

## Uproar Lasts Long after Pittsburgh VA Destroyed Pathogen Collection

Administrators at the Veterans Affairs (VA) Pittsburgh Healthcare System (VAPHS) in Pittsburgh, Pa., arranged for an estimated 8,000 specimens in the VAPHS Special Pathogens Laboratory to be destroyed abruptly in December 2006 — giving rise to acrimony and recriminations that are yet to subside. The collection, developed by microbiologists Victor Yu, Janet Stout, and their collaborators, consisted mainly of *Legionella* and other pneumonia-causing bacterial pathogens, many of them resistant to antibiotics. An outside group of microbiologists and infectious disease experts earlier this year described the destruction of that collection as “an affront to science and scientific study.”

Clamor over loss of the collection struck a chord with several members of Congress, particularly Rep. Brad Miller (D-NC), who chairs the Investigation and Oversight subcommittee of the House of Representatives Committee on Science and Technology. Miller not only convened a hearing, “Biobanking: How the Lack of a Coherent Policy Allowed the Veterans Administration to Destroy an Irreplaceable Collection of *Legionella* Samples,” last September, he also had his staff investigate the matter and has pledged to introduce legislation that will safeguard other such collections. Full testimony from the hearing is available at <http://www.legionella.org/vaspl.asp>.

It is an understatement that there are profound disagreements between Yu, Stout, and their immediate collaborators on one side and VA administrators on the other.

“Initially, I was not concerned about the transfer of the collection from the VA,” Stout testified. With the Special Laboratory closed, she and Yu were working at the University of

## Nobel Prizes and Special Lasker Award 2008

Several of the 2008 Nobel Prizes touch either specifically or indirectly on microbiology, while the 2008 Lasker Special Achievement Award in Medical Science went to a microbiologist:

- The Nobel Prize in Medicine or Physiology is shared by Harald zur Hausen, of the German Cancer Research Centre, Heidelberg, Germany; Françoise Barré-Sinoussi of Institut Pasteur, Paris, France; and Luc Montagnier of University of Paris and Director, World Foundation for AIDS Research and Prevention, both in Paris, France. Among his efforts, zur Hausen determined that the human papilloma virus (HPV) causes cervical cancer, the second most common cancer among women. Barré-Sinoussi and Montagnier are recognized for discovering the human immunodeficiency virus (HIV). More information can be found online at [http://nobelprize.org/nobel\\_prizes/medicine/laureates/2008/](http://nobelprize.org/nobel_prizes/medicine/laureates/2008/)
- The Nobel Prize in Chemistry is being shared by Osamu Shimomura at the Marine Biological Laboratory (MBL), Woods Hole, Mass., and Boston University Medical School, Mass.; Martin Chalfie of Columbia University, New York, N.Y., and Roger Y. Tsien at the University of California, San Diego, La Jolla, Calif. Shimomura isolated the green fluorescence protein (GFP) from the jellyfish *Aequorea victoria*, while Chalfie first used GFP as a visual tag for analyzing various biological phenomena, and Tsien contributed toward understanding how GFP fluoresces and also extended its palette beyond green, enabling other researchers to tag proteins and cells with different colors. More information can be found online at [http://nobelprize.org/nobel\\_prizes/chemistry/laureates/2008/](http://nobelprize.org/nobel_prizes/chemistry/laureates/2008/)
- The Lasker Special Achievement Award went to Stanley Falkow of Stanford University in Stanford, Calif., for many achievements, including his development of our understanding pathogenesis, new molecular tools for studying it, and his role in founding the discipline of molecular epidemiology. More information can be found online at <http://www.laskerfoundation.org/awards/2008special.htm>

Pittsburgh, where they planned to transfer their collection. “I knew that other VA investigators had left the VA and taken their collections of specimens with them,” she says. Further, several VA administrators assured her that they would “facilitate” that planned transfer. The 8,000 specimens collected between 1979 and 2006 included strains of *Legionella*, staphylococci, *Pseudomonas*, *Klebsiella*, enterococci, streptococci, and *Candida*.

