Ant guts could pave the way for better drugs

March 25 2008

Scientists have discovered two key proteins that guide one of the two groups of pathogenic bacteria to make their hardy outer shells -- their defense against the world.

The work, they said, could allow researchers to create new antibiotics against gram-negative bacteria, like E. coli and salmonella, that would destroy these bacteria by disabling the mechanism that produces their protective coating.

"A long-term goal is to find inhibitors of these proteins we have discovered," said Natividad Ruiz, a research molecular biologist at Princeton University and the lead author on the paper describing the work. "Small molecule inhibitors could become antibiotics that subvert the outer membrane."

The research, conducted by Ruiz, Thomas Silhavy, Princeton's Warner-Lambert Parke-Davis Professor of Molecular Biology, and others from Harvard University, is described in the online edition of the April 8 *Proceedings of the National Academy of Sciences*.

The team discovered the proteins through an extended process of elimination. The scientists looked at microbes in the guts of carpenter ants. The bacteria, which have lived there for millions of years -- passed on over many generations -- have lost many of the traits necessary for survival in the outer world. As a result, their collection of genes, known as a genome, is far smaller and simpler than the genome of E. coli.

Scientists sequenced the genome of the model bacterium E. coli 11 years ago, yet they still do not understand the functions of about 40 percent of the thousands of proteins produced by those genes, according to Ruiz. Proteins are the workhorses of cells, directing and producing the creation of many key cell structures and functions.

In contrast, the genome of the bacteria found in the ant gut, Blochmannia floridanus, contains the instructions for only 583 proteins. Since the bacteria are closely related, nearly all of Blochmannia's genes -- 564 -- are found in E. coli. The scientists reasoned that they could find the protein containing the instructions for building the germ's outer casing.

"We designed a computer-based search that filtered out proteins that lacked the characteristics essential for outer membrane construction," Ruiz said. "In the end, only two of the 564 proteins remained."

They found the two missing proteins of a pathway that ferries one of the key components of the outer shell, called LPS, to the cell surface.

Members of Silhavy's laboratory use E. coli as a model system to better understand the workings of the cell, such as how it senses changes in its environment. Silhavy is a bacterial geneticist who has made fundamental contributions to the field of cell biology.

Source: Princeton University