Researchers focus efforts on ‘super bug’ weak point

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“Development of High-Throughput Assay for Inhibitors of Aerobactin Synthesis”

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The “classical” *Klebsiella pneumoniae* (cKP) bacteria strain is a common human pathogen involved in infectious outbreaks in hospitals and long-term care facilities. However, a hypervirulent strain (hvKP), which first appeared in the Asian Pacific Rim in the 1980s, has become increasingly prevalent in the United States, including three cases which presented in Buffalo. Of even greater concern, more recently hvKP has demonstrated increasing antimicrobial resistance, making it a genuine double-threat “super bug.”

Researchers at UB’s Jacobs School of Medicine and Biomedical Sciences and the Hauptman-Woodward Medical Research Institute who are working on the problem have focused their efforts on a weakness in the hvKP life cycle involving biosynthesis of the siderophore aerobactin. The hvKP bacteria must manufacture aerobactin in order to adapt to the limited iron availability in its human hosts. If researchers can find a safe and effective compound that disrupts aerobactin biosynthesis they will have a powerful new treatment for hvKP infection.

Principal investigator Andrew M. Gulick, PhD, of the Hauptman-Woodward Institute and UB’s Department of Structural Biology, and co-PI Thomas A. Russo, MD, in the Department of Microbiology and Immunology, Jacobs School of Medicine and Biomedical Sciences, are developing two high-throughput screens to identify small molecule inhibitors of aerobactin production. Both assays have already been demonstrated in low-throughput format. The pilot screening study uses three commercially available chemical libraries totaling 4,400 compounds, including a panel of FDA-approved drugs. The initial screening of the biochemical assay will be conducted at the Small Molecule Screening Center at Roswell Park Cancer Institute.

The $25,000 research award from the Clinical and Translational Science Award is funded by the National Center for Advancing Translational Sciences of the National Institutes of Health (NIH) under Award Number UL1TR001412. The project represents an interdisciplinary team approach that involves several Buffalo Translational Consortium partners, with good potential for securing additional funding from NIH.