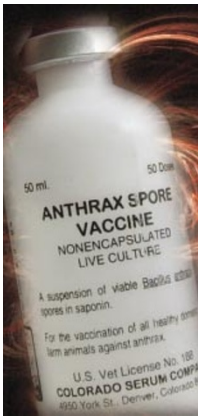


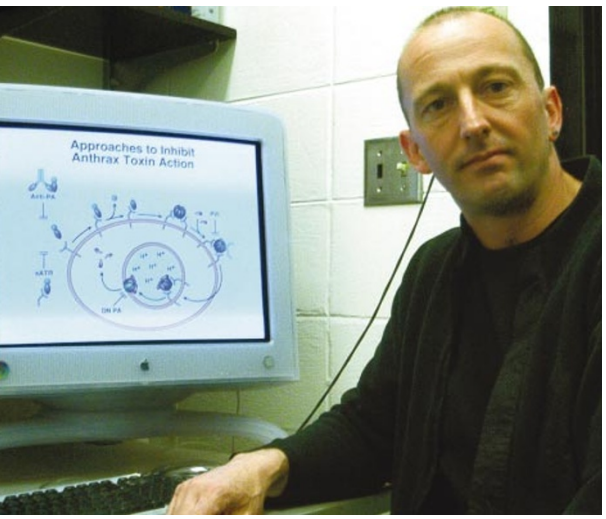
Funding increases for biodefence research in the United States will have a sizable impact on the landscape for jobs, says Eugene Russo.

John Young's colleagues used to wonder why he worked on anthrax. "It was an intellectual curiosity, really, that drove the project," says Young, a professor of cancer research at the University of Wisconsin, Madison. Since the events of last autumn, Young's intellectual pursuits have acquired national security implications.

In 1999, Young, who originally trained as a retrovirologist, began investigating anthrax toxin receptors. He was attracted to the project in part because anthrax toxin and the avian retrovirus he had been studying use similar mechanisms for cell entry.

Driven by the joint interests of graduate student Ken Bradley in the Young lab and of postdoc Jeremy Mogridge in John Collier's lab at Harvard Medical School, the high-risk project went forward with limited resources. But it would pay big dividends. Last November, the group reported the first cloning of an anthrax toxin receptor (K. A. Bradley *et al. Nature* **414,** 225–229; 2001). The team submitted the paper to *Nature* just a few days before the first anthrax cases were reported in the United States. Since then, Young has devoted more time to anthrax and now collaborates with scientists from several fields.

Young's story may not be typical, but it exemplifies one way in which biodefence concerns have already affected research. The impact will intensify with the massive increase planned in federal US funding.



John Young: curiosity about anthrax proved to be timely.

Support for basic research in biodefence through the National Institute of Allergy and Infectious Diseases (NIAID) is slated to increase by $1.5 billion in fiscal year 2003, in addition to the $270 million already budgeted. The boost is part of a proposed $4.5-billion funding increase for general biodefence spending in 2003, up 319% from 2002.

The NIAID's funding boost is likely to affect the research landscape for microbiologists, cell biologists, virologists and chemists. Indeed, some of these specialists have even begun to band together into 'biodefence interest groups' to share expertise and jointly apply for funding. Anthony Fauci, the NIAID's director, who has heard from a few such groups, is enthusiastic about the prospect of funding them because, he says, their multidisciplinarity increases their chances of success.

BROAD-BASED STRATEGY

The anthrax attacks of last autumn, although tragic, had a relatively minor public-health impact. How can the planned huge funding boost be justified, especially if further attacks do not materialize in the near future?

There is one obvious answer: the need to be prepared. The other, according to Fauci, is the need not only to bolster biodefence but to improve scientists' understanding of both the immune system and the pathogenesis of infectious diseases in general. "We want to include bioterrorism in the big umbrella of emerging and re-emerging infections," says Fauci.

Research targets will go well beyond the designated 'category A' bioterrorist agents such as anthrax, botulism, plague and smallpox. Although these have been the focus of media attention, Fauci emphasizes the importance of bolstering manpower and infrastructure, and fostering general study of host-defence interactions, immunotherapy and adaptive immunity. Work on diagnostics, therapeutics and vaccines is also likely to have broader applications.

"The idea is to design a platform technology for application against any pathogen," says Adel Mahmoud, head of vaccine research at drug firm Merck. The company is collaborating with the NIAID on the development of an HIV vaccine.

