

# Ethical Issues Raised by Human Microbiome Research

## Human Microbiome Science: Vision for the Future

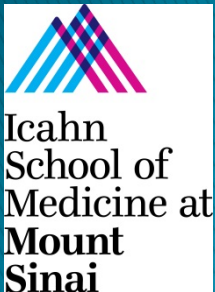
Bethesda, July 24, 2013

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Icahn School of Medicine at Mount Sinai

The Graduate Center, CUNY

Union Graduate College



**“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



ELSI

## Self-Identity

- ▶ 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

## Germ Farm



Scrub'em!

[www.1st-in-handwashing.com](http://www.1st-in-handwashing.com)

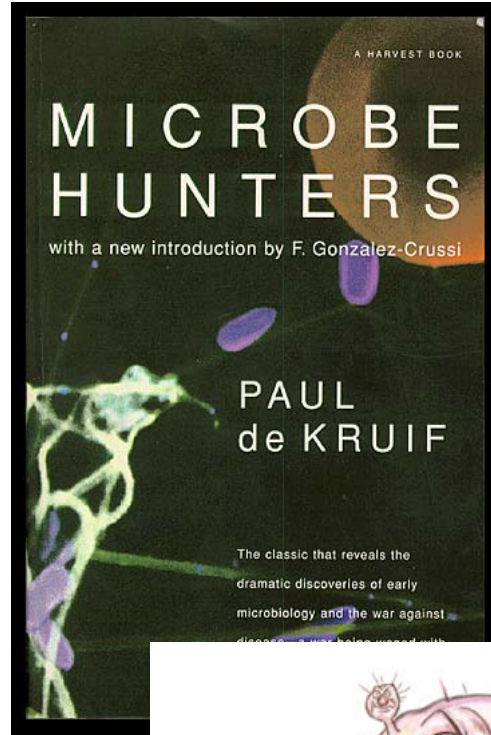


Illustration: Don Smith



PETE MOORE BSC, PHD  
**THE NEW KILLER  
GERMS**

AVIAN FLU • MRSA • SARS • ANTHRAX • EBOLA  
LEGIONNAIRE'S DISEASE • MONKEY POX  
NEW-VARIANT CJD



**WHAT YOU NEED TO KNOW ABOUT DEADLY  
DISEASES OF THE TWENTY-FIRST CENTURY**



## Positive View of Microbes



# ELSI



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“Privacy” or “confidentiality”



# Privacy

- Shared HMP samples include microbiome DNA & human DNA
- Individuals might have unique metagenomic genotypes  
Schloissnig S. et al. Genomic variation landscape of the human gut microbiome. *Nature*. 2013 Jan 3;493(7430):45–50. doi: 10.1038/nature11711. Epub 2012 Dec 5.
- 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.

# ELSI -- Property:

- 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:

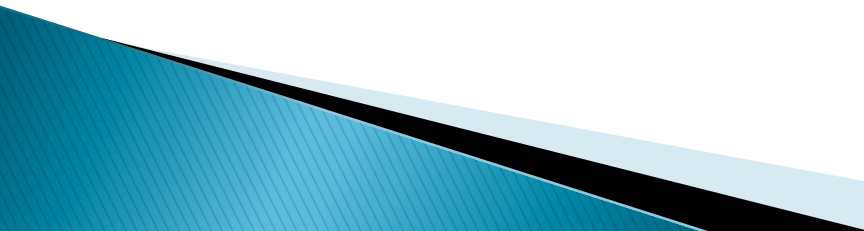
- Property law is a dynamic patchwork
- Laws and policies related to the microbiome should be designed to:
  - Avoid harm to individuals
  - Promote the social good
  - Avoid undermining important social projects



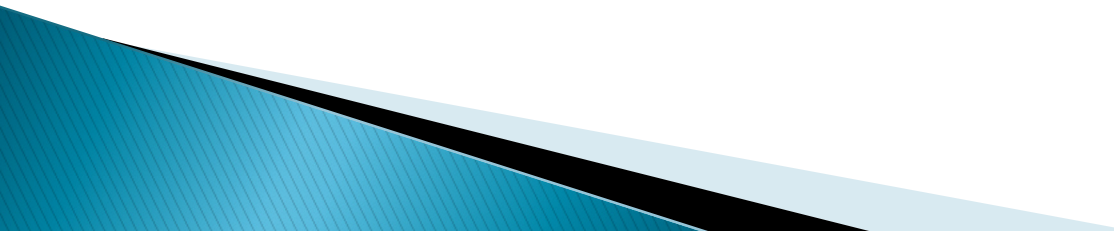
# Controversial Genetics Property Cases

- ▶ 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)
- 

# (1) 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?
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# ELSI Biobanks



