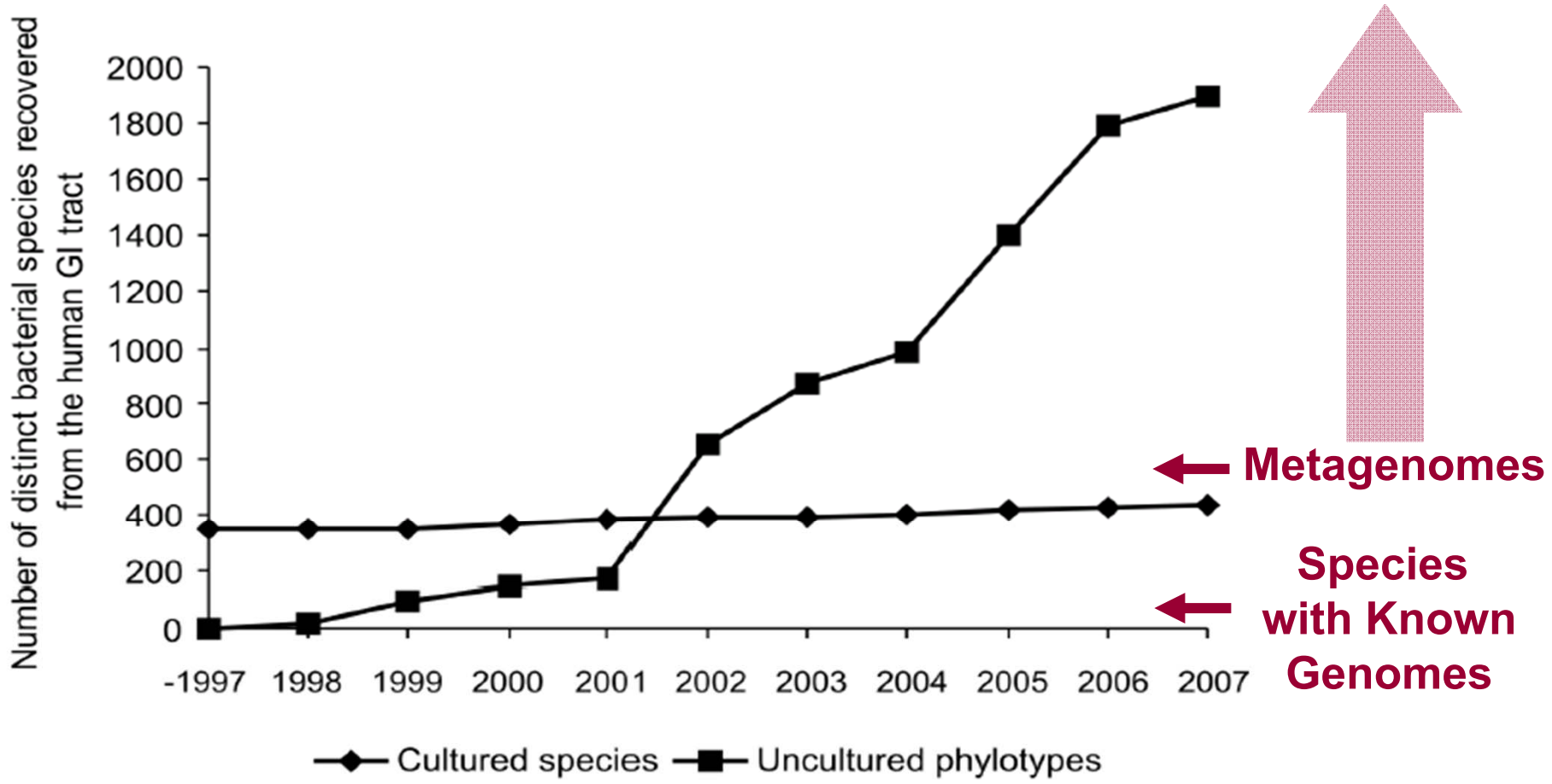


Omics Based Approaches

Global Description of Intestinal Microbiota

Zoetendal EG, M Rajilić-Stojanović & WM de Vos
High throughput diversity and functionality analysis of the gastrointestinal tract microbiota.
Gut 57 (2008) 1605-15

New Generation Technology Seq



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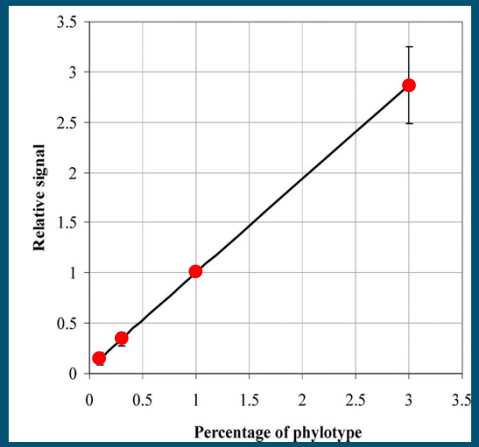
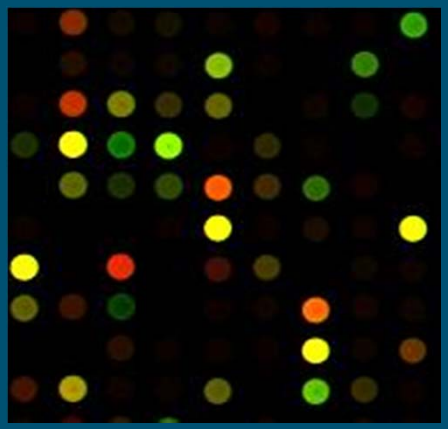
Microbiota Differences in Health & Disease

