



THE UNIVERSITY OF CHICAGO

MICRONEWS

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Microbiology—A New Year

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Dear Friends,

Fall Quarter 2005 is under way! One hallmark of the new quarter is the return of Microbiology faculty to teaching duties. As you can imagine, preparation for instruction begins much before the classes start in September. This year's preparations were influenced by the Pritzker Initiative – a University of Chicago Pritzker Medical School effort in self study and curriculum reform. It's impossible to list all circumstances triggering the Pritzker Initiative. Certainly, we received valuable comments from extramural referees during the LCME review, the accreditation process of the American Association of Medical Colleges. Such comments provide food for thought and liberate much needed energy for reform. I applaud the BSD Dean for Medical Education, Dr. Holly Humphrey, for boundless energy, enthusiasm and launching of this effort. Colleagues in BSD Departments and of course colleagues in the Department of Microbiology are looking both inside and out. What are our achievements in medical school instruction? What do other institutions teach? Where are the educational frontiers, challenges and

opportunities in our fields? For me, this seems a great opportunity to explain our navigation of Medical Microbiology education.

Looking out, is it at all important to teach medical students microbiology and infectious diseases? The toughest of all questions for those working in the field of Microbiology was not always answered "yes." Many medical schools abolished wet laboratories for Medical Microbiology and chiseled away, reduced or even dissolved what is commonly appreciated as the classic medical microbiology course (systematic review of microbes, their infectious diseases, diagnosis, therapies and preventions). Affected Departments of Microbiology and their faculty are now pursuing other educational frontiers. In abandoned arenas arrive instructors without research expertise in host-pathogen interactions, such as clinical infectious disease specialists, pathologists or physiologists. This results in a rudimentary discourse of microbes and infectious diseases or even invitation for medical student "self study."

Origins of such development can reside in curricular reform. There are two extremes. Students are either taught the hu-

man body plan and its bodily dysfunctions as a sequence of organ systems or they are instructed that human organisms are the sum of physiologically connected systems with biochemical or molecular basis. In reviewing the former, learning anatomy is much like the study of geography – limbs, organs, the great circulation, all a network of roads and rails with stops for function. What great relief for medical students and physicians that many diseases respect boundaries (heart failure occurs in the heart, cancers originate in organs, pneumonia is an infection of the lung). The comfort and diagnostic security generating anatomical view allows physicians to leaf through volumes of organ-based disease symptoms searching for tables with clues on how to derive diagnosis. In maintaining this status quo, isn't it perfectly obvious that the entire medical school curriculum, including microbiology and infectious diseases, must be taught in an organ based schedule? A resounding "yes" rings in my ears, whether I talk with medical students, pathologists, surgeons or medical experts in the dozen or so organ-based disciplines that make up the Department of Medicine.

**Alumni: Where are you?
What have you been doing?
Please send us an update
and we will include it in
future newsletters.**

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Glenn Randall, Ph.D.



Pictured left to right: Andrew Fischer, Glenn Randall, and Jake Cooper

The first of three new faculty members in the Department of Microbiology to arrive this year, Glenn Randall, Ph.D., received his B.S. with distinction in Microbiology from the University of Illinois, Urbana-Champaign. After an internship at Abbott Laboratories, he

pursued graduate studies at the University of Chicago in the laboratory of Bernard Roizman. His doctoral thesis describes mechanisms by which herpes simplex virus I establishes a latent infection. He then joined the Laboratory of Virology and Infectious Disease at Rockefeller University in New York. His American Cancer Society post-doctoral fellowship was under the mentorship of Charles Rice. His research focused on hepatitis C virus (HCV)-host interactions with an emphasis on the interaction between HCV and cellular RNA interference (RNAi) pathways. He joined the Department of Microbiology at the University

of Chicago in August of 2005.

Glenn's research investigates the roles of hepatitis C virus (HCV)-host interactions in viral replication and pathogenesis. He has applied RNAi interference as a genetic approach to identify host genes required for HCV infection. These genes are likely to regulate diverse steps of the viral life cycle, including entry, viral translation, protein processing, replication, assembly, and egress of virus. Additionally, numerous genes involved in cellular stress response pathways were found to regulate

HCV replication. His laboratory is currently exploring the function and roles of a subset of these host genes in viral replication.

Glenn is building his laboratory and program on the 7th floor of Cummings Life Science Center. Jacob Cooper and Andrew Fischer, Research Technicians, are assisting Glenn in this task. We welcome Glenn, Jake, and Andy and look forward to new scientific discoveries from this excellent lab.

