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Genome study shows how strep throat germ circumvents our immune system

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(PhysOrg.com) -- Investigators at The Methodist Hospital Research Institute in Houston examined for the first time the long-term response to strep throat on a genome-wide level, shedding light on how group A streptococcus interacts with the patient's immune system and attempts to circumvent it. Results were published today in the *Proceedings of the National Academy of Sciences (PNAS).*

In the United States, the human bacterial pathogen group A streptococcus causes an estimated 30 million cases of strep throat annually, and also causes rheumatic fever that damages the heart.

"This study has discovered previously unknown ways that a common bacterial pathogen communicates with its host during an infection episode. The result is a new, much higher level of understanding of how infection causes disease," said Dr. James Musser, senior scientist on the study and co-director of The Methodist Hospital Research Institute. "These discoveries have already provided a wealth of information for future research into new treatments and vaccines, not only for strep throat, but also for other types of life threatening group A strep infections as well."

"Our results are significant because despite the prevalence of strep throat, currently relatively little is known about what happens on a molecular level regarding interaction between group A streptococcus and the host during a throat infection, said Dr. Patrick Shea, scientist at TMHRI who is the first author of the study. "Advances in genome-wide

analyses occurring in the last decade have facilitated the study of global gene changes that occur during microbial infection, giving us important new clues on how better to fight and prevent infections," he said.

About the study

Incorporating molecular biology and sophisticated computational techniques, the researchers determined which groups of host and bacterial genes had similar changes in magnitude and pattern of expression over the course of the 32-day infection.

In the study, 509 host genes and seven biological pathways were differentially expressed throughout the entire 32-day infection cycle. GAS infection produced an initial widespread significant decrease in expression of many host genes, including those involved in cytokine production, vesicle formation, metabolism, and signal transduction.

This repression lasted until day four, at which time a large increase in expression of host genes was observed, including those involved in protein translation, antigen presentation, and GTP-mediated signaling. This "interactome" analysis identified 73 host and pathogen gene pairs with correlated expression levels. The team discovered significant correlations between transcripts of GAS genes involved in hyaluronic capsule production and host endocytic vesicle formation, GAS GTPases and host fibrinolytic genes, and GAS response to interaction with neutrophils. Also identified was a strong signal suggesting interaction between host γδ T cells and genes in the GAS mevalonic acid synthesis pathway responsible for production of isopentenyl-pyrophosphate, a short-chain phospholipid that stimulates these T-cells. Taken together, the results provide the first comprehensive understanding of the host-pathogen interactome during mucosal infection by a bacterial pathogen.

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