GENOMES TO GLOBAL HEALTH: THE COMPUTATIONAL BIOLOGY OF INFECTIOUS DISEASE A SAMSI Program for Academic Year 2004-2005.

- Principal Organizer: Thomas B. Kepler, Departments of Biostatistics & Bioinformatics and Immunology, Duke University Medical Center
- Co-organizer: Denise Kirschner, Department of Microbiology and Immunology. University of Michigan
- Co-organizer: Lindsay Cowell, Department of Biostatistics & Bioinformatics, Duke University Medical Center

## Introduction

The eradication of naturally-occurring smallpox in 1980 marked the culmination of two centuries of work and stands as one of humankind's greatest achievements. This singular event, and the steady progress made leading up to it, contributed to an optimism that infectious disease would no longer be a threat to the industrialized world. The next year, a strange new illness appeared that would later become known as AIDS. Infectious disease remains a major cause of suffering and death among people in the developing world; globalization ensures that the developed world is only marginally safer. The emergence of HIV and SARS as novel viral agents, readily transported from rural and underdeveloped areas to the west, resulting in human and economic devastation in both regions underscores the seriousness of this concern. Some African countries such as Swaziland have adult HIV infection rates approaching 40%. The World Health Organization estimates economic cost of the SARS epidemic at about \$30 billion. The WHO further estimates that 3000 African children die each day from malaria. Drugs once effective against the infectious agent, Plasmodium falciparum no longer work. Similarly, tuberculosis, once a fearsome killer of children in the developed world, and then virtually eradicated, has made a stunning recovery; drug-resistant Mycobacterium tuberculosis is now a significant health concern in New York City as well as in Bombay.

The near-completion of the human genome project brings with it the promise of a more complete understanding of human disease, including infectious disease, but the path from the genome sequences of the human hosts and their microbial pathogens is exceedingly complex and will require significant contributions from the mathematical sciences for its elucidation.

The primary aims of this year of research and study are to identify those areas where mathematical innovation may have the greatest impact on the basic science and medicine of infectious disease, to progress materially toward major research efforts in these areas, to establish a greater sense of community among the researchers with skills and interests in these areas, and to contribute to the training of the next generation of mathematically literate biomedical researchers, originating in both the biological and the mathematical sciences.

We envision the program as consisting of three intertwining strands representing different scales of resolution: genomics & molecular biology, cellular dynamics & physiology, and

epidemiology & global health. Each of these strands represents a specific window onto the world; a major concern of ours will be to integrate the views revealed from these disparate perspectives, to explore novel multiscale approaches to the fundamental problems.

## Program Activities.

**Opening Workshop.** We will kick off the year's activities with the Opening Workshop, 19-22 September 2004. Tutorials covering basic material in immunology, microbiology, statistics and mathematical modeling will be on Sunday the 19<sup>th</sup>, with the research portion of the workshop running from Monday through Wednesday. We will feature talks by prominent researchers representing the three major strands mentioned above, and the major action item for the workshop participants is to define a set of topics around which to structure the ongoing activities of the working groups.

**Working groups.** Working groups will meet throughout the year, and will consist of local faculty members, postdocs, grad students and resident visiting scholars as well as short-term visitors. The focus topics of these working groups will be developed in the foundational workshop and refined over the course of each semester. Examples of such topics include influenza evolution, molecular evolution of mycobacterial pathogenicity, signaling in leukocytes, ecology of commensalisms and pathogenicity, vaccine design. individual-based models for epidemiology, global patterns of disease spread, etc.

**Visiting Scholars.** We are extremely fortunate to have Byron Goldstein, of Los Alamos National Laboratories joining us as the SAMSI University Fellow for this program. His expertise is in mathematical modeling of signal transduction in cells of the immune system, and he will be teaching a course on that topic during his residency in the Spring semester.

Other scholars with expertise in diverse topics in immunology, microbiology, epidemiology, mathematics, statistics and computational biology, will be joining us for periods of varying duration. Most will be invited, but we are soliciting applications as well.

**Graduate courses**. In addition to the course in mathematical models of signal transduction, we are developing and will offer a full-semester course in *Computational Immunology and Immunogenomics* with Tom Kepler and Lindsay Cowell in the fall semester and *Mathematical Epidemiology* with Alun Lloyd. The signal transduction course will be half-semester, with the other half devoted to *Microbial Genomics*.

**Postdoctoral fellows**. SAMSI will appoint two postdoctoral fellows for this program, both of whom will continue with research in the second year of their appointment at a related organization or laboratory, typically in the Triangle.

**Transitional workshop.** The formal program will draw to a close with a workshop during May 22-24, 2005. The primary aims of this workshop will be to disseminate the

results of the working groups over the course of the year and to strategize about preserving the momentum of built during the year, and preserving the community built in that time.

## Leadership

Tom Kepler, Primary organizer Denise Kirschner, co-organizer Lindsay Cowell, co-organizer.

## Local committee

Name	Discipline	Affiliation
Atchley, William	Genetics	NCSU
Elston, Tim	Applied Mathematics	UNC
Nobel, Andrew	Statistics and Operations Research	UNC
Schmidler, Scott	Statistics and Decision Sciences	Duke
Thorne, Jeff	Statistical Genetics	NCSU
Global committee		
Name	Discipline	Affiliation
Anderson, Roy	Theoretical Epidemiology	Imperial College, London
Antia, Rustom	Biology	Emory
Bergstrom, Carl	Biology	University of Washington Albert Einstein College of
Casadevall, Arturo Castillo-Chavez,	Microbiology and Immunology	Medicine
Carlos	Mathematical Biology	Arizona State University
Gupta, Sunetra	Mathematical Epidemiology	Oxford
Perelson, Alan	Theoretical Biology and Biophysics	Los Alamos
Tan, Man-Wah	Immunology	Stanford
Liu, Jun	Statistics	Harvard