

# Hope for Patients at Risk



*E. coli*

As resistance to the miracle antibiotics grows, OU researcher Anne Pereira joins the attack on hospital-acquired infections with a new and potent weapon.

BY DEBRA LEVY MARTINELLI  
PHOTOS BY ROBERT TAYLOR



Twenty years of research by OU Health Sciences Center scientist Anne Pereira have gone into the development of the CAP37 peptide, an antibiotic that targets hospital-acquired bacterial infections.

As a young microbiology student at the University of Melbourne in the late 1970s, Anne Pereira heard some disconcerting news: Resistance to antibiotics—that 20<sup>th</sup> century marvel cure for a multitude of bacterial infections—was on the rise. A few years later, when she was a graduate student at a Melbourne children's hospital, the Australian native witnessed firsthand an outbreak of antibiotic-resistant *Staphylococcus aureus*, or staph infection.

Those two events, plus a post-doctoral fellowship at Emory University with a researcher investigating a solution to the antibiotic resistance challenge, sealed Pereira's professional destiny. For more than 20 years, she has doggedly pursued a viable therapy for hospital-acquired infections.

Her persistence has paid off.

Pereira, associate professor of pathology at the University of Oklahoma Health Sciences Center, has developed an antibiotic from a protein that, oddly enough, occurs naturally in the human body.

By synthesizing the small portion of the protein responsible for killing bacteria, Pereira and her research team have created CAP37, a compound to which hospital-acquired bacterial infections are particularly susceptible. CAP37 is unique for three reasons: It both binds and neutralizes the toxin that generates most of the harmful effects of a severe infection; it destroys those infection-causing bacteria in

such a unique way that the chances of resistance patterns developing are very low; and there is no evidence thus far that it is toxic to healthy cells.

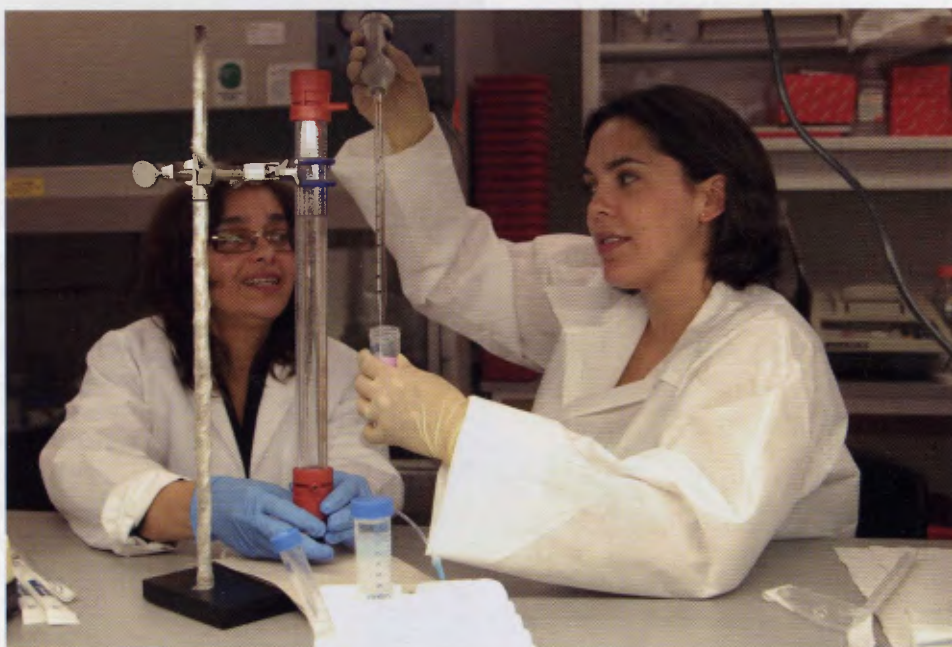
“We managed to isolate the protein at a time most infectious disease specialists were having problems with antimicrobial resistance against various antibiotics that were on the market,” Pereira explains. “Our whole premise was that we could look at the human body and come up with a native protein that might work as a new antibiotic and circumvent the problems of antibiotic resistance.”

CAP37 is particularly potent against such organisms as *Pseudomonas*, *E.coli* and *Acinetobacter* that plague hospital patients, especially those on ventilators and with indwelling devices like catheters, whose immune systems already are significantly weakened by illness, trauma or surgery. Others at risk are infants, the elderly and people with immune system disorders and other chronic diseases.

Pereira teamed with Alpha BioPartners Inc., a life sciences business consulting firm, to determine the need for a new antibiotic and assess all aspects of commercializing CAP37—from patent protection to product scale-up potential and market viability. After months of analysis and consultation with other experts around the world, they concluded the answer was a resounding “yes” on all counts. In 2005, they formed start-up Biolytx Pharmaceutical Corp. and negotiated with OU, which holds the patents on CAP37—eight issued patents with three more pending—for an exclusive worldwide license.

Biolytx is one of 30 companies created around University technology since 1998. Half of those came from discoveries made at the OU Health Sciences Center.

“Dr. Pereira is one of the latest examples of an OUHSC faculty member who is an accomplished basic scientist and has chosen the path of translational research to make her discovery available to patients in need,” says Joe Waner, vice president for



TOP: A single bacterium can grow and divide numerous times to form a circular colony, such as these bacterial colonies grown in Petri dishes in Pereira’s laboratory.