Human Intestinal Tract (HIT) Chip:
Analysis of Thousands of Intestinal Species

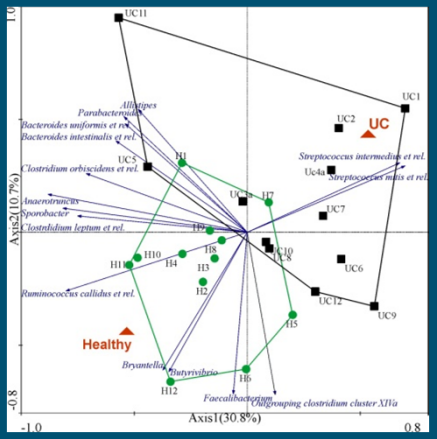


Accurate Over Large Dynamic Range



benchmarked to FISH & pyrosequencing

Each Individual Has A Unique Microbiota



PCA of Healthy & Ulcerative Colitis

Twin Studies Show Genetic Impact

Aberrant Microbiota in Intestinal Diseases

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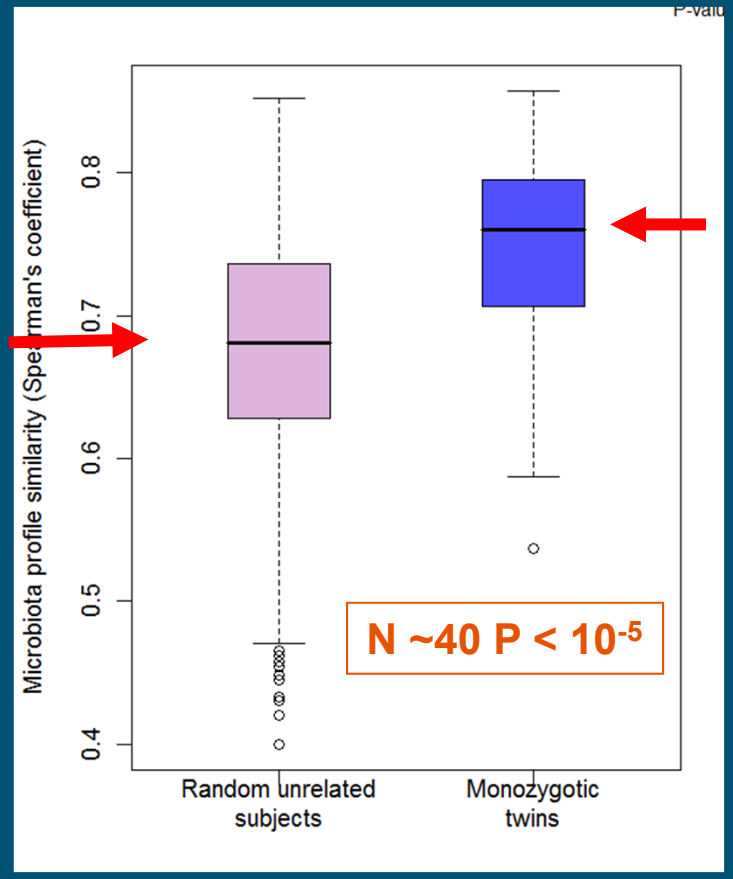
Rajilic-Stojanovic M, H Heilig, D Molenaar, K Kajander, A Sukara, H Smidt & WM de Vos (2009) Environ Microbiol 11: 1736-1743

Individual Microbiota - Twins Have Similar Microbiota



confirms earlier family studies of 10 years ago

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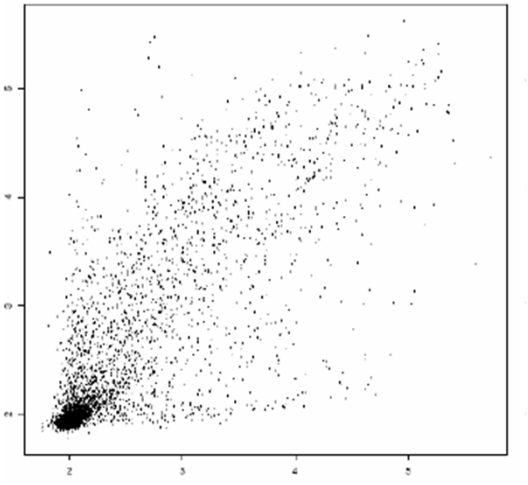
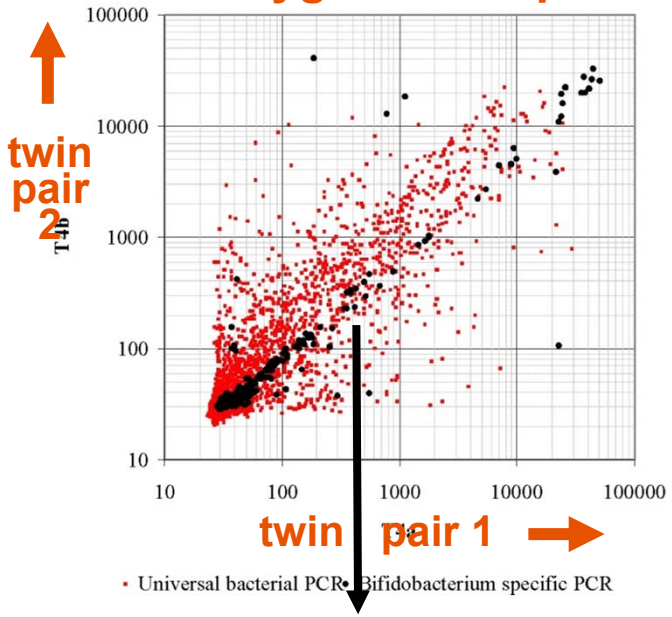
24. Zoetandal, E. G., Akkermans, A. D. L., Akkermans-van Vliet, W. M., de Visser, J. A. & de Vos, W. M. The host genotype affects the bacterial community in the human gastrointestinal tract. *Microb. Ecol. Health Dis.* **13**, 129–134 (2001).

