Mutant gene lessens devastation of flesh-eating bacteria

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(PhysOrg.com) -- Scientists at The Methodist Hospital Research Institute in Houston recently discovered a simple gene mutation that decreases the chance people will get a flesh-eating disease called necrotizing fasciitis. Further, they proved that inactivating this section of the gene lessens the devastating disease in humans.

Results of this research, funded by the National Institutes of Health and the American Heart Association, appear online this week in the Proceedings of the National Academy of Sciences (*PNAS*).

“The study of genomics has opened a wealth of information on how disease develops on a molecular level,” said Musser, co-director of The Methodist Hospital Research Institute. “When we identify a gene mutation that has a direct effect on a disease - like we have done for the flesh-eating bacteria - this opens up doors to designing drugs that provide treatments and cures.”

Necrotizing fasciitis is rare but serious. It is lethal in approximately 30 percent of those who develop it. The most common cause is the group A Streptococcus (GAS) bacteria, the same bacteria that causes step throat.

“Single-nucleotide changes are the most common cause of natural genetic variation among members of the same species, but there is remarkably little information on how these common genetic mutations affect the infectious and damaging nature of some bacteria,” Musser said. “It is one of these single-nucleotide mutations in the GAS genome

that is associated with decreased human necrotizing fasciitis, or flesh eating disease."

Dr. James Musser and his team analyzed the genomic sequences of 12 GAS strains taken from patients with several strep-related diseases, including necrotizing fasciitis. This analysis revealed a naturally occurring mutation in the strep genome that decreases necrotizing fasciitis in humans. It also showed that the mutation caused a segment of the gene to "turn off," which reduced the disease's ability to destroy soft tissue, spread from the infection site, and cause human necrotizing fasciitis and death.

Musser's lab compared 255 GAS genomes collected from patients in Ontario, Canada, over an 11-year period, to genomes of the 12 strains found in patients with the mutation, a naturally occurring single-nucleotide insertion in the MtsR (metal transporter of streptococcus regulator) gene. Using an integrated systems biology strategy, the study showed that the MtsR mutation results in early termination of the MtsR protein, and that MtsR inactivation is responsible for the decreased necrotizing fasciitis phenotype observed in human patients.

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