SOUTHWESTERN NEWS

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BACTERIA'S IRON-ABSORBING MECHANISMS MAY OPEN GATES FOR NEW TYPES OF ANTIBIOTICS

DALLAS – March 5, 2002 – Researchers at UT Southwestern Medical Center at Dallas have brought to light new information about how bacteria capture iron from the human body, and the work has implications for the design of novel antibiotics.

Dr. Andrew Ferguson, a postdoctoral researcher in the laboratory of Dr. Johann Deisenhofer, professor of biochemistry and investigator in the Howard Hughes Medical Institute at UT Southwestern, led the study published in *Science*.

Bacterial cells use a series of transporters to actively pump iron through their outer membranes and into the cells. These iron-acquisition mechanisms are vital for bacterial pathogens to establish and maintain bacterial infections. Ferguson and his colleagues deciphered the three-dimensional structure of the iron transporter FecA and showed that this receptor undergoes dramatic changes before transporting iron through the outer membrane.

"We have shown that the receptor changes its conformation," Ferguson said.

Bacteria lent themselves well to the study because the protein-based process that gets nutrients and other necessary elements across bacterial cells' protective outer membranes has been widely studied. The extensive base of existing research allowed the team to focus on the iron-absorption mechanism.

The three-dimensional structure of FecA includes a barrel that is open on both ends. A plug inside the barrel fills its middle, leaving open pockets at the barrel's top and bottom. When iron is added, the top pocket closes, triggering absorption of the iron.

Ferguson said bacteria's high-affinity iron uptake systems could have clinical applications. With an alarming rise in the reported number of harmful, drug-resistant bacteria, scientists may be able to design new antibiotics that physically resemble the natural iron carriers that the transporters recognize. Because these "Trojan Horse" antibiotics would be specifically recognized and actively pumped into the cell, they may eventually provide an alternative weapon

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to treat systemic bacterial infections.

"Understanding the mechanism of iron transport is an important first step toward this goal," said Deisenhofer, winner of the 1988 Nobel Prize in chemistry.

Other authors on the March 1 study in *Science* included Barbara S. Smith of the Howard Hughes Medical Institute at UT Southwestern, and researchers from East Tennessee State University and the University of Victoria in British Columbia.

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