



PRESS RELEASE

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HWI Scientist Makes Breakthrough In Studies of Protein from Infectious Bacteria *Dr. Andrew Gulick's Work Published in Prestigious Scientific Journal Biochemistry, Dubbed "Hot Article"*

Dr. Andrew Gulick, Hauptman-Woodward research scientist, has just published a significant discovery in the scientific journal *Biochemistry*. Dubbed a "Hot Article" by the journal, the study confirms Gulick's hypothesis as to how an enzyme performs two half-reactions in a ping-pong mechanism.

Since 2001, Gulick and his lab have been working on understanding a family of proteins that is known for making antibiotics. Four years ago, they solved a new structure of a member of this protein family and proposed that the enzyme catalyzes a two-step reaction by a major change in conformation from one step to the next.

Also working on the project is Albert Reger, a graduate student in the Department of Structural Biology at the University at Buffalo. Gulick and Reger have determined the structures bound to different ligands that trap the enzyme in the active conformations for either the first or second half-reaction. These studies have allowed them to propose that members of this family of enzymes adopt two different conformations: The enzyme first catalyzes the initial adenylation step in one conformation. Then, to catalyze the second half-reaction, one part of the enzyme rotates by 140° to adopt a second conformation that is competent to catalyze the second half-reaction. This unusually large rotation is interesting in that it allows the enzymes to use a mobile domain to reconfigure a single active site. Residues from two different faces of the C-terminal domain are contributed to the active site to catalyze the distinct half-reactions.

"This is an exciting development for us because we needed this information to determine how other, larger bacterial proteins are being impacted. These other proteins can perhaps be engineered to make novel antibiotics or, in some cases, may serve as targets for the development of new antibiotics," Gulick said. "We have tested several other enzymes and expect to publish reports on how studies with those enzymes also support our hypothesis."

About Gulick

In addition to his position as an HWI research scientist, Gulick is an assistant professor of Structural Biology at the University at Buffalo. He received his Ph.D. in Experimental Oncology and Biochemistry from the University of Wisconsin-Madison in 1994 and his bachelor's degree in Biochemistry from Brown University in 1989. Gulick's research is focused primarily on the use of X-ray crystallography as a tool to study the structure and function of enzymes that catalyze interesting reactions. A major target in the lab is a family of proteins from *Pseudomonas aeruginosa*, a bacteria that causes chronic infections in patients with cystic fibrosis.

About HWI

With more than 50 years of exceptional scientific research, HWI is an independent, non-profit facility specializing in the area of fundamental biomedical research known as structural biology. Hauptman-Woodward's team of more than 75 staff members is committed to improving human health by studying the causes of diseases, as well as potential therapies, at their basic molecular level. HWI is located in the heart of the Buffalo Niagara Medical Campus in downtown Buffalo, New York, in a new state-of-the-art structural biology research center at 700 Ellicott Street. For more information, visit HWI's website at www.hwi.buffalo.edu or call 716-898-8600.