BOTTOM: Research assistant Heather Hinsley, right, gains valuable laboratory experience under the guidance of Pereira, an associate professor of pathology at OUHSC.

research on the Oklahoma City campus.

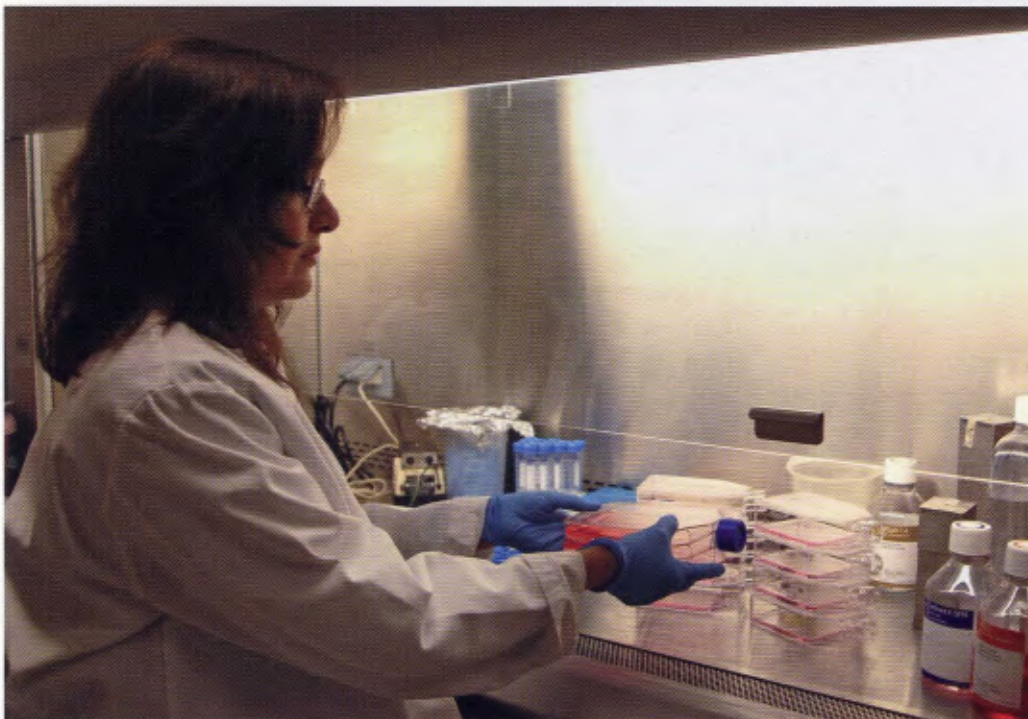
Alpha BioPartners founder Bill Hagstrom, who serves as Biolytx’s initial CEO, notes that historically antibiotics have been developed by large pharmaceutical companies. Today, however, Big Pharma, as the industry is known, focuses mostly on treatments for chronic diseases and conditions.

“This leaves a void for new drug antibiotic candidates, especially for severe hospital-acquired infections,” he says. “Biotechnology firms have been filling that void and Big Pharma has



ABOVE: CAP37 has a very strong kill capacity for *Pseudomonas*, *Salmonella*, *E.Coli* and *Acinetobacter*. Pereira carefully analyzes her data to determine those specific capabilities.

BELOW: Pereira takes a hands-on approach to producing the CAP37 protein in her OU Health Sciences Center laboratory.



aggressively been acquiring them.

“We hope to raise enough capital to advance CAP37 to FDA approval. At that point, we expect Big Pharma to be very interested in acquiring Biolytx.”

Getting there will take a bit more time.

“Our studies thus far confirm that this compound works in Petri dishes and in rodents,” Pereira says. “With the necessary funding, we hope to expand those studies to include such disease states as lung and eye infections to ascertain efficacy in various organs. That would take about six months to complete.”

The next steps would be to enlarge the screen further to include 70 different pathogens, determine the compound’s half-life (how long it circulates in the body without breaking down) and produce an initial drug compound through a contract manufacturer. Then would come toxicology or safety studies followed by submittal to the FDA of an Investigation of New Drug application. Clinical trials could begin shortly thereafter.

Hagstrom says this is the stage at which private investment is most critical. “Once we get the product closer to an IND, we can raise money from the venture capital community,” he explains. “It is important that we move this process along efficiently so we can quickly get to clinical trials and have a much better chance of getting the drug to market and benefit patients.”

Scientifically speaking, antibiotic clinical trials are short when compared to those for certain cancer drugs or therapies for Alzheimer’s, heart disease and other chronic conditions. “We will know within a few weeks whether there is any toxicity,” says Pereira.

Also, antibiotic trials require fewer participants and cost less than most clinical trials. If all goes well, CAP37 could be on the market within three to four years of IND approval.

By that time, Pereira will have been at this pursuit for nearly three decades. Although she has heard her share of naysayers and even had some occasional doubts herself about her ability to move a drug from the laboratory to the market, she has never lost her resolve.

“If you know you have something worthwhile, and you know deep down everything you’ve done is naturally going in a certain direction, you know you’re doing the right thing. I always tell my students, ‘If you love it, and you’re willing to stick with it, do it.’ ”

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