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News Release

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Burton Dickey, M.D.

Aerosol Launches Immune Response in Lungs to Wipe Out Lethal Infections

Preclinical research presented at ASCB shows swift killing of bacteria, viruses, fungi

M. D. Anderson News Release 12/03/07

An inhaled immune system stimulant protects mice against lethal pneumococcal pneumonia and other deadly bacterial, viral and fungal infections of the lungs, a research team led by scientists at The University of Texas M. D. Anderson Cancer Center reports at a major scientific meeting.

Their findings have implications for protecting immuno-compromised patients against infection and the general public against respiratory epidemics and biological weapons. The research is a featured presentation at the annual meeting of the American Society for Cell Biology Dec. 3 in Washington, D.C.

"This aerosol stimulates an innate immune system response in the lung lining fluid that kills the invading pathogens virtually on contact," says Brenton Scott, Ph.D., post-doctoral fellow in M. D. Anderson's Department of Pulmonary Medicine, and first author of the abstract presented at ASCB. "It also works in mice with suppressed immune systems."

The innate immune system is the body's inflammatory first response to infection or injury. It produces proteins and peptides that act as natural antibiotics to broadly kill invading bacteria, viruses or fungi.

"Pneumonia is a leading cause of death from infection in the United States and a major cause of death among cancer patients and others with suppressed immune systems," says Burton Dickey, M.D., professor and chair of pulmonary medicine and senior author of the research.

Untreated mice exposed to S. pneumoniae, the most common form of bacterial pneumonia, died within days. Mice treated with the Aerosolized Lung Innate Immune Stimulant (ALIIS), developed by the researchers, two hours before exposure had an 83% survival rate. All of the mice treated between 4 and 24 hours before exposure survived.

The effect slowly declines over five days, Scott says. Giving the stimulant after infection also provides some protection.

The team got similar results testing ALIIS as a protectant against lethal doses of several other types of pneumonia, as well as influenza virus, the mold aspergillus, and the Class A bioterror agents anthrax, bubonic plague, and tularemia.

ALIIS consists of a purified extract of a common bacterium, Haemophilus influenzae, that causes ear and sinus infections in children. The bacterium is essentially broken open, purified and administered as an aerosol.

Preclinical research continues, with early clinical trials - most likely to test a protective role in cancer patients - at least a year away.

The innate immune system indiscriminately targets invading pathogens and also recruits the adaptive immune system to launch a more targeted, pathogen-specific response. The adaptive immune system takes a few days to respond, Dickey says.

"Here the innate immune system is so effective, infections are cleared before the adaptive response even gears up," Dickey says.

The battle also is over before white blood cells called neutrophils, part of the innate immune system, can be called in to help. That's potentially important, Dickey says, because chemotherapy, particularly for leukemia, often wipes out a patient's neutrophils.

Dickey and Scott believe the entire defense against invaders is accomplished by local cells in the lung's lining, called the epithelium. Their research shows the epithelium floods its lining fluid with anti-microbial polypeptides in response to ALIIS inhalation. These natural antibiotics are virtually lying in wait for microbes to kill.

The team is now trying to understand exactly which of these polypeptides kills the pathogens.

Lungs are exposed to infectious agents with every breath, Scott notes, and the innate immune system plays an important role in routinely keeping the lungs healthy.

"We study airway inflammation, and mostly we think about that in a negative context - how to stop inflammation, as in the allergic inflammation that causes asthma," says Dickey. "But surely the ability of airways to become inflamed is there for a good reason. So we asked can we set off a type of inflammation that strengthens protection against infection. The answer is yes."

Research is funded by the George and Barbara Bush Endowment for Innovative Cancer Research, M. D. Anderson's Odyssey Fellowship program, and grants from the National Institutes of Health, National Heart, Lung and Blood Institute.

Dickey and others involved in the research have a patent on ALIIS. Dickey, Scott and co-author Michael Tuvim, Ph.D., associate professor in the Department of Pulmonary Medicine, own stock in Pulmotect, LLC, which has licensed the ALIIS technology from M. D. Anderson. These arrangements are managed in accordance with M. D. Anderson's conflict of interest policies.

Co-authors with Scott, Dickey and Tuvim are Cecilia Clement, M.D., and Scott Evans, M.D., both of M. D. Anderson's Department of Pulmonary Medicine; Bryan E. Gilbert, Ph.D. of Baylor College of Medicine's Department of Molecular Virology and

Microbiology; and Johnny Peterson, Ph.D., The University of Texas Medical Branch at Galveston Department of Microbiology and Immunology.

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