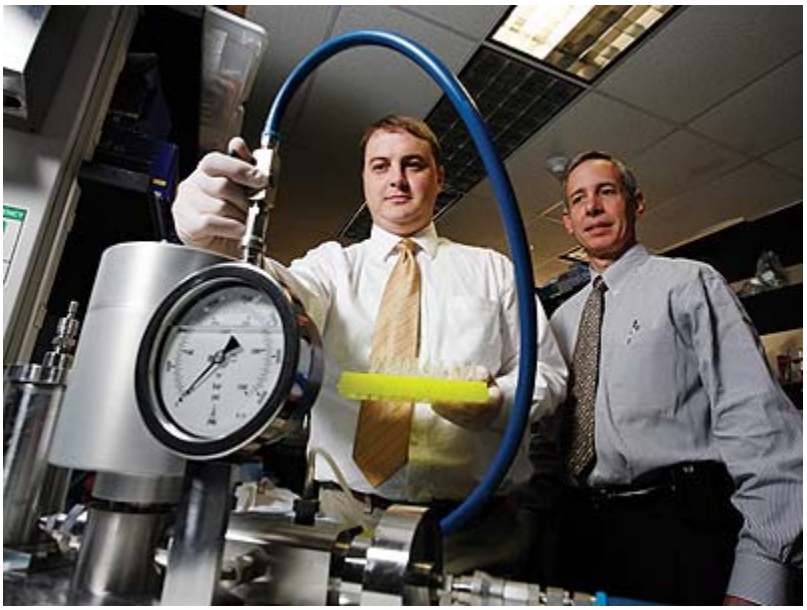
messenger

In Our Labs: Wiping Out Lethal Infections

By Carol Bryce

Ever pass by one of the hundreds of labs on our campuses and wonder what researchers were doing in there? This periodic series takes you inside to find out.



Above, from left: Brenton Scott, Ph.D., and Burton Dickey, M.D., work with a cell disruptor, which breaks the bacterial cells used to make Aerosolized Lung Innate Immune Stimulant. ALIIS stimulates the immune system to protect against infection.

Like many scientific discoveries, this one started with a problem.

Chemotherapy kills cancer cells. But it also destroys patients' infection-fighting white blood cells and weakens their immune systems. Potentially life-threatening illnesses such as pneumonia can result.

"The lungs are delicate structures that are exposed to infectious agents in the environment with every breath, so pneumonia is pretty common in all populations," explains Burton Dickey, M.D., chair of pulmonary medicine. "Among cancer patients and others with suppressed immune systems, pneumonia is a major cause of death."

Dickey and his colleagues wanted to find out if anything could be done to protect cancer patients against pneumonia as well as staphylococcal infections and other infectious agents.

"We wanted to see if we could set off a type of airway inflammation that would strengthen protection against infection. So we decided to try to kill all the pathogens in the lungs, the body's first line of defense, before they could penetrate into the rest of the body," he says.

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"We mainly tend to think of airway inflammation in a negative context, such as how to stop the inflammation that causes asthma. But surely the ability of airways to become inflamed is there for a good reason," Dickey adds.

The researchers' idea led to the development of an inhaled aerosolized stimulant that not only protects mice against pneumonia but also defends them against other deadly bacterial, viral and fungal infections of the lungs.

"We've found that this aerosol stimulates an innate immune system response in the lung lining fluid that kills the invading pathogens virtually on contact. It also works in mice with suppressed immune systems," says Brenton Scott, Ph.D., postdoctoral fellow in Pulmonary Medicine. Scott was first author on an abstract of the research that was featured at the 2007 annual meeting of the American Society for Cell Biology.

To conduct the research, the scientists exposed two groups of mice to the most common form of bacterial pneumonia: a pathogen called S. pneumoniae. Before exposure, one group of mice was placed in a plastic container and treated for 20 minutes to a very fine mist of Aerosolized Lung Innate Immune Stimulant. The other group of mice received no treatment.

The ALIIS, developed by the researchers, contained a purified extract of a common bacterium, Haemophilus influenzae, that causes ear and sinus infections in children. The mice inhaled the ALIIS through a nebulizer — an inexpensive device that's commonly used to administer medication to people with asthma and other respiratory diseases.

The untreated mice died within days of exposure. But the mice that were treated two hours before exposure had an 83 percent survival rate. And all of the mice that were treated 4-24 hours before exposure survived. The protective effect lasted for 3-5 days. Giving the ALIIS after infection also provided the mice some protection.

Both human beings and mice have two types of immune systems: innate and adaptive. The aerosol treatment the researchers developed targets the innate immune system, which is found in nearly all living things and is the body's inflammatory first response to infection or injury. The adaptive immune system is more specialized and exists only in higher vertebrates such as birds and mammals. Vaccines, which help the body establish immunity to a disease, target the adaptive immune system.

"Unlike vaccines, which usually have to be administered before exposure and take a few weeks to work, we found out that our system protects very quickly," Scott explains.

Beyond Cancer

In addition to S. pneumoniae, the researchers also tested the effectiveness of the ALIIS against lethal doses of other types of pneumonia, as well as the influenza virus, the mold aspergillus, and Class A bioterror agents including anthrax and bubonic plaque. The ALIIS offered mice similar protection against all of these pathogens.

Based on these results, the researchers believe this technology has many potential applications, and they've started a company to transition the technology for use by patients. The next step will be to try the therapy in larger animals. If that research is successful, Phase I clinical trials in cancer patients will follow.

"This is a 'platform technology,' which means it has multiple uses," Dickey explains. "Our findings not only have implications for guarding cancer patients against infection, but also they potentially offer the general public protection against both biological weapons and respiratory epidemics such as avian flu. And while most of our results so far have involved prevention, this technology has treatment applications as well."