Microbiology—A New Year (continued)

Some schools broke new ground with a curriculum of systems-based learning, series of self-contained yet interacting pathways involving genetics, cell biology, pharmacology and microbiology - immunology. These pathways do eventually involve anatomy and pathology, yet they also intended to provide glue and function beyond the rigors of anatomical boundary. There is some evidence to suggest that present day medical students still prefer anatomical analysis over systems biology approaches.

Why are Medical Schools still so determined to impregnate the brains of medical students with pathological-anatomy? An answer seems easy - in medicine one views instructional value as the student's ability to arrive at the correct diagnosis. Pathological-anatomy is the current yard stick of diagnosis, both pre- and post-mortem. Other diagnostic tools, including chemical, physical and microscopic tests follow this paradigm. Even microbiological diagnosis is conducted by Pathology Departments and,

although *strictu sensu* not organ-based, microbes have been ruled under the same yoke.

Such views were first challenged with the demonstration that microbes represent disease causing entities. The shocking revelation was that microbes infect healthy hosts, do not respect organ boundaries, do not always cause the same symptoms, bring rapidly fatal or chronic illnesses, and can spread vertically or horizontally through populations, afflicting single or multiple species, mammals, plants, even insects. For some time such findings triggered a medical revolution, generated appreciation for an ever-increasing load of infectious agents and their disease causing entities. Microbiologists provided simultaneously diagnostic tools and preventions that transformed the threat of infectious diseases, the way we teach it, and the way microbiology was perceived. Eventually, microbiologists provided cures and, with powerful antibiotics in hand, medicine could return to pathological-anatomical diagnosis and organ-based teaching. The underlying mantra is "one doesn't have to

make a microbiological diagnosis as long as one can treat the infection."

In 1967, United States Surgeon General William H. Stewart concluded that "we could close the book on infectious disease." Many agreed. There have been regrets, as the AIDS pandemic single-handedly changed the way we think about infectious diseases. Those who have not yet appreciated the re-emergence of infectious diseases are invited to learn microbiology and infectious diseases in the University of Chicago Medical Microbiology course (MTWRF 8:30-9:20 AM, BSLC115).

As University of Chicago faculty engage in debate over their curriculum, many of you will also grapple with educational reform. We would love to hear your experience, views and recommendations. Please visit the Department of Microbiology website to look at the syllabus of our Medical Microbiology course. I am sorry to say that we cannot post

lecture notes and class material for general web access. However, we can answer e-mail queries about our lectures. The Department of Microbiology teaches a total of 50 class room lectures and 40 hours of wet laboratory instruction on microbial diseases. Two readers are distributed to each student one on Bacterial Diseases and one on Viral, Parasitic & Fungal Diseases with a total of 1,000 printed pages and 1,000 color images. Eight full time faculty and four teaching assistants engage 105 second year medical students for one quarter. Testing includes one midterm and one final exam as well as seven unknown samples for wet laboratory diagnosis.

Medical Schools cannot teach Microbiology history but must focus on frontiers. Microbiology frontiers are now much more clear than thirty years ago - cures for infectious diseases such as AIDS, malaria, tuberculosis, flu or drug-resistant bacteria, prevention of an ever increasing load of

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infectious diseases and improved-diagnostics. On the way, Microbiology scientists will explore new diagnostic tools, analyzing host molecules as beacons for disease. Improved technologies in physical separation and detection, including capillary electrophoresis, nanofluidics and mass spectrometry will provide molecular and even anatomical resolution of host-pathogen interactions. Eventually, this will include real time diagnosis of disease and pathogen identification using molecular beacons of both. For me the question is not whether this technology will become available but rather when it will be achieved. I therefore feel

that we must prepare medical students for the navigation of such advanced diagnostics with information on the molecular basis of disease. Even today's students will be exposed to diagnostic changes. As the molecular biology revolution finally transforms medicine, I presume we will teach infectious disease causing processes as the complex interplay between microbial and host molecules. Therapeutic strategies will be reviewed as perturbations imposed by small

molecules that allow physicians to change the molecular equilibrium in the patient's favor. With this in mind, I cannot recommend that modern medical microbiology return to organ-based teaching. In my mind this would represent a bankruptcy statement on the same scale as "infectious diseases are conquered." Medical Microbiology courses now offer the unique opportunity of driving student appreciation for the molecular basis of disease, of engaging frontiers of pathogen-based

and host response-based learning. Our challenge is also that Microbiology represents the most advanced field in examining the molecular basis of disease. Microbiologists should not stand on the sidelines of organ-based learning. Isn't it time we lead the way to Medical School curricular reform?