Some Groups Identical in Adult Twins Living Separately

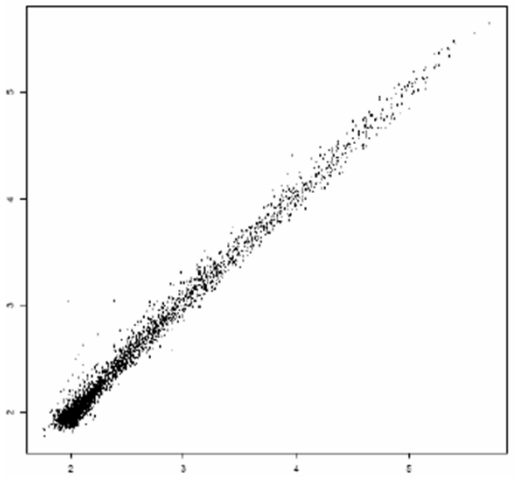
unrelated subjects



monozygotic twin pair



reproducibility



Bifidobacterium spp.- early colonizers **p=0.0152**

Mother, Milk & Microbes….
Specific Host-Microbe & Other Interactions

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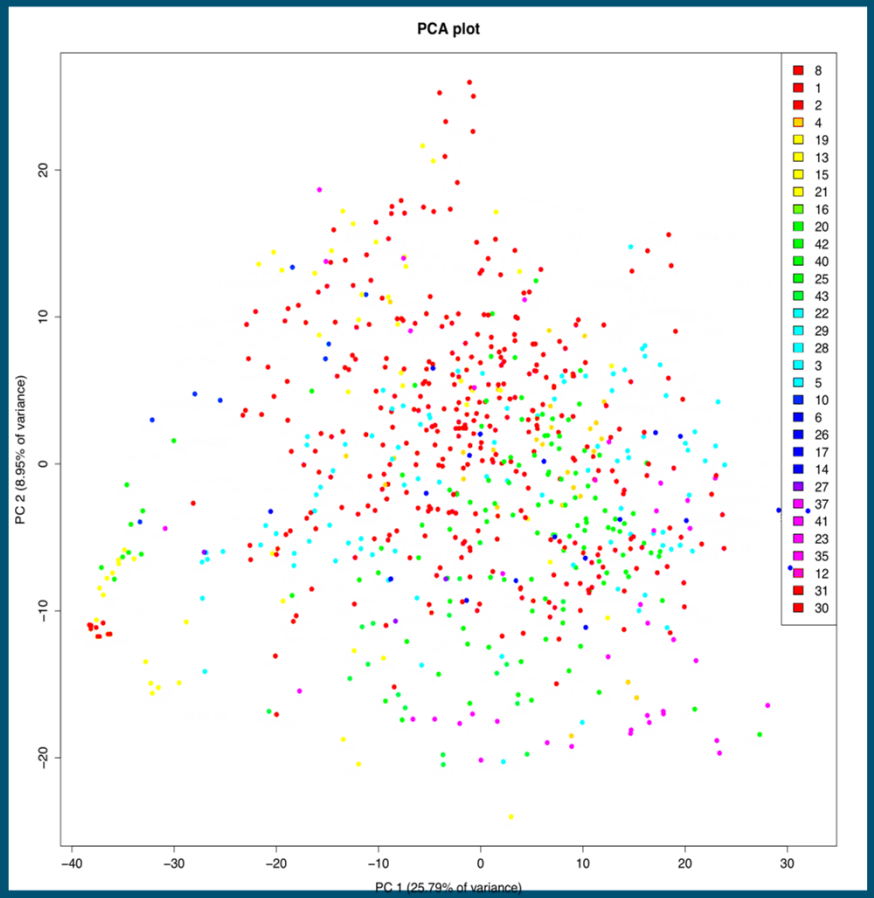
1000 Intestinal Samples – PCA of HITChip Analysis



Advanced Computational & Machine Learning Tools

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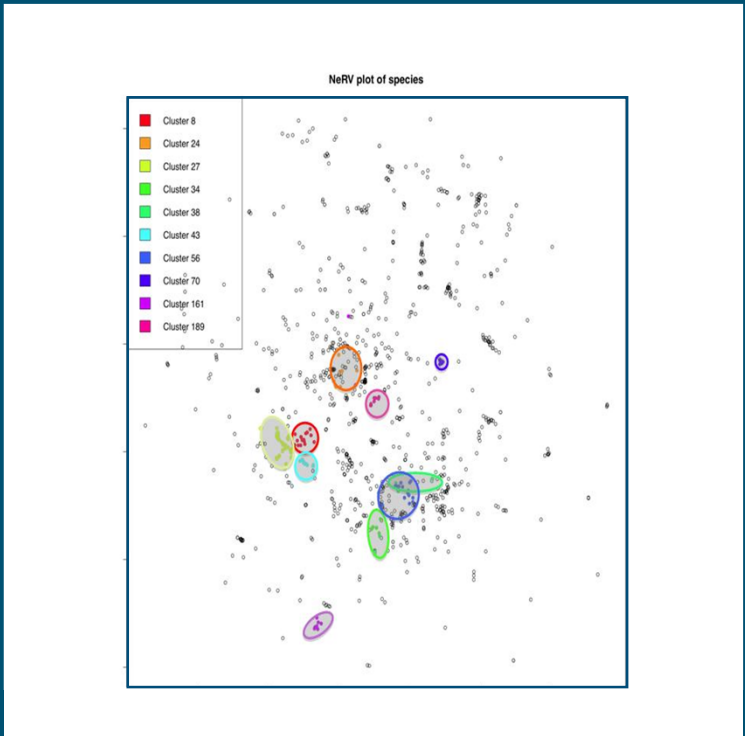
J Nikkila & WM de Vos (2010) J Clin Gastroenterol 44-S1-S5

Meta-Analysis Shows Common Networks



Various Networks of Specifically Interacting Bacteria

Clustering of Human Subjects: *Enterotype Hypothesis* (Nature 2011)

