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'Arms Race' Targets MRSA

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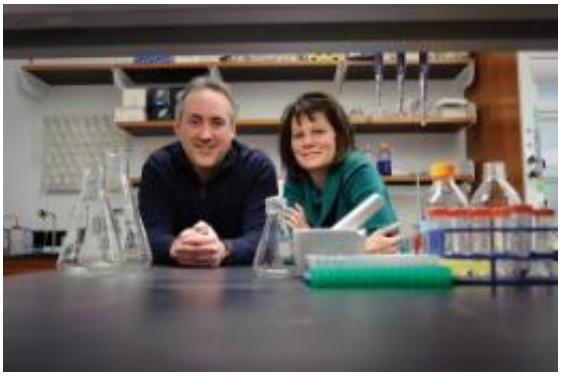

Researchers Amy Anderson and Dennis Wright are developing new strategies and drugs to treat infections.

(PhysOrg.com) -- Amy Anderson and Dennis Wright, both associate professors of medicinal chemistry in the School of Pharmacy, are fighting a small, but potent enemy - methicillin-resistant Staphylococcus aureus, better known as MRSA.

The bacteria's resistance to many antibiotics makes it difficult to treat, with systemic MRSA infections often becoming fatal. As the MRSA bacteria adapt to survive treatment with new antibiotics, scientists like Anderson and Wright must develop new strategies to treat infections.

"It's an arms race," says Wright. "We're always trying to stay one step ahead. I doubt we'll ever discover the 'ultimate antibiotic.' We'll just keep creating new ones."

The research of this husband and wife research team focuses on the development of new drugs to treat MRSA infections as well as other infectious diseases. One of their approaches involves working with an enzyme called dihydrofolate reductase, or DHFR, which supports key metabolic functions in living things, including bacteria. By inhibiting or changing DHFR's ability to function, it is possible to weaken and kill harmful bacteria like MRSA.

Anderson and Wright design drug compounds that have the potential to inhibit DHFR. These compounds - synthesized in Wright's lab with the assistance of graduate and postdoctoral students - are composed of small molecules that are designed to bind with the DHFR enzyme, effectively thwarting its capacity to function.

"There's a 'pocket' where the drug binds, and it's our job to figure out how big it is and its shape," says Anderson.

Jennifer Beierlein, a Ph.D. candidate in medicinal chemistry and a graduate assistant in the Anderson and Wright labs, likens compound synthesis to playing with a Mr. Potato Head. "You add on pieces to the molecule until you get a shape that will fit into the enzyme," she says.

Anderson and Wright are working with 10 strains of MRSA from Hartford Hospital, each of which has a slightly different susceptibility to antibiotics. With excellent results in the lab, they plan to move toward testing the drug compound on animals. Although developing a new class of antibiotics to fight MRSA infections is at the forefront of their research, they are also using the same technologies to develop drugs that fight other infections, including anthrax. With small tweaks in design, the DHFR inhibitors can have antibacterial, antifungal and antiprotozoal properties, says Anderson.

The researchers, whose work is largely funded by the National Institutes

of Health, were both professors in the chemistry department at Dartmouth before arriving in Storrs in 2006. “Coming from a small, liberal arts school, UConn is much different,” Anderson says. “It’s exciting to be in an environment that is so focused on drug research. We have great colleagues; even our informal conversations give way to new information, new ways of looking at things.”

This supportive collegial environment is evidenced by a University grant awarded to Anderson and colleague Victoria Robinson, assistant professor of molecular and cell biology in the College of Liberal Arts and Sciences, for an X-ray diffraction system that will collect data and allow Anderson and Robinson to “see” the structures of molecules, including how they bind to the drug compounds.

Anderson and Wright will continue to explore DHFR in the treatment of various diseases. Their new projects will focus on developing drugs that treat cancer. Infections and cancer are very similar from a treatment perspective, according to the couple. Says Wright, “You’re still trying to kill fast-growing cells.”

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