MedicalXpress

Team finds mechanism of toxin's inflammatory effect on lungs

December 29 2014

A study released Dec. 23 describes a never-before-seen mechanism by which a bacterial toxin leads to severe inflammation in asthma and other acute and chronic pulmonary diseases. Researchers from The University of Texas Health Science Center at San Antonio said the discovery could result in development of therapeutic strategies that improve health in individuals who suffer from airway diseases.

The offending party is the *Mycoplasma pneumoniae* Community Acquired Respiratory Distress Syndrome (CARDS) toxin. The CARDS toxin, discovered at the Health Science Center in 2006, is considered the first major bacterial respiratory toxin discovered since the days of diphtheria and pertussis.

Persistent and harmful

M. pneumoniae is a common and persistent infection in the lungs and airway. Once there, it produces the CARDS toxin and a cascade of harmful effects. Specifically, CARDS toxin reacts with NALP3, a key molecule that regulates inflammatory pathways, leading to excessive activation of pro-inflammatory reactions.

"Inflammation is important for self-protection from infection and any injury, but when a microbial factor such as the CARDS toxin controls inflammation, bad things happen," said study author Joel B. Baseman, Ph.D., professor of microbiology and immunology in the School of

Medicine at the UT Health Science Center and director of the Center for Airway Inflammation Research (cAIR). "Through this mechanism, CARDS toxin triggers exaggerated and prolonged inflammation that results in tissue injury, airway narrowing, mucus hypersecretion, wheezing and coughing."

Multiple infections

"Because *M. pneumoniae* infections occur so frequently in children and adults and CARDS toxin is such a powerful inducer of inflammation, it is likely that co-infections involving *M. pneumoniae,* CARDS toxin and other respiratory pathogens result in enhanced severity of disease," said Santanu Bose, Ph.D., study co-author and associate professor at Washington State University.

"Now that we have identified this pathway of disease development, our goal is to prevent the wide range of airway pathologies caused by CARDS toxin with drugs, vaccines and protective antibodies," said study co-author Thirumalai R. Kannan, Ph.D., associate professor/research in the Department of Microbiology and Immunology at the UT Health Science Center and also a member of cAIR. "We are undertaking those studies now."

Provided by University of Texas Health Science Center at San Antonio

Citation: Team finds mechanism of toxin's inflammatory effect on lungs (2014, December 29) retrieved 13 May 2024 from https://medicalxpress.com/news/2014-12-team-mechanism-toxin-inflammatory-effect.html

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