Yours sincerely,
Olaf Schneewind

Entering Class of 2005

Graduate students pictured left to right
Top row: Laure Case, Todd Oakland, and Cameron MacDearmid
Bottom Row: Kelly Riordan and Yvonne Chan



Laure Case	Yvonne Chan	Cameron MacDearmid	Todd Oakland	Kelly Riordan
Hometown: Reading, PA	Hometown: Waipahu, HI	Hometown: Newcastle, Maine	Hometown: Sycamore, IL	Hometown: Middletown, MD
Degree: B.S., Lehigh University	Degree: B.A., University of Pennsylvania	Degree: B.A., Swarthmore College	Degree: B.S., Purdue University	Degree: B.S., University of Maryland, College Park
Research/Interests: A mainline defense against viral infections involves humoral immune responses, including the production of antiviral antibodies. Retroviruses, however, are generally able to escape humoral immune responses because of their rapid mutation rate, leading to the selection of immune escape variants. Interestingly, the retrovirus-resistant I/LnJ mouse strain produces antiviral antibodies throughout their lifetime. We are currently investigating the cellular, molecular and genetic mechanisms that allow I/LnJ mice to produce virus-neutralizing antibodies resulting in resistance to retroviral infection.	Research/Interests: I am interested in bacteria and host/pathogen interactions. I used to study the Type IV secretion system in the context of DNA conjugal transfer in E. Coli and Agrobacterium tumefaciens. My current rotation concerns the study of toxin secretion in Anthrax, looking at the lipoproteins hypothesized in playing a role in the process. My winter rotation will look at the sufficiency of a particular host surface molecule in Rickettsia attachment and invasion.	Research/Interests: I am currently studying mouse mammary tumor virus (MMTV), a well-characterized retrovirus that causes tumors in susceptible mice, to investigate virus-host interactions. The YBR/Ei mouse strain demonstrates a novel mode of resistance to MMTV that is controlled by a single gene. I aim to identify the gene and mechanism that control MMTV resistance in the YBR/Ei mouse strain. Studying virus-host interactions is critical not only for understanding the genetics of resistance to retroviral infection, but also for learning basic biological processes.	Research/Interests: I'm interested in virus-host interactions, as well as other aspects of virology, like replication and assembly. How something as minimal as a virus is capable of making such profound changes to a host has always fascinated me. As an undergrad, I worked on the generation of a stable cell-line constitutively expressing flavivirus sub viral particles. Currently, I am rotating with Dr. Schneewind. I am working with beta-lactam antibiotic resistant <i>Staphylococcus Aureus</i> in an attempt to find a bacterial chromosome localized gene responsible for conferring resistance.	Research/Interests: I am studying the type III secretion system in <i>Yersinia enterocolitica</i> . <i>Yersinia</i> , as well as other pathogenic gram negative bacteria, use this needle-like system to inject proteins into the extracellular milieu as well as the host cell cytoplasm. I am interested in the soluble factors that regulate YscN, an AAA-ATPase that may function in chaperone release and unfolding of effector proteins. It is our hope that, by understanding how substrates get recruited to the secretion complex and how this complex is regulated, we will gain insights into the complexities of type III secretion and how this relates to host pathogenesis.



THE UNIVERSITY OF CHICAGO

**COMMITTEE ON MICROBIOLOGY
DEPARTMENT OF MICROBIOLOGY**

The Howard T. Ricketts Symposium on Microbiology

"Bistable switches and cannibalism in bacteria"

Richard Losick, Ph.D.

Harvard College Professor and Maria Coors Cabot Professor of Biology,
Department of Molecular and Cellular Biology
Harvard University

**"Tailed bacteriophages: how they assemble, how they package their
dsDNA genome into their proheads and how they infect their hosts"**

Michael Rossmann, Ph.D.

Hanley Distinguished Professor of Biological Sciences,
Department of Biological Sciences
Purdue University

**"The assembly of surface proteins in the envelope of gram positive
bacteria"**

Olaf Schneewind, M.D., Ph.D.

Professor and Chair,
Department of Microbiology
The University of Chicago

Thursday, December 15, 2005

1:00p.m.-5:00p.m.

The Biological Sciences Learning Center

Room 115

924 East 57th Street