

Biological questions addressed by metagenomic analysis

Introduction

- Bacteria amongst us
- Human Microbiome Project
- Clinical microbiomics
- Interactions of host and microbiome (What causes what?)

Different environments harbor unique communities of microorganisms



Microbes interact

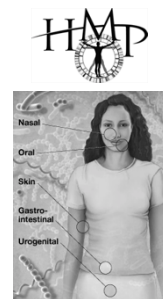
- With each other
 - Via regular ecological mechanisms (competition)
- With the host
 - Produce and metabolize hormones and common nutrients
 - Host immune response
- With the environment

Microbiome and metagenome

- Joshua Lederberg: the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space and have been all but ignored as determinants of health and disease. microbiome
- Complete collection of genes contained in the genomes of microbes living in a given environment
- Numbers Human shelter 100 trillion microbes (10¹⁴), (we are made of 10 trillion cells) It is estimated that there are 1000 species of bacteria live in the human gut.
- Metagenome: Composition of all genes present in an environment (soil, gut, seawater), regardless of species.

Human Microbiome project

- Determining whether individuals share a core human microbiome
- Understanding whether changes in the human microbiome can be correlated with changes in human health
- Developing the new technological and bioinformatic tools needed to support these goals
- Addressing the ethical, legal and social implications raised by human microbiome research.

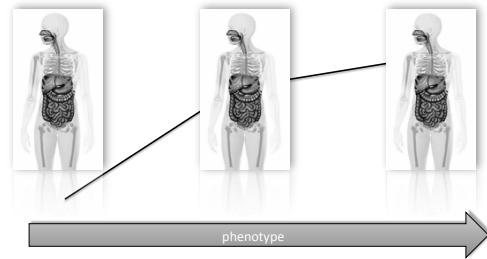


<https://commonfund.nih.gov/hmp/>

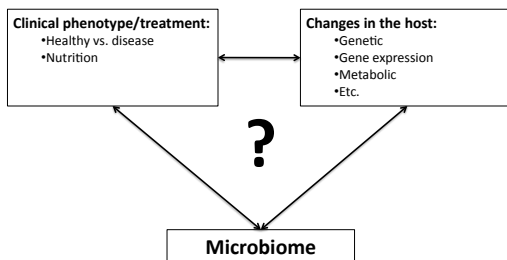
HMP Goals is to address the following questions

- What are the microbes that inhabit human body sites? → Microbiomics
- What do they do? → Metagenomics
- What microbes contribute to human diseases? → Clinical microbiomics
- What are the mechanisms of interaction of microbes with their host? → Clinical metagenomics

What changes in phenotype can be attributed to commensal or pathogenic microbes?



Are the microbes drivers or passengers in disease mechanisms?



A sample of clinical microbiomics projects underway

- The role of antibiotics in obesity
- Microbiomic determinants of psoriasis
- Microbial markers of foregut adenocarcinoma
- Microbiomic markers of severe early childhood caries
- Microbiome in estrogen driven malignancies
- The role of gut microbiome in newborn immune development

Some studies with published results

- Co-Evolution of primates and their flora
 - R. Ley, C. Lozupone, M. Hamady, R. Knight and J. Gordon, *Nature Reviews Microbiology* 6, 776 (2008).
- Certain diseases
 - T. Nelson, S. Holmes, A. Alekseyenko, M. Shenoy, T. DeSantis, C. Wu, G. Andersen, J. Winston, J. Sonnenburg, P. Pasricha and A. Spormann, *Neurogastroenterology & Motility* (2010).
- Biogeography of Bacteria:
 - P. B. Eckburg, E. M. Bik, C. N. Bernstein, E. Purdom, L. Dethlefsen, M. Sargent, S. R. Gill, K. E. Nelson and D. A. Relman, *Science* 308, 1635 (Jun 2005).
 - E. Costello, C. Lauber, M. Hamady, N. Fierer, J. Gordon and R. Knight, *Science* 326, p. 1694 (2009).
 - Gray RR, Tatem AJ, Johnson JA, Alekseyenko AV, Pybus OG, Suchard MA, Salemi M. Testing spatiotemporal hypothesis of bacterial evolution using methicillin-resistant *Staphylococcus aureus* ST239 genome-wide data within a bayesian framework. *Mol Biol Evol.* 2011 May;28(5): 1593-603.
- History of Bacteria
 - C. Palmer, E. Bik, D. DiGiulio, D. Relman and P. Brown, *PLoSbiology* 5, p. e177 (2007).