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Researchers find possible target to treat deadly bloodstream infections

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Researchers at the University of Illinois at Chicago have discovered a possible target to treat bloodstream bacterial infections.

Most bacterial pathogens can invade the bloodstream, which can lead to severe sepsis, a syndrome that kills about 215,000 of the 750,000 people affected in the United States each year, according to a study published in the journal *Critical Care Medicine*.

"The growth of bacterial pathogens in blood represents one of the most dangerous stages of infection," said Alexander Mankin, professor and associate director of UIC's Center for Pharmaceutical Biotechnology. "Before we can discover an antibiotic to treat bloodstream infections, we first had to discover which enzymes are essential for bacteria to live in the bloodstream.

"Our major goal was to identify genes that are critical for the survival and growth of bacteria in blood."

The study appears in the February issue of the journal *PLoS Pathogens*.

A graduate student in Mankin's laboratory, Shalaka Samant, infected human blood in a test tube with E. coli bacteria, a major cause of bloodstream infections in hospitalized patients.

Using a novel technique developed in Mankin's laboratory, Samant discovered that 19 E. coli mutants out of more than 4,000 she tested

could not grow in blood. The majority of the mutants carried a deletion of a gene involved in making nucleotides, the building blocks of DNA and RNA.

The result suggested that the biosynthesis nucleotides is crucial for the growth of the bacteria in human blood, Samant said.

Samant expanded her research to another bloodstream pathogen -- Bacillus anthracis, the causative agent of anthrax.

"There are few treatment options available for the late stages of anthrax infections," Samant said. "We found that, similar to E. coli, anthracis bacilli that could not biosynthesize nucleotides also were unable to grow in blood."

To add to Samant's study, a team of researchers led by Dr. James Cook, chief of infectious diseases, immunology and internal medicine at the University of Illinois Medical Center at Chicago, showed Bacillus anthracis mutants that were unable to synthesize nucleotides were not able to infect mice. After they were infected with anthrax, the mice remained healthy, with no bacteria detected in their blood.

Mankin said the enzymes of nucleotide biosynthesis could make excellent antibiotic targets. The UIC Center for Pharmaceutical Biotechnology is now working to identify drugs that inhibit these enzymes.

Source: University of Illinois at Chicago