Potential for Personalized Diets Targeting Intestinal Microbiota

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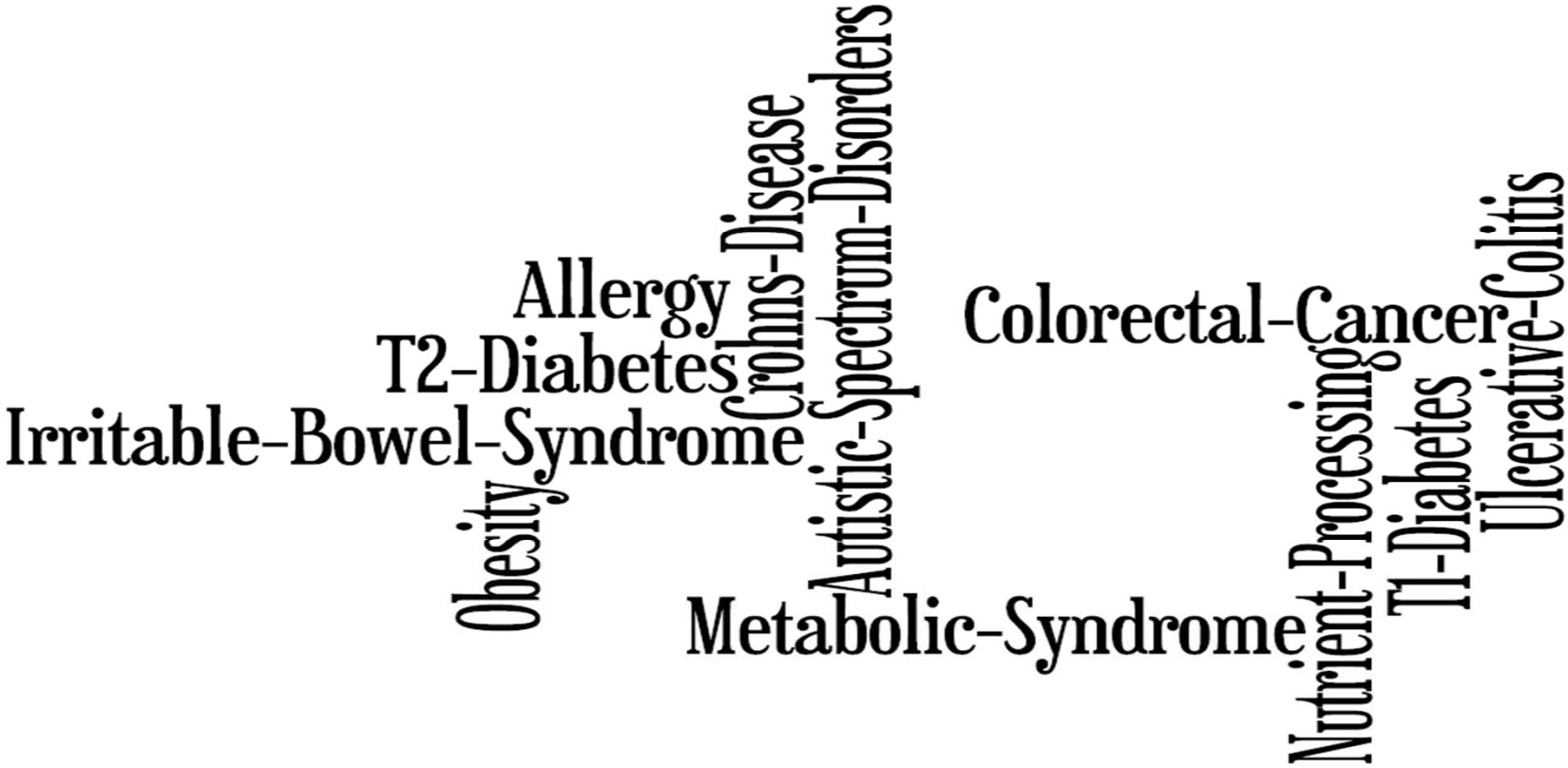
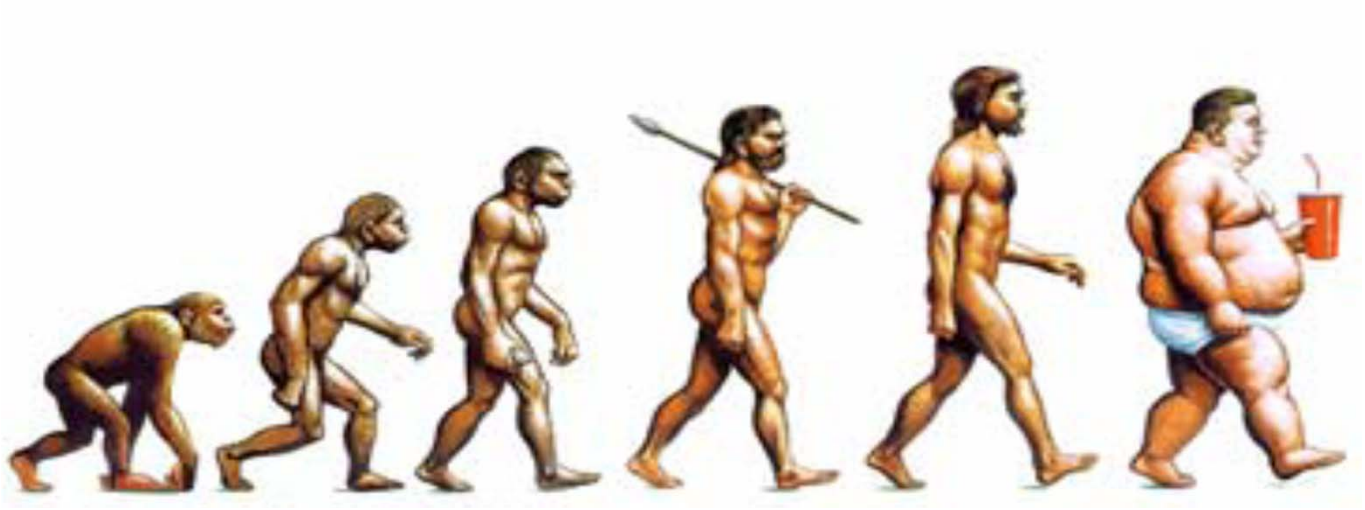
Large Impact of Human GI Tract Microbes



Correlation Studies !

