Ethical Issues Raised by Human Microbiome Research

Human Microbiome Science: Vision for the Future

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“Microorganisms impact just about everything, animals and plants are merely along for the ride.”

Prof. Lee Kump
Scientific Background

- The ultimate goal of the HMP is to understand our microbial ecosystems to make people healthier

- Microbiome influences our susceptibility and resistance to disease

- For example:
  - H. pylori may cause ulcers and stomach cancer and protect against esophageal cancer
  - Bi-products of bacteria on the surface of skin modulates inflammatory response during minor skin trauma
  - Probiotics, prebiotics, and phages can be used as clinical treatment
Science influences what we think.

The HMP is likely to reshape our notions of self-identity (who I am) somewhat.

The HMP is unlikely to effect the philosophical problem of personal identity over time.
Self –Identity

- Research on the human microbiome may change:
  - our concept of the human organism
  - affect the distinction between us and our environment
  - transform how we think of microbes
Negative view of microbes
“Privacy” or “confidentiality”
Privacy

- Shared HMP samples include microbiome DNA & human DNA

- Individuals might have unique metagenomic genotypes

- FBI and Homeland Security are already interested in using the microbiome in their investigations

- Something akin to The Genetic Information Nondiscrimination Act (GINA) should be developed to cover the human microbiome.

- Samples collected for research should be subpoena proof, safeguarded from criminal and immigration investigations.
The concept of “property” is socially constructed.

Some features of the microbiome make us think of it as property:
- it is in or on your body
- obtaining some samples require permission

Other features of the microbiome do **not** incline us to think of it as property:
- discarded items
- things we don’t value at all
  (e.g., excrement)
Property:

- Property law is a dynamic patchwork

- Laws and policies related to the microbiome should be designed to:

  - Avoid harm to individuals
  - Promote the social good
  - Avoid undermining important social projects
Controversial Genetics Property Cases

- Ananda Mohan Chakrabarty tried to patent a bacterium that he had modified to break down crude oil and help clean up oil spills. Diamond v. Chakrabarty

- Myriad Genetics, a biotech company, holds patents for two breast cancer–related genes and a diagnostic test for the genes’ presence. (Association for Molecular Pathology et al. v. U.S. Patent and Trademark Office, Myriad Genetics, et al. 6/13/13

- Cells from Henrietta Lacks, a poor black woman who was being treated for cervical cancer, were taken for research. They were preserved as the HeLa “immortal” cell line, a valuable tool in medical research. Rebecca Skloot. *The Immortal Life of Henrietta Lacks*. 2010

- John Moore’s spleen was removed during his leukemia treatment. His doctor used his tissue to create a cell line, patent it, and profit from it. Moore v. Regents of the University of California, et al.
3 types of microbiome research

- Collection of samples from a broad spectrum of subjects to answer very general questions

- Examination of individuals to understand the role of microbiota in the development of specific diseases

- Intervention (probiotics or bacteriophages) for the cure or amelioration of specific diseases (clinical trials)
To understand how microbial communities are structured and how they function (observational)

- What sorts of bacteria, viruses, and fungi comprise the human microbiome?

- How many kinds of microbiota are common to all humans?

- Are changes in the human microbiome correlated with changes in human health?
Advances in Personalized Medicine require widespread participation in biobanks.

Knowledge gained from microbiome studies will be broadly applicable.

Once samples are collected, biobank research will pose only negligible physical risks.
Two points re: (1)

- Samples from multiple sites on a very large number of individuals

- Very time-consuming & costly process
  - Storing and processing samples
  - Record keeping
  - Extracting genetic material
  - Running genetic sequencing
  - Generating useful data is a complex

- To have a significant research payoff, samples and data have to be widely available to researchers for use in many studies.
(2) To develop our understanding of disease processes  

- To determine whether microbiome differences are causes or effects of the target condition.

- Studies require the participation of individuals with & without the target disease.

- Comparison of site-specific microbial samples from affected and non-affected individuals.
Research on the effectiveness of probiotics will resemble:

- Research involving infectious disease
- Resemble drug development research

(3) investigations of the effectiveness of probiotics, phages, and lysins *(clinical trials)*
Not all studies require the same level of oversight.

Different rules may be appropriate for different kinds of research.
Informed consent is not always ethically necessary because:

- Research using previously collected microbiome samples involves only hard to imagine *de minimis* physical risks or harms.
- The benefits of findings to future patients could be significant.
- It is often difficult and sometimes impossible to obtain consent for studies after samples have been collected.
- Specified informed consent for future uses of samples should not be required.

Surveillance and tracking are public health tools

Public health measures, quality assurance (QA) and quality improvement (QI) efforts involve data collection

Gathering needed personal information may infringe upon privacy

The social good provided by such studies can justify small infringements on privacy.
The current regulatory definition of “research” distinguishes it from “public health surveillance,” “QA,” and “QI.”

- Scientific activities
- Employ data collection and analysis
- Designed to produce generalizable knowledge

Ethical oversight and restriction should be based on:
- risk
- benefits
- need to know
- costs
- feasibility
Biobank studies, public health, QA, and QI already employ significant confidentiality protections.

NIH Certificates of Confidentiality provide inadequate protection.

A legally sanctioned mechanism that extends medical confidentiality protections to biobank, public health, QA and QI studies should be established.
Human intervention & the human microbiome: Antibiotics

- Antibiotics kill bacteria
  - Bad bacteria
  - Good bacteria

- Antibiotic use leads to the development of drug-resistant bacteria

- Antibiotic use changes the human microbiome
  - Obesity?
  - Inflammatory bowel disease?
  - Allergies?
  - Asthma?
Human intervention & the human microbiome: Probiotics

- Probiotics are live bacteria said to be safe and to provide a health benefit (*e.g.*, *fecal transplants*)

- They are not evaluated as drugs for safety or efficacy by the FDA

- Manufacturers are not required to provide information about their products or demonstrate that the ingredients are actually alive and present
We are not sure about products sold as Probiotics & Prebiotics:

- What they are
- What they do
- Whether they survive in the gut
- How long they survive
- What effects they have on patients
- What effects they have on others
Phage Therapy Center, Tbilisi Georgia is now accepting patients with chronic, difficult, antibiotic-resistant bacterial infections that do not respond to conventional antibiotic therapies.

http://www.phagetherapycenter.com/pii/PatientServlet?command=static_home
Probiotics, Phages, & Synthetic biology

Synthetic biology could be used in the future:

- To increase the life span of bacteria and viruses
- To make probiotics and viruses more resistant to mutation
- To help probiotics and phages survive during transport to their target environment
Conclusions

- Scientists are just beginning to understand the human microbiome.

- A great deal will have to be learned before microbiome intervention becomes a feasible human.

- Bacteria have altered the planet and they can do so in the future, so foresight and caution are needed.
27 Interdisciplinary Participants

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