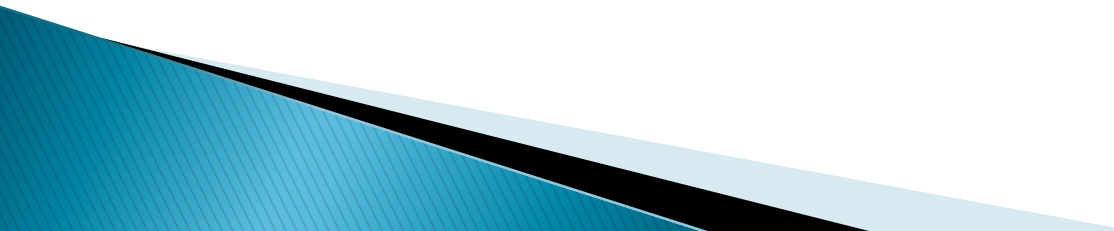
- ▶ Advances in Personalized Medicine require widespread participation in biobanks
- ▶ Knowledge gained from microbiome studies will be broadly applicable
- ▶ Once samples are collected, biobank research will pose only negligible physical risks

# 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.



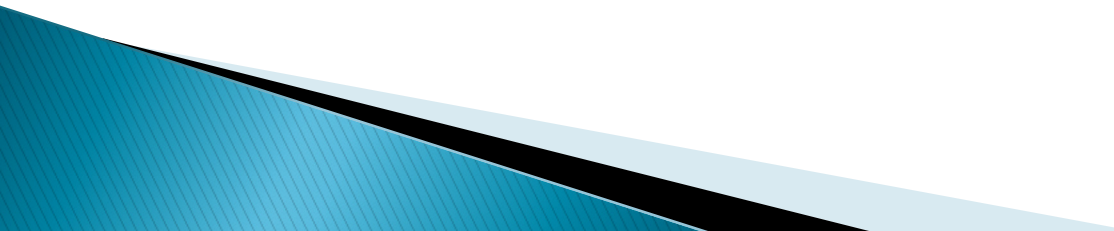
## (2) To develop our understanding of disease processes (observational)

- ▶ 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.
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### (3) investigations of the effectiveness of probiotics, phages, and lysins (clinical trials)

- ▶ Research on the effectiveness of probiotics will resemble:
  - Research involving infectious disease
  - Resemble drug development research


# ELSI: Microbiome Research

- ▶ Not all studies require the same level of oversight.
  - ▶ Different rules may be appropriate for different kinds of research.
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# ELSI: Biobank Studies & Informed Consent

- 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.
    - Rhodes R. et al., *De Minimis Risk: A Proposal for a New Category of Research Risk. American Journal of Bioethics*. 2011; 11(11): 1–7.

## ELSI -- Public Health & Privacy Protections

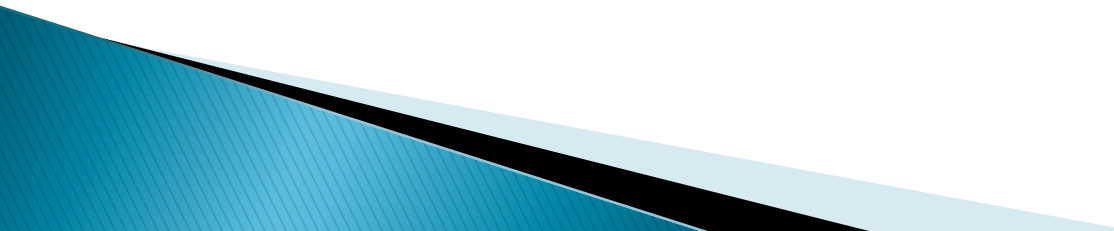
- ▶ Surveillance and tracking are public health tools
  - ▶ Public health measures, quality assurance (QA) and quality improvement (QI) efforts involve data collection
  - ▶ Gathering needed personal information may infringe upon privacy
  - ▶ The social good provided by such studies can justify small infringements on privacy.
- 

# ELSI -- Public Health

- 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



## ELSI -- Public Health & Privacy Protections

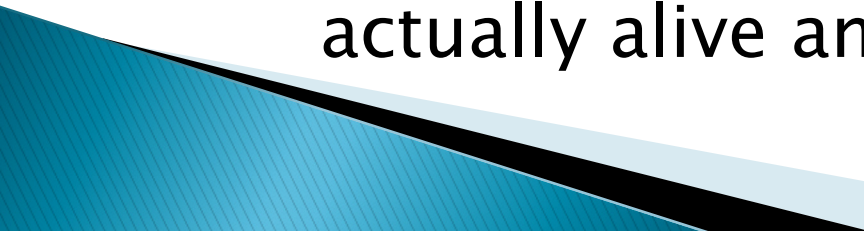
- ▶ Biobank studies, public health, QA, and QI already employ significant confidentiality protections
  - ▶ NIH Certificates of Confidentiality provide inadequate protection
  - ▶ A legally sanctioned mechanism that extends medical confidentiality protections to biobank, public health, QA and QI studies should be established
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# 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
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# Probiotics and Prebiotics