Impact of GI Tract Microbes on Obesity



Vol 444|21/28 December 2006|doi:10.1038/nature05414 nature

ARTICLES

Nature 2006
Xmas Issue

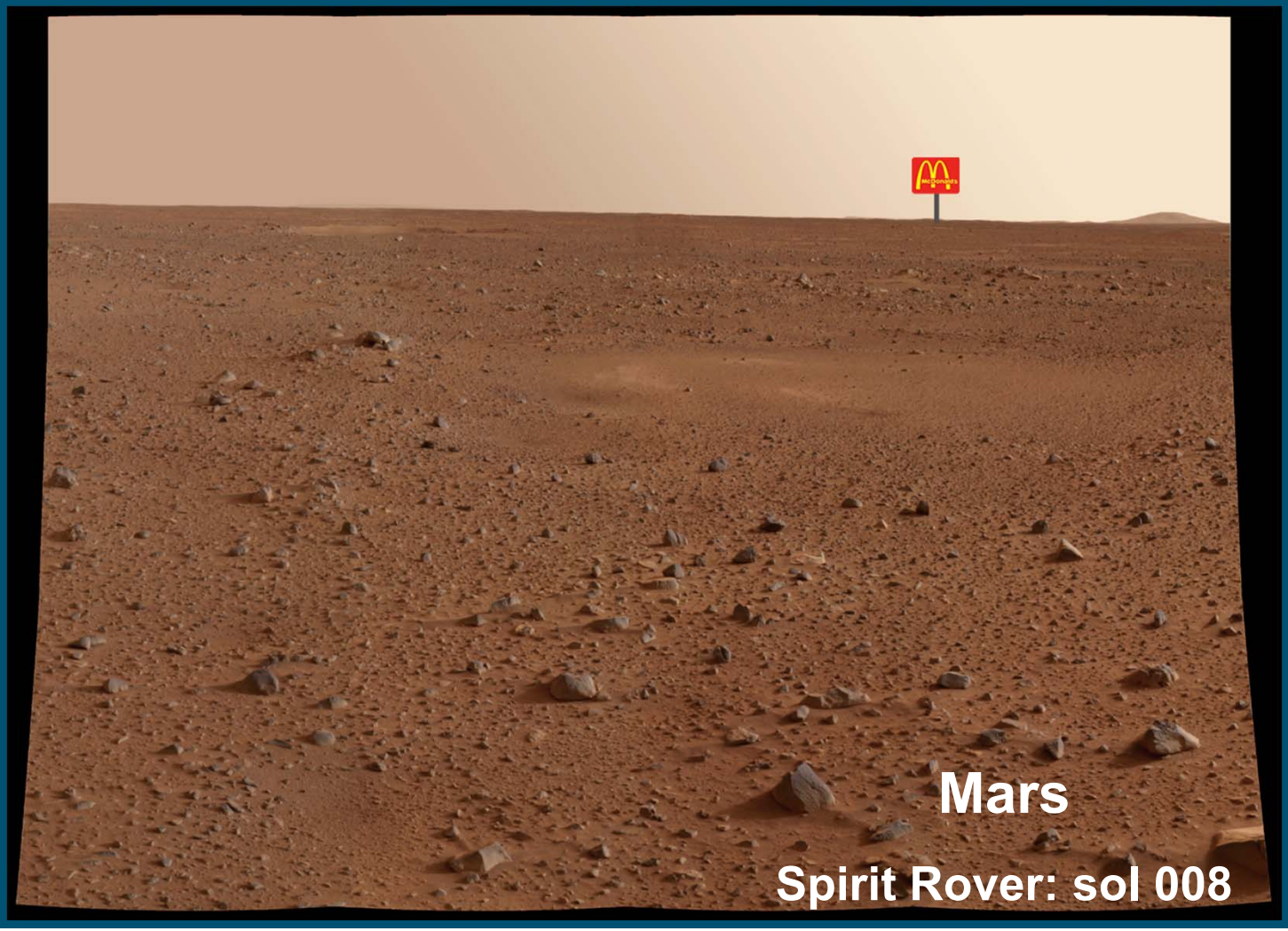
An obesity-associated gut microbiome with increased capacity for energy harvest

Peter J. Turnbaugh[1], Ruth E. Ley[1], Michael A. Mahowald[1], Vincent Magrini[2], Elaine R. Mardis[1,2] & Jeffrey I. Gordon[1]

MICROBIAL ECOLOGY

Human gut microbes associated with obesity

Controversial Results -Food Is Everywhere -Effect of Diet

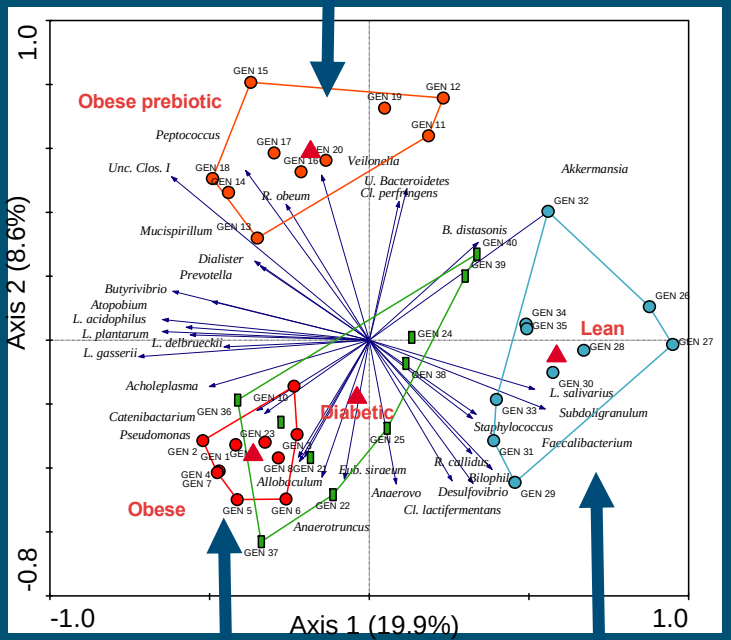


Microbiota Differences in Obese versus Lean Mice

Obese ob/ob mouse

Lean wt mouse

Obese + Prebiotic Diet



Obese **Lean**

Marked Effect of Diet

Mouse Intestinal Tract (MIT) Chip Data

Patrice Cani & Muriel Derrien

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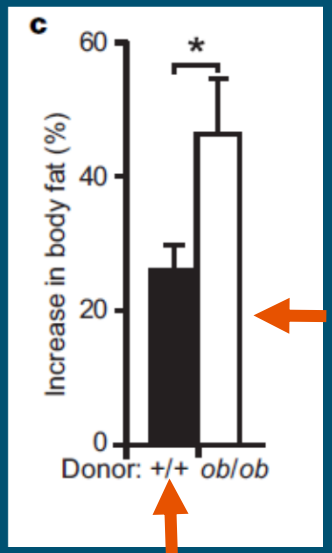
Impact of GI Tract Microbes on Obesity