Despite those assurances, however, the collection was not saved. “The attack and destruction of our work is justified with bureaucratic jargon,” Yu says. “Nowhere in the testimony of the VA bureaucrats was there any regret or compunction of the gravity of their offense. In contrast, the Congressmen were easily able to comprehend the fact that the public and the scientists themselves were egregiously harmed.”

The subcommittee report recom-



## Combining Antibiotics Enhances Activities, Raises Questions

Three antibiotics—myxopyronin, coralopyronin, and ripostatin—inhibit bacterial RNA polymerase (RNAP) through interactions with the RNAP “switch region,” a hinge-like structure that opens and closes around the active-center of this enzyme, according to Richard Ebright and Eddy Arnold of Rutgers University in New Brunswick, N.J., and their collaborators. Together these three antimicrobial agents potently inhibit both gram-positive and -negative bacterial growth, while showing no cross-resistance with other antibacterial agents. Further, by targeting RNAP, this trio of compounds can effectively target both growing and dormant pathogens, including *Mycobacterium tuberculosis*. Another plus is that they bind to the hinge region of that key enzyme, a site that is distant from where other antibiotics, notably rifamycin which is used in treating tuberculosis, bind this molecule. Details appear in the October 17 issue of *Cell*.

mends that the President’s Office of Science and Technology Policy “develop a focused policy for biospecimen collection management” and asserts that “Biobanking cannot succeed if its basic policy structure is honored more in the breach than in the observance.”

While destroying the collection irreparably damaged the careers of these microbiologists, Stout and Yu draw specific lessons from their experience that could prove instructive for other microbiologists when called on to protect similarly valuable collections. In other words, some simple steps could help in protecting important biological materials, according to Stout. Thus, she recommends that microbiologists and other researchers (i) keep duplicates of all research, including records from institutional review boards (IRBs) and other research and development (R&D) files; (ii) become familiar with and adhere to rules governing IRBs and with other R&D practices because, even if they are not being strictly observed, they may be invoked later; (iii) check consent forms to ensure that they cover future uses of retained specimens; and (iv)

make sure commitments from administrators are in writing, and pester for such assurances whenever necessary.

### Jeffrey L. Fox

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## How Infection Status Affects Subsequent Infections and Immune Responses

Chronic underlying infections sometimes modulate host responses to superimposed and acute, albeit self-limiting, bacterial infections, according to David Schauer of Massachusetts Institute of Technology (MIT), Cambridge, Mass., and his collaborators, whose report appears in the November *Infection and Immunity* (76: 4851–4858). Their research “is the first to study the interaction between a chronic bacterial infection and a superimposed acute bacterial infection,” says Vincent Young of the University of Michigan (UM), Ann Arbor, who did not collaborate in the MIT-led re-

search. That research thus “supports the hypothesis that prior exposure to one pathogen may influence the clinical course due to” another.

As part of the study, Schauer and his collaborators exposed mice to *Helicobacter hepaticus*, which colonizes the gut but causes no clinical symptoms. About two months later, the researchers exposed those mice to *Citrobacter rodentium*, which infects mice and causes symptoms such as diarrhea similar to those caused by enteropathogenic *Escherichia coli* in humans.

Typically, such infections—in mice and humans—are self-limiting. However, in these experiments with mice, the initial subclinical infection with *H. hepaticus* not only lengthened the course of the subsequent *C. rodentium* infection, but it also altered the host immune response by suppressing expression of interferon- $\gamma$  and boosting expression of interleukin-17. Altogether, these changes led the mice to develop colitis. These findings suggest that “an individual’s infection status . . . is important in determining the outcome of infection, immune-mediated disease, or even immunization,” Schauer says.

The germ of this research was the hygiene hypothesis, Schauer continues. It holds that childhood exposure to unclean conditions harboring various microorganisms and parasites “can lead to immune responses that influence outcomes of infectious and immune-mediated diseases,” he says. “We wanted to provide proof of principle and begin to define the mechanism for such interactions.” They chose *H. hepaticus* because it behaves much like *H. pylori* in humans, giving rise mainly to subclinical infections in situations where hygiene practices are suboptimal.

In more general terms, the multiply infected mice “reflect a more realistic situation for what humanity faces in terms of the body’s constant fight