Jon Gilbert Fox

FOUNDATION FUNDING ADVANCES THE FIGHT AGAINST MRSA

Postdoctoral fellow Dhanalakshmi Nair (left) collaborates with Ambrose Cheung, a professor of microbiology and immunology, to knock out the resistance in methicillin-resistant Staph.

STAYING ONE STEP AHEAD OF MRSA—or methicillin-resistant *Staphylococcus aureus*, as it's technically known—is an ongoing challenge for health-care workers and scientists. But Ambrose Cheung, PhD, a professor of microbiology and immunology at Geisel, hopes to send MRSA two steps back by developing a compound that re-sensitizes the bacteria to common antibiotics. Supporting his efforts is a grant from the Gustavus and Louise Pfeiffer Research Foundation, a 70-year-old family foundation that funds university medical and pharmacological research projects.

MRSA is a tiny organism with a fearsome reputation. Resistant to most antibiotics, not just methicillin, MRSA spreads through direct and indirect contact and can be especially dangerous if it infects the bloodstream, lungs, or a wound. Approximately 75,000 people (or 24 in 100,000) contract invasive infections of MRSA each year in the U.S., according to a 2012 estimate by the Centers for Disease Control, resulting in 20 percent mortality.

Several years ago, Cheung's lab discovered that it was possible to re-sensitize MRSA to the antibiotic oxacillin by knocking out a particular protein in the bacteria called PBP4. Since then, Cheung and his postdoctoral associate Dhana Nair have screened more than 60,000 synthetic compounds to find ones that are capable of re-sensitizing MRSA and appear safe enough to give to humans. They've narrowed their search to two such compounds.

"New antibiotics may come on the market for MRSA, but we know that the bacteria can develop resistance very quickly," says Cheung. "Our strategy is to reduce the emergence of resistance so we can stay ahead in the game."

So far, Cheung hasn't figured out exactly how either compound works. They appear to disrupt PBP4 and another protein related to resistance called PBP2, but so far, it is not clear if those are the compounds' primary target—the mechanism by which they disarm MRSA's resistance to antibiotics.

"I'm hopeful that we can find the target within a year or two," says Cheung. "If you know the target, you can design a better drug." Knowing the target will also give him a better chance of securing grants from the National Institutes of Health (NIH) and partnering with a pharmaceutical company to develop, test, and market the drug.

"It's very hard to get money from the NIH for drug development," Cheung explains. "It's also hard to get support from a pharmaceutical company without having strong preliminary data. Grants from private foundations are so important to bridging that gap."

Private foundations, such as the Pfeiffer Research Foundation, often help researchers make the leap from basic science findings to translational research and clinical trials.

"That's a big jump," says Cheung. "People think that's an easy thing to do but that is the hardest part."

If Cheung's efforts pay off, MRSA's fearsome reputation will likely take a major hit.

JENNIFER DURGIN