Deborah Dean, MD, MPH, a veteran infectious diseases researcher, focuses her career on understanding and fighting one deadly and widespread bacterium.

Chlamydia Warrior

WRITTEN AND PHOTOGRAPHED BY TOM LEVY

"We are mostly bacteria," said veteran Children's Hospital Oakland researcher Deborah Dean, MD, MPH, pointing out that 90 percent of the cells in the human body are non-human. "Our whole body is an ecosystem."

With that image in her mind, it's no wonder that after completing medical school—at the Albert Einstein College of Medicine in Bronx, N.Y., and residency at the University of California, San Francisco (UCSF)—Dr. Dean decided to do a postdoctoral fellowship in microbial pathogenesis at Stanford University as well as an Infectious Disease fellowship.

During her fellowship, Dr. Dean worked at Santa Clara County Hospital. "I saw stuff there you wouldn't see unless you were in a developing country," she said.

Dr. Dean also got invaluable clinical experience as an assistant professor and Infectious Disease attending at San Francisco General Hospital, a UCSF teaching hospital. It was the "fascinomas" she puzzled over at The General that finally led Dr. Dean to her chosen career. Not always knowing what was going on when a patient had an unknown infectious disease trained her to keep an open mind. "With infectious diseases you're like a detective," said Dr. Dean.

During a project in South India, she noticed how many people had eye problems. This led to Dr. Dean's decision to specialize in Chlamydia, an ocular and sexually transmitted disease (STD) that leads to more blindness and bacterial STDs around the world than any other cause.

The more she learned about Chlamydia, and the body's bacteria-laden ecosystem, the more she became convinced of something else, something revolutionary. Microorganisms, and even human cells, swap DNA all the time. They're more promiscuous than a rooster in a henhouse.

But because Chlamydia is not able to live outside the body, it wasn't thought this family of organisms participated in this DNA-swapping marathon. Dr. Dean's suggestion, as a younger researcher, that Chlamydia also have "mobile DNA," was thought heretical. Now the idea is becoming mainstream among other Chlamydia researchers.

"I firmly believe that some of the youngest people to enter a lab have some of the most novel ideas and they don't know it yet," said Dr. Dean. "They haven't been brainwashed in the field yet."

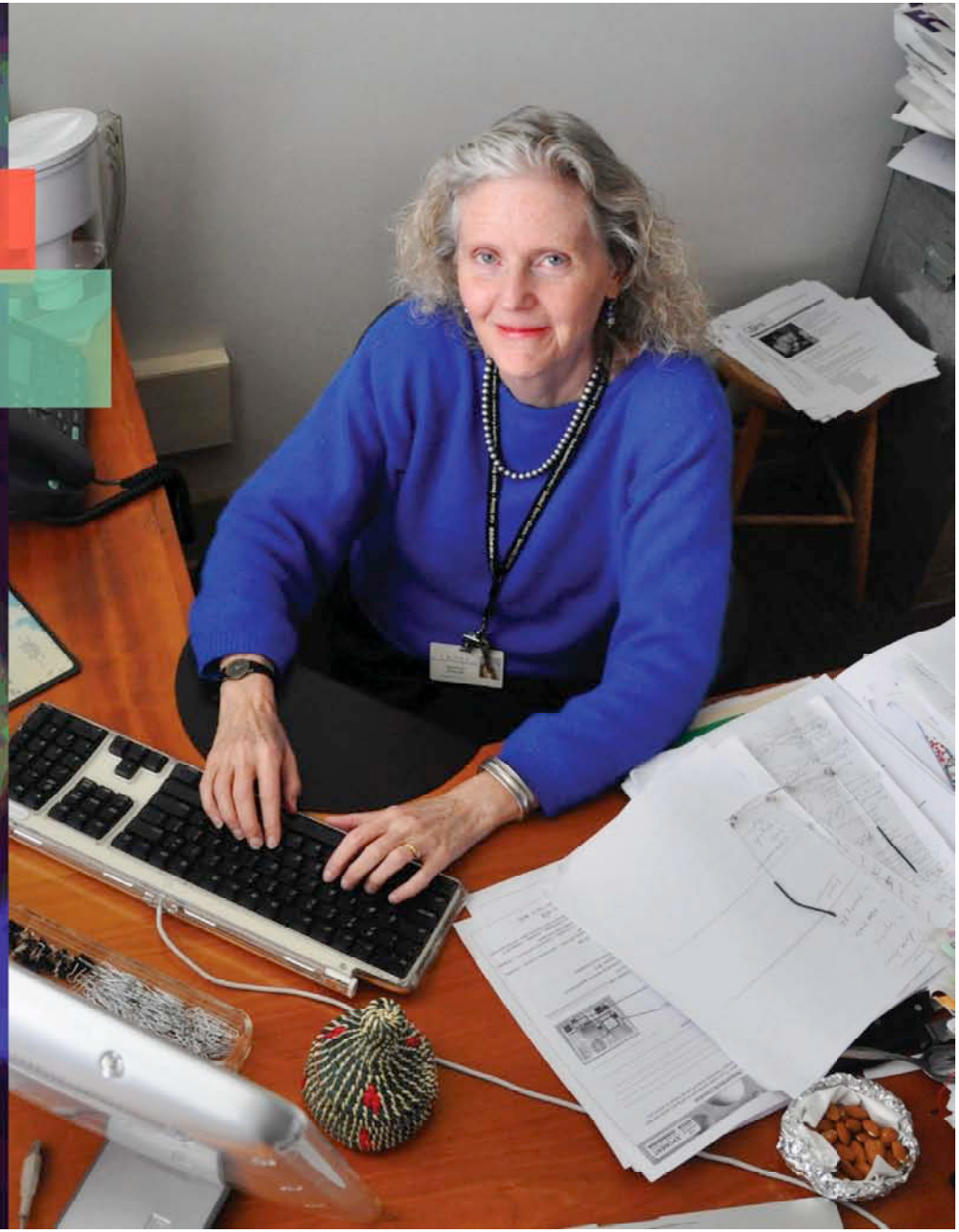
That's why, in addition to doing her work, Dr. Dean is always on the lookout for new postdocs and graduate students to bring in to her lab.