Obese Lean

Fecal Transplantion
Into Germ-Free Mice



Obese Donor

Lean Donor

Vol 444|21/28 December 2006|doi:10.1038/nature05414 nature

ARTICLES

An obesity-associated gut microbiome with increased capacity for energy harvest

Peter J. Turnbaugh[1], Ruth E. Ley[1], Michael A. Mahowald[1], Vincent Magrini[2], Elaine R. Mardis[1,2] & Jeffrey I. Gordon[1]

Washington University in St. Louis School of Medicine

The Gordon Lab

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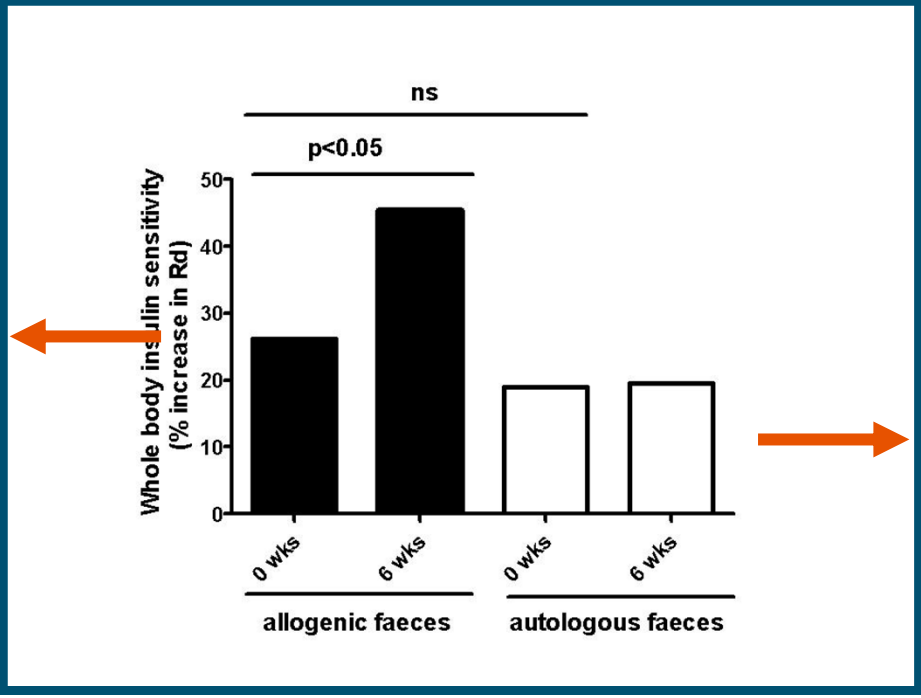
Microbiota Transplantation Improves Insulin Sensitivity

Metabolic effects of transplanting gut microbiota from lean donors to subjects with metabolic syndrome

Wednesday, Sep 22, 2010, 12:00 PM -12:15 PM

A. Vrieze[1], F. Holleman[1], M.J. Serlie[2], M.T. Ackermans[2], G.M. Dallinga-Thie[1], A.K. Groen[3], E. van Nood[1], J.F.W. Bartelsman[4], R. Oozeer[5], E. Zoetendal[6], W.M. de Vos[6,7], J.B.L. Hoekstra[1], M. Nieuwdorp[1];

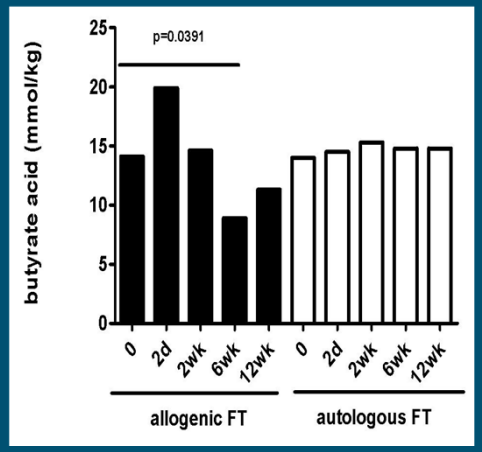
Lean Donors
Allogenic (n=9)

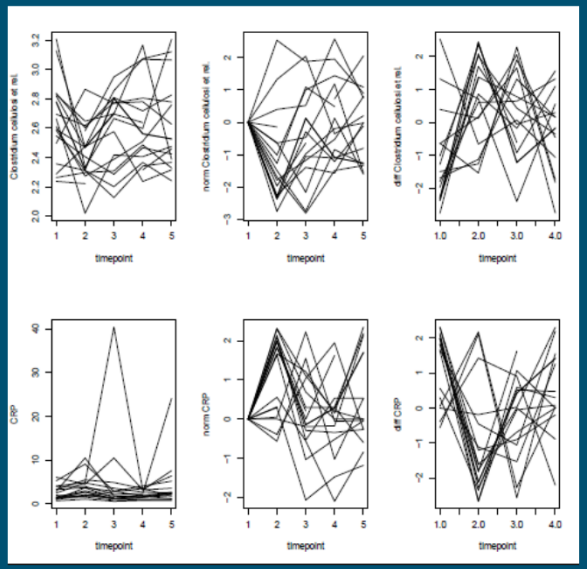


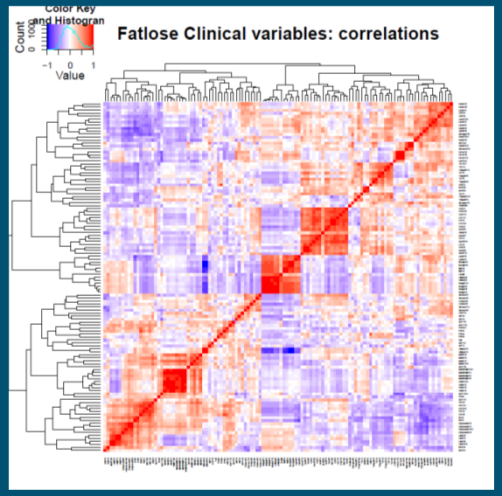
Patient Donors
Autologous (n=9)

