Medical Xpress

Cancer fighter can help battle pneumonia

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The tip of an immune molecule known for its skill at fighting cancer may also help patients survive pneumonia, scientists report.

A synthesized version of the tip of tumor necrosis factor appears to work like a doorstop to keep sodium channels open inside the air sacs of the lungs so excess fluid can be cleared, according to a study published in the *American Journal of Respiratory Critical Care Medicine*.

This TIP peptide is attracted to the sugar coating at the mouth of the sodium channel. Once the two connect, they move inside the small but essential number of cells that help keep the lungs clear by taking up sodium, said Dr. Rudolf Lucas, vascular biologist at the Medical College of Georgia at Georgia Regents University and the study's corresponding author.

Inside these cells, TIP binds to the most critical part of the sodium pump, the alpha subunit, and fluid starts moving again. Sodium comes in the channel, water follows, and the sodium pump pushes the fluid into the body's natural drainage network, called the lymphatic system.

"The more sodium you take up, the more water will be taken up by these cells," Lucas said. "That is the way it's supposed to work.

Fluid in the lungs' 266 million air sacs interferes with breathing as well as the important transfer of oxygen from air sacs to capillaries so it can be distributed throughout the body. TNF, known for its tumor-killing capacity, actually has been viewed as a "bad guy" in the lungs where it

can block the sodium channel. In fact, excessive TNF production can put patients into shock.

"We found that there is another side on the tip of this molecule, which recognizes sugar groups and this side counteracts that side," Lucas said. "We knew we could stimulate liquid clearance in animal models with this peptide and we also knew we could increase the uptake of sodium. Now we know more about how it works."

Pneumonia and influenza together are the eighth leading cause of death in the United States with pneumonia overwhelmingly the most deadly, according to the American Lung Association. The elderly, children, and the chronically ill are at highest risk.

Ironically, lung problems can actually worsen with pneumonia treatment. Viruses and bacteria are major causes of pneumonia, with bacteria typically producing the most severe cases. When antibiotics are given to kill the bacteria, the dying organisms release toxins that reduce expression of the sodium channel and help keep it closed at a time when it needs to work even harder. "The natural system is being impaired by an infection," Lucas said.

TNF weighs in as well. It's recruited as part of the body's natural defense against the bacterial infection, producing reactive oxygen species to help destroy the organism but also blocking the sodium pathway. It can even produce more fluid in the lungs by making capillaries leaky.

The TIP peptide appears to help the body do what's needed at that moment: keep sodium channels open, intact, and safe from bacterial toxins. "You have two opposing sides within the same TNF molecule," Lucas said. "We give much more of the positive part so we can actually help it function much better than the normal response."

Mice with less expression of this sugar-loving TIP experience a lot more swelling, or edema, and those missing the alpha subunit of the sodium pump can't survive.

For the laboratory studies, scientists used the strongest toxin produced by the pneumonia-causing bacteria so next steps include looking at the entire infection. Lucas is also looking at the effect of the TIP peptide in the flu with fellow MCG scientist Dr. Andrew Mellor and in kidney failure with MCG Medicine Chair Dr. Michael Madaio.

His studies in mice and pigs have shown the peptide increases fluid removal fourfold and improves blood oxygen levels.

Recent clinical trials of the peptide at the Medical University of Vienna in patients with pulmonary edema, or swelling, who were at high risk of multiple organ failure and dying, showed that fluid removal occurred earlier and was significantly better in patients receiving the synthesized peptide. It worked best in the sickest patients and no side effects have been reported.

The biotechnology company APEPTICO has a patent on the peptide and funded the clinical studies in which it was given twice daily through the ventilator mask helping support breathing.

In healthy individuals, sodium channels are pretty much always open, people make very little TNF, and there is very little fluid in the lungs.

Provided by Medical College of Georgia