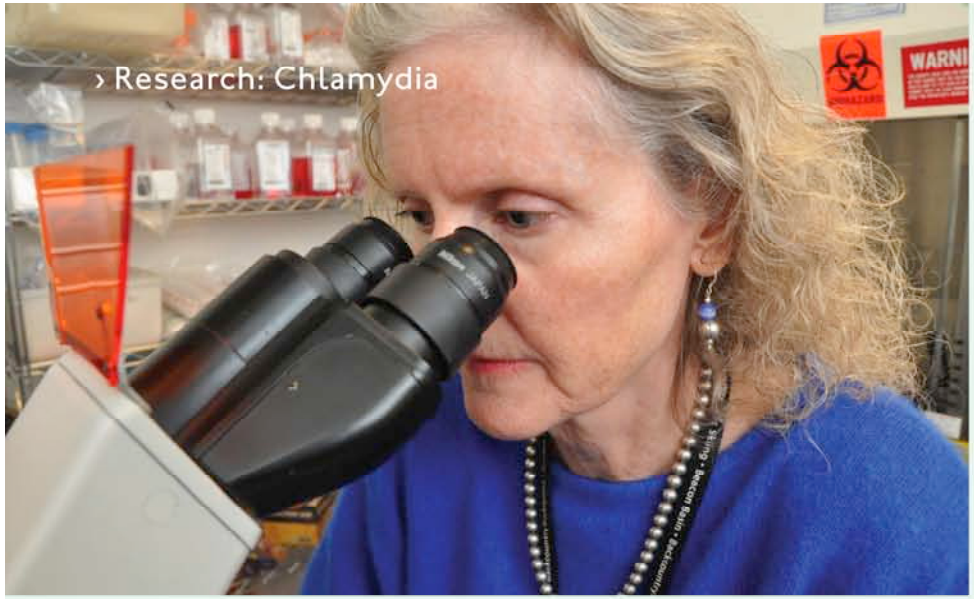
As the mother of 12-year-old fraternal twins, a boy and a girl, Dr. Dean also has young people at home to keep her on her toes. "I don't want to be a workaholic like you, Mom," said her daughter recently.

Dr. Dean chose to make this challenge a teachable moment. "There's a difference between being a workaholic and doing something you love," she replied.

And because she loves her work, in 1999 she moved her lab to Children's Hospital Oakland Research Institute. There, the strictures of doing research in an academic institution don't exist.

"I saw the potential for what could be done at Children's," she said. "There's so much going on that breaks a lot of boundaries. It's a jewel of a place in terms of being given the freedom to grow your own research program."





Focusing on the family tree

$1 million genomic study of Chlamydia strain that may jump from animals to humans

WRITTEN AND PHOTOGRAPHED BY TOM LEVY

Domestic livestock are the last thing you would expect a scientist at Children's Hospital Oakland to study, especially if that scientist is international Chlamydia expert Deborah Dean, MD, MPH.

But maybe you, like Dr. Dean, know that the Chlamydiaceae family—responsible for more cases of sexually transmitted disease (STD) and human blindness worldwide than any other—contains eight other species of microorganism that also infect sheep, goats, pigs and cattle. These species—which can cause reduced fertility in cattle, reproductive failure in pigs, and severe respiratory and intestinal disease in poultry—are also thought to be capable of mutating and jumping into humans.

Dr. Dean has long wanted to thoroughly understand the dynamics of Chlamydiaceae as it interacts with the oft-intertwined human and livestock communities. But because money for this kind of research is hard to come by, Dr. Dean used an unorthodox strategy to get funded.