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

## Bacteriophage Therapy for Patients Across the Globe

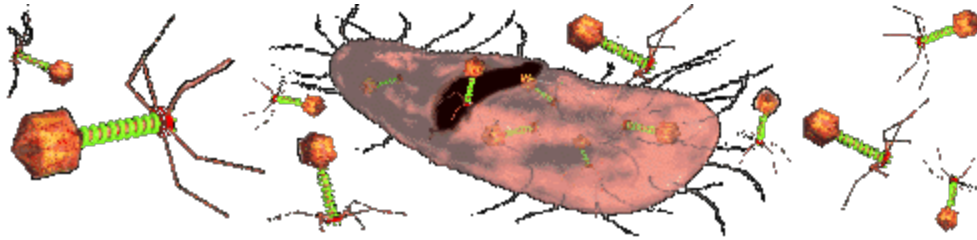
- Phage Therapy Center, Tbilisi Georgia is now accepting patients with chronic, difficult, antibiotic-resistant bacterial infections that do not respond to conventional antibiotic therapies.



- [http://www.phagetherapycenter.com/pii/PatientServlet?command=static\\_home](http://www.phagetherapycenter.com/pii/PatientServlet?command=static_home)

# Probiotics, Phages, &

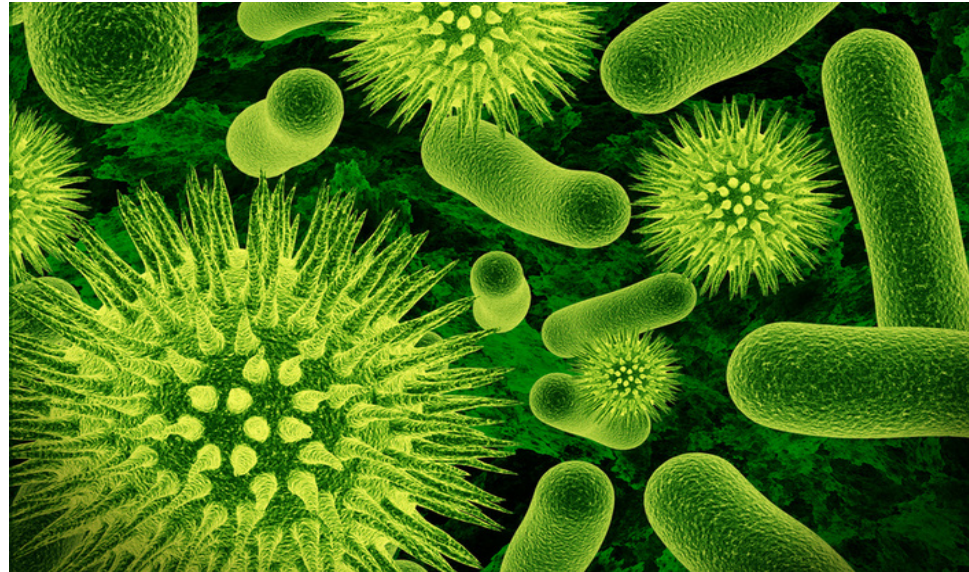
# Synthetic biology



- ▶ **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

Jody Azzouni, PhD, **philosophy**  
Mary Ann Baily, PhD, **economics**  
Stefan Baumrin, PhD, JD, **philosophy, law**  
Keith Benkov, MD, **pediatric gastroenterology**  
Martin Blaser, MD, **microbiology**  
Barbara Brenner, Dr PH, MSW, **sociology**  
Joseph Dauben, PhD, **history**  
Bill Earle, PhD, **philosophy**  
Lily Frank, ABD, **philosophy**  
Nada Gligorov, PhD , **philosophy**  
Joseph Goldfarb, PhD, **pharmacology**  
Kurt Hirschhorn, MD, **genetics**  
Rochelle Hirschhorn, MD, **genetics**

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Debbie Indyk, PhD, **sociology**  
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Daniel Moros, MD, **neurology**  
Sean Philpott, PhD, MSB, **microbiology**  
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Rosamond Rhodes, PhD, **philosophy**  
Lynne Richardson, MD, **emergency medicine**  
Henry Sacks, PhD, MD, **preventive medicine**  
Abraham Schwab, PhD, **philosophy**  
Rhoda Sperling, MD, **gynecology**  
Brett Trusko, MBA, PhD, **business, informatics**  
Arnulf Zweig, PhD, **philosophy**

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