New finding in ribosome signaling may lead to improved antibiotics

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(PhysOrg.com) -- Researchers at the University of Illinois at Chicago have discovered a signaling mechanism in the bacterial ribosome that detects proteins that activate genes for antibiotic resistance.

"The ribosome is one of the most complex molecular machines in the cell," said Alexander Mankin, UIC professor and director of the Center for Pharmaceutical Biotechnology. It is responsible for the production of all proteins in the cell, and in bacteria it is one of the major antibiotic targets.

Understanding how signals are generated and transmitted within the ribosome, Mankin said, may one day lead to better antibiotics.

Mankin's research, funded by the National Science Foundation, has been published in the journal *Molecular Cell*.

The ribosome is responsible for activating some antibiotic resistance genes in the presence of certain proteins. For that to occur, special sensors in the ribosome must recognize cellular cues and the structure of the regulatory protein. Once the signal is detected, it is then transmitted to the functional centers which alter the ribosome's performance.

Mankin's latest research has found at least one of the signal pathways in the ribosome. He and his coworkers found that the presence of the regulatory protein as it is made within the ribosome changes the properties of the ribosome's catalytic center.

Under normal conditions, the ribosome's catalytic center can accept any of the 20 natural amino acids, which are then added to the growing protein chain.

However, if the ribosome has synthesized the regulatory protein in the presence of an antibiotic, the catalytic center rejects some or even all amino acids. As a result, synthesis of the regulatory protein stops, and the genes of antibiotic resistance are activated.

"This is one of the strategies used by pathogenic bacteria exposed to antibiotics to regulate expression of antibiotic resistance genes," Mankin said.

In previous studies, Mankin and his research team pinpointed some of the ribosomal RNA residues that interact with the growing regulatory peptide, thus serving the function of the peptide sensors.

Provided by University of Illinois at Chicago