"I've been discovering that microbial communities are very important in human health. But it's hard to get National Institutes of Health funding to really investigate them thoroughly because these types of comparative genomic studies are so expensive," said Dr. Dean.

"Instead, I decided to try coming at it from a different direction, to look at the diversity of strains and species that specifically affect animals and domestic livestock, that may then jump hosts, like the current H1N1 flu strain."

In September 2009, she received a three-year $1 million joint National Science Foundation (NSF) and United States Department of Agriculture (USDA) grant to study the diversity of Chlamydiaceae bacterial strains responsible for infections in domestic livestock.

Unlike the National Institutes of Health (NIH), which focuses on research directly relevant to people and their health, the NSF and USDA traditionally have more interest in evolution, fundamental biology, educational training or animal well-being. In this case, the NSF partnered with the USDA to request a microbial genome project.

These kinds of studies can help us learn how a bacteria like Chlamydiaceae can jump from animals to humans, a critical public health question. Dr. Dean's grant is one of the few NSF grants a Children's Hospital Oakland researcher has ever received. Her project will compare the genomes—all the genes that make up a bacteria species—of all the known species of the bacterium, as well as a selection of the strains that infect birds, mammals and humans.

Dr. Dean will look for evidence of an evolutionary strategy, and how these organisms might be better classified. She hopes to see what kind of genetic reassortment and reshuffling is going on and how that has affected Chlamydiaceae evolution, including the emergence of new species and strains.

"This grant provides the opportunity to take the field to a whole different level in terms of understanding this very important organism and how different species and strains of the organism may or may not interact," said Dr. Dean.

The questions Dr. Dean hopes to answer include: How stable is the organism and how rapidly does it change, recombine and form new species?

What she learns will help build a new classification system that scientists can use to more quickly identify which strains are more or less virulent, understand how the organisms recombine to form new strains and invade new host niches, and which strains could jump to humans.

"Understanding the mechanisms of recombination would also help us develop a way to genetically manipulate the organism, significantly accelerating our understanding of disease pathogenesis as well as guiding appropriate drug and vaccine design," said Dr. Dean.

She's optimistic about the potential for combining NSF and NIH research goals. "I think this marks the beginning of a new era in understanding that there should be more cross-fertilization between NSF research and research traditionally undertaken by the NIH," said Dr. Dean. "I think scientists are recognizing that we need a much greater understanding, not of just of one particular niche of how the organism functions, but a more global perspective, and it's very exciting to be a part of it."

› Research: Chlamydia

Diagnostic in a box

Developing a faster point-of-care Chlamydia diagnostic

In addition to investigating chlamydia's animal-human link, Children's senior scientist Deborah Dean, MD, MPH, is also working on a fast point-of-care diagnostic for sexually transmitted chlamydial diseases in humans.

Existing diagnostic tools are expensive and don't work well, so they're not widely used. "There is no accurate screening," said Dr. Dean. "The prevalence could be 10-fold higher than what's reported."

Chlamydia trachomatis—the largest cause of blindness and bacterial sexually transmitted diseases worldwide—infected more than 1 million people in the United States last year, according to the World Health Organization, and more than 92 million worldwide. It's also a leading cause of pelvic inflammatory disease and sterility.

And because up to 70 percent of women and 50 percent of men who are infected may be asymptomatic, millions more may be at risk without knowing it.

To develop the faster diagnostic, Dr. Dean teamed up with Network Biosystems—a Massachusetts-based bio-tech firm—to land a five-year $3.8 million Small Business Innovation Research grant from the National Institute of Allergy and Infectious Diseases. Dr. Dean is a principal investigator on the project, along with Richard Selden, MD, PhD, of NetBio.

Network Biosystems—founded in 2000 by a group of engineers from the Massachusetts Institute of Technology—is best known for its expertise in rapid DNA analysis. NetBio has already developed a half-a-shoe-box-sized device designed to quickly detect bioterrorism agents for the Department of Defense.

It is this device that Dr. Dean and the team hope to modify to do a two-part detection of Chlamydia. First, does this person have Chlamydia? Second, which strain is it? Is it a virulent strain?

With a diagnostic this fast, infection can be determined in minutes and treatment can begin immediately. That's crucial if your patient is a teenager or young adult who may not follow up for test results, or you're examining patients in rural Southeast Asia or equatorial Africa.

Setting up appointments and monitoring treatment is difficult in those environments. So starting treatment right away is essential. It's also handy to have a device that can confirm the success of treatment by quickly telling you Chlamydia is no longer present in your patient.

Here's how the device works: The tip of a sample-laden swab is placed into a "cassette" where it enters a buffer solution. The cassette is inserted into the machine where DNA is extracted, enters a microfluidics system and is matched against possible target organism strains.

"Because we have the technology and could run with it and we had great preliminary data: That's how we got funded," said Dr. Dean. "The sky's the limit in terms of what we can do. From a research perspective it's fantastic too. I can take this into the field with me and get real-time data to help me with what I'm doing."