MRSA Researchers Identify New Drugs For Superbugs

In two separate studies, researchers at The Ohio State University Wexner Medical Center have discovered a new class of treatment against methicillin-resistant Staphylococcus aureus, as well as evidence of a growing need to quickly genotype individual strains of the organism most commonly referred to as the “superbug.” “The public is most familiar with the dramatic progression of skin infections caused by MRSA, but MRSA is responsible for a range of difficult to treat illnesses,” noted Dr. Kurt B. Stevenson, primary investigator of one of the studies following the transmission of MRSA infections in communities. “While we’ve seen a decrease in the number of MRSA cases, identifying new drug treatments and tracking methods will be critical to stopping these infections before they can start.”
In the August issue of *Bioorganic and Medicinal Chemistry,* researchers detail the results of a study that began 10 years ago, when Ching-Shih Chen, professor of medicinal chemistry at Ohio State College of Pharmacy, and a team of researchers were creating a library of anti-cancer agents built around he scaffold of the molecules of celecoxib, a popular arthritis treatment in a family of drugs known as cyclooxygenase-2 (COX-2) inhibitors. This effort yielded OSU-03012 (AR12), a compound that is currently in a Phase I clinical trial as anti-cancer agent at the OSU Comprehensive Cancer Center.

After observing how OSU-03012 acted within breast cancer cells, Hao-Chieh Chiu, a then post-doctoral researcher in Chen’s laboratory, realized that the derivatives were suppressing a mechanism that bacteria use to take over their host cells. Chiu decided, with the support of Dr. Chen, to focus his research on testing this compound library against a variety of bacteria. “When these compounds showed anti-bacterial activity against Salmonella and Francisella, we began testing efficacy against a variety of pathogenic bacteria, including Staphylococcus aureus, Enterococcus, and Streptococcus,” said Chiu, who is now an assistant professor at the Department of Clinical Laboratory Sciences and Medical Biotechnology at National Taiwan University. “It became clear that these analogues had a unique anti-bacterial activity, and they appeared to be most potent against Staph aureusand other MRSA strains.”

The researchers narrowed the library down to a single agent (dubbed “compound 46”) and moved to testing in MRSA-infected mice. Published in the August issue of *Bioorganic and Medicinal Chemistry*, the authors report that an intraperitoneal administration of compound 46 resulted in increased survival in MRSA-infected mice versus untreated mice. “It was particularly gratifying to see that these compounds, originally designed as anti-cancer agents, work as a novel class of anti-bacterial agents based on the same principle in bacterial cells,” said Chen.

The researchers are hopeful that this early work will ultimately provide insights on

the development of a treatment for antibiotic resistant infectious diseases. The team is already working with scientists at the Ohio State Center for Microbial Interface Biology, led by Dr. Larry Schlesinger, to use this technology to develop novel agents against tuberculosis, another public health threat facing similar issues with drug resistance.

Investigators in the Division of Infectious Diseases at the Ohio State College of Medicine have created a statewide “roadmap” of MRSA infections that is helping them better predict how – and where – MRSA will spread. The team is funded by the Centers for Disease Control and Prevention.

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