Reverse Engineering: Analysis of Effector Microbes & Exploitation

Large Datasets – Systems Approaches Needed







COBIOT 781 1–12 ARTICLE IN PRESS

Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Biotechnology

ELSEVIER

Systems biology of the gut: the interplay of food, microbiota and host at the mucosal interface

Vitor Martins dos Santos[1,*], Michael Müller[2,*] and Willem M de Vos[3,4,*]

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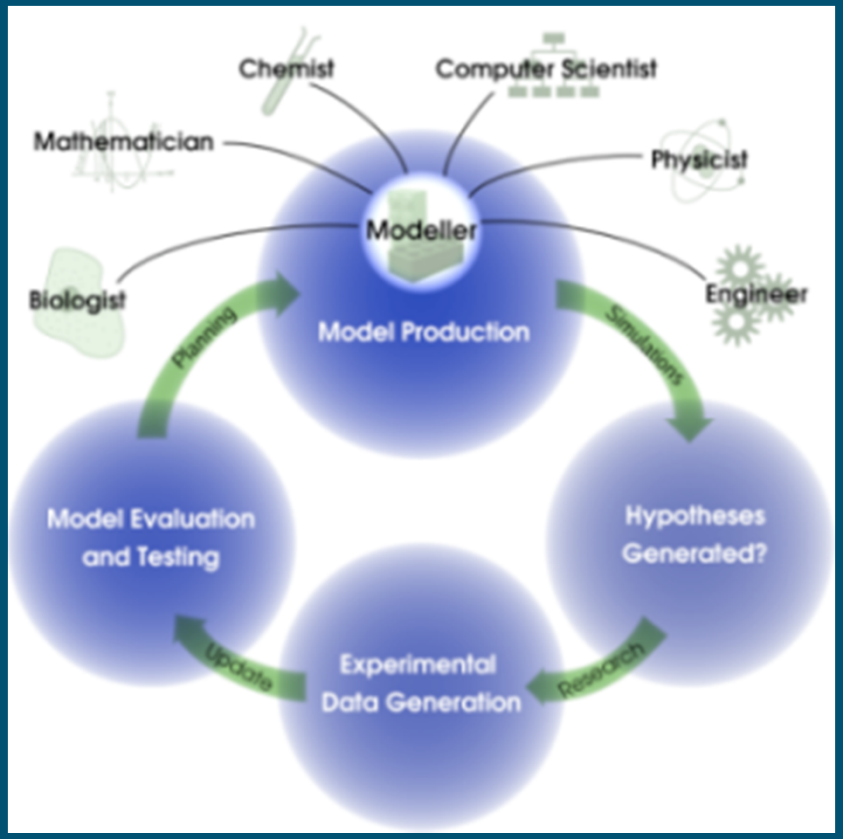
Systems Approaches – Model Production



Quantitative Understanding of Dynamic Interactions Between Components of Living Systems

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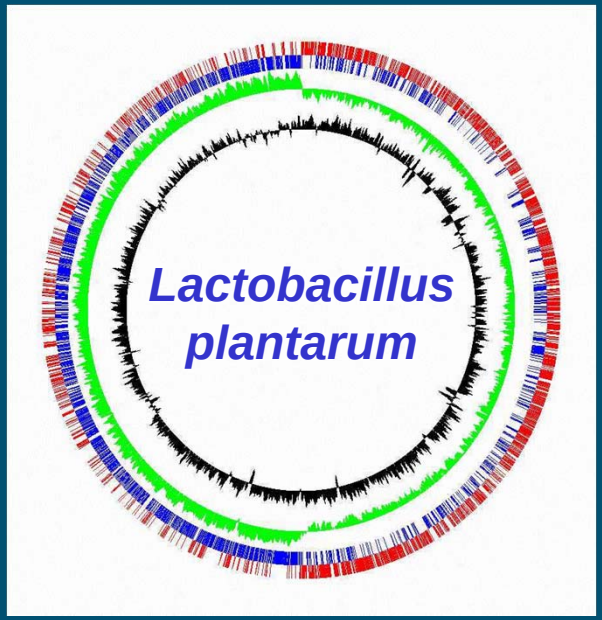
Systems Approaches – Model Example

