Aging, obsolete cells prime the lungs for pneumonia

May 26 2011

Cells that are supposed to die because of DNA damage, but don't, are linked to pneumonia risk in older mice. This finding is described in a research article in the journal Aging Cell. The senior author is Carlos Orihuela, Ph.D., pictured, of the Department of Microbiology and Immunology and the Barshop Institute for Longevity and Aging Studies at The University of Texas Health Science Center San Antonio. Credit: UT Health Science Center San Antonio

Community-acquired pneumonia is the leading cause of infectious death among the elderly. Newly published research from The University of Texas Health Science Center San Antonio suggests why older people are vulnerable and offers a possible defense.

The researchers found that when it comes to aging and pneumonia, one bad apple can ruin the barrel. Lung cells that were supposed to die due to DNA damage — but didn't — were 5 to 15 times more susceptible to

invasion by pneumonia-causing bacteria. These bad apples also increased the susceptibility of normal cells around them. The research was published Wednesday [May 25] in the journal *Aging Cell.*

Close to 1 billion adults worldwide are at risk for pneumonia. They include more than 800 million adults who are older than 65 and an estimated 210 million with chronic obstructive pulmonary disease (COPD).

Injurious effects

Both age and COPD are associated with senescent cells, which are unable to die due to dysregulated function. These cells have increased levels of proteins that disease-causing bacteria stick to and co-opt to invade the bloodstream. The cells also spew out molecules that increase inflammation, and make normal cells nearby do the same.

"Senescent cells prime the lungs for infection," said Pooja Shivshankar, Ph.D., research scientist in microbiology and immunology at the UT Health Science Center and first author on the study.

Controlling the inflammatory molecules' release could short-circuit pneumonia risk in the elderly, said the senior author, Carlos Orihuela, Ph.D., assistant professor of microbiology and immunology, also at the Health Science Center.

"We can't stop aging, but our findings suggest that preventing inflammation might be the next best thing," Dr. Orihuela said. "This opens up possibilities for anti-inflammatory drugs as treatments for pneumonia."

Mouse study

The scientists compared aged and young mice, all healthy. The older mice were found to have increased lung inflammation with higher levels of senescence markers; this was consistent with previous studies in the literature.

The lung cells in aged mice also proved to be more susceptible to infection by Streptococcus pneumonia, the bacterium that causes pneumonia. This was determined by increased levels of proteins to which the bacteria adhere and by testing bacterial adhesion to the lung cells.

Four different experiments — on senescent cells, on normal lung cells exposed to senescent cells, on aged mice and on young mice exposed to gene-damaging stress — revealed increased susceptibility to pneumonia infection.

"This potentially helps to explain why the elderly and individuals with COPD are predisposed to community-acquired pneumonia," Dr. Orihuela said.

More information: Cellular senescence increases expression of bacterial ligands in the lungs and is positively correlated with increased susceptibility to pneumococcal pneumonia. Pooja Shivshankar, Angela Boyd, Claude Le Saux, I-Tien Yeh, Carlos Orihuela. *Aging Cell* DOI: 10.1111/j.1474-9726.2011.00720.x

Provided by University of Texas Health Science Center at San Antonio