The biodefence research agenda, in fact, has several similarities with the research onslaught that resulted from the HIV epidemic in the 1980s. Fauci believes that that mammoth task will provide lessons for this one. As with the HIV/AIDS research strategy, he foresees extensive collaborations with industrial partners, partly solicited through challenge grants for bioterrorism-related research projects.

Over the next few years the NIAID will also establish 6–10 centres of excellence in emerging diseases and biodefence at universities and institutes. The first of these will be funded from the 2003 budget.

AP

On the hunt: the US is ploughing millions of dollars into the search for countermeasures to biological warfare.

The centres will have biosafety level 3 and level 4 handling facilities to contain the most dangerous pathogens, facilities that are currently in short supply. As with many of the anti-bioterrorism grant proposals, the NIAID will use an accelerated form of peer review to decide which centres to fund.

As with the HIV/AIDS research programme, the NIAID's funding strategy will ideally be broad enough from the start to attract established immunologists and infectious-disease specialists. "It's going to be a combination of programmatic direction, together with *de novo*, investigator-initiated projects," says Fauci.

Dennis Kasper, a Harvard Medical School professor of microbiology and molecular genetics, suggests that attracting top people to HIV research took some time. He hopes that this time more top scientists will get involved sooner. "You've got to have a way to attract the top-level scientists into the field," he says.

INFECTIOUS ENTHUSIASM

Fauci hopes not only to encourage infectious-disease investigators to make their work more relevant to biodefence, but also to help to train young students and postdocs with a "substantial recruitment and training effort". Early signs indicate that students may have already started to respond.

Applications to graduate biology programmes at major universities have increased 15% this year according to Kasper, an executive dean for academic programmes at Harvard Medical School. Kasper attributes the increase to a sagging computer-sciences job market and a general renewed interest in biology since bioterrorism hit the news. "Whether that will translate into more graduate students in microbiology, I hope so, but I don't know," he says.

Senior scientists are already showing interest in biodefence-related basic research. Young recently visited oncovirologist Peter Vogt at the Scripps Research Institute in San Diego, California. To Young's surprise, Vogt announced that he had started working on anthrax toxins. "That's all he wanted to talk about," recalls Young.

Since late last year, Vogt has been participating in a biodefence interest group studying several bioterrorism agents. For years, Vogt has collaborated with Scripps chemists to develop high-throughput tests for specific cancer targets. It was only a small step from the search for small molecules that inhibit biologically active compounds to the search for molecules that might inhibit bacterial toxins.

Last year, Vogt's collaborator Barry Sharpless, Scripps chemist and Nobel laureate, found a very potent enzyme inhibitor in the context of their cancer research. But they recognized its potential for more widespread use. "We started thinking about toxins before 11 September," says Vogt. But after that date, "the obvious candidate immediately became anthrax".

Vogt has become fascinated by specific actions of the toxin and is surprised by the small number of experts studying these actions. He contends that this is much more than derivative applied work. "These are fantastically interesting scientific questions that are really challenging," he says. ■

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NIAID counter-bioterrorism research agenda
www.niaid.nih.gov/dmid/pdf/biotresearchagenda.pdf
NIAID funding
www.niaid.nih.gov/dmid/bioterrorism

Genomics still holds the key

Already a hot area, genomics is to be a key component of the National Institutes of Health's anti-bioterrorism basic-research strategy. Although all the 'category A' agents, such as anthrax and smallpox, have been sequenced or targeted for sequencing, finding genetic differences between strains will be essential, says Claire Fraser, director of The Institute for Genomic Research (TIGR) in Rockville, Maryland.

"Having a single genome sequence for an important pathogen is probably not enough if you want to understand all of the variability you're going to find out there in nature," she says.

Last November, TIGR received $25 million from the National Institute of Allergy and Infectious Diseases (NIAID) to establish the Pathogen Functional Genomics Resource Center. Its aim is to determine the biological function of pathogen genes and their protein products. TIGR and its collaborators recently submitted a proposal to NIAID to work on several anthrax strains.

TIGR has not yet hired more researchers, but bioinformatics experts are constantly in demand for all sequencing-related projects. "Bioinformatics is one area where we've never been fully staffed," says Fraser. E.R.

Anthony Fauci sees a multidisciplinary approach as the key to success.