First Complete Genome Sequenced in NL -2000 Greenomics-WCFS



3.3 Mb Genome – 3052 genes
Paradigm for Lactic Acid Bacteria
Genome-Based Modelling

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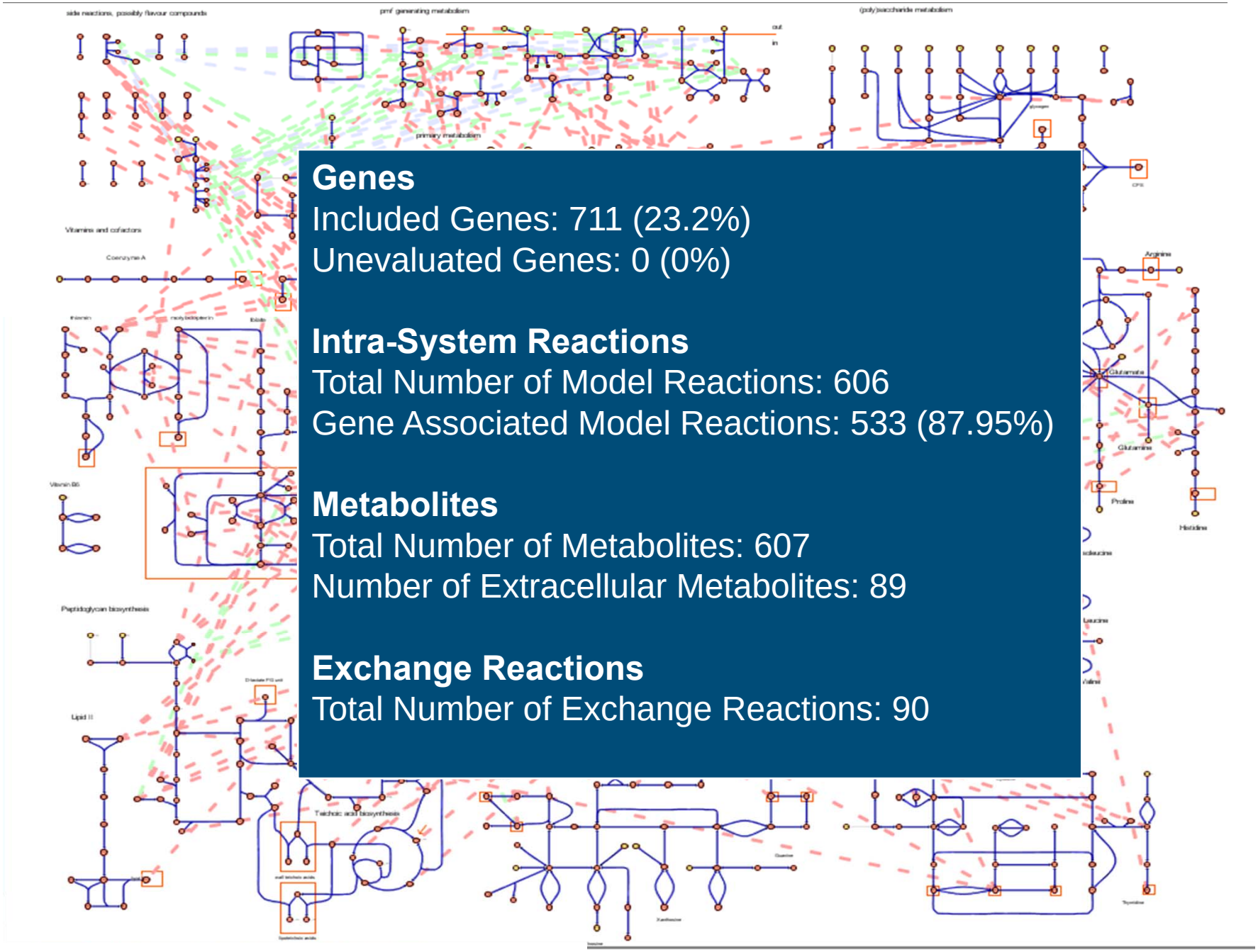
Kleerebezem et al. PNAS 100 (2003) 1990



Teusink et al. Analysis of Growth of L. plantarum Using a Genome Scale Model J Bi

Model-Based Engineering

A Good Model is A Good Hypothesis

Prediction of O_2 and NO_3 Respiration – Experimentally Verified & 3-Fold Yield Improvement

Growth Predicted on Glycerol – Verified after 500 Generation of Adaptation – NGT Reseq Reveals Mutations

Brooijmans et al & Teusink et al - Patent Pending

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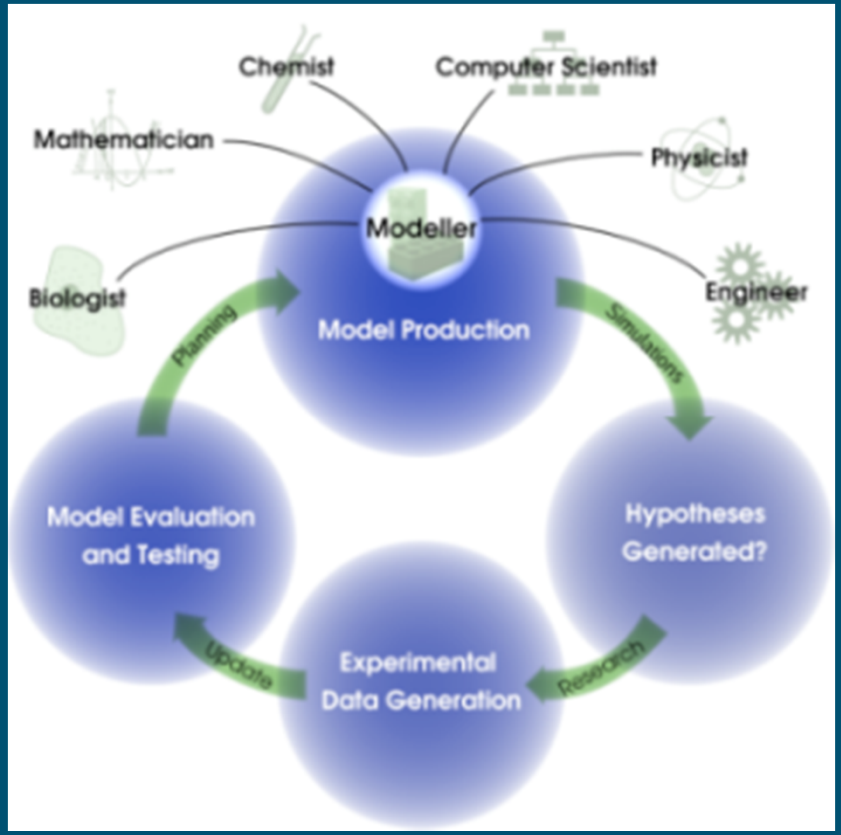
TI FOOD NUTRITION

Systems Approaches – New Biology

Describe & Understand



Predict & Control

Quantitative Understanding of Dynamic Interactions Between Components of Living Systems

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The Genome Revolution Is Only Just Starting

Microbiota & Personalized Nutrition – Systems Approache

You Never Walk Alone…

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Conclusion

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