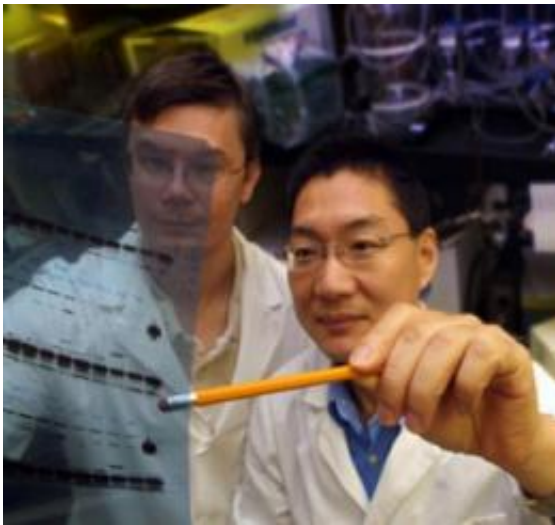


# Powerful free radical causes lung damage from oxygen therapy

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Drs. Yunchao Su and Dmitry Kondrikov have found a major cause of the lung damage that can result from use of oxygen therapy in the critically ill or injured. Credit: Phil Jones Campus Photographer

The most toxic free radical appears responsible for much of the lung damage that can result from oxygen therapy in the critically ill or injured, Medical College of Georgia researchers report.

Within just a few days, ventilators and oxygen chambers used to significantly increase oxygen levels can also dramatically increase levels of peroxynitrite, an oxidant powerful enough to break down DNA and cause proteins to malfunction, said Dr. Yunchao Su, pharmacologist in

the MCG Schools of Medicine and Graduate Studies.

Oxygen toxicity is the most severe side effect of oxygen therapy in newborns and adults. The lungs take the brunt of the damage, which can include inflammation, hemorrhaging and swelling that may result in death or chronic lung problems, said Su, corresponding author of the study published in the [Journal of Biological Chemistry](#).

"We knew it was bad but we did not know why," Su said. The good news is they may also have a solution.

Researchers found that within five days, mice placed in small oxygen chambers that mimic oxygen levels given in intensive care have dramatically elevated levels of peroxynitrite in their lungs. Free radicals, such as peroxynitrite, result from oxygen use and are safe at low levels. While it's a given that oxygen therapy produces free radicals, the significant increase in peroxynitrite was not known.

The trouble begins when high oxygen levels prompt [endothelial cells](#) that line blood vessels and tiny air sacs in the lung to make more [nitric oxide](#), the precursor of peroxynitrite. At high levels, nitric oxide, most often a helpful compound, combines with other free radicals produced by excess oxygen use to form the powerful peroxynitrite. "As oxygen levels increase, nitric oxide levels increase and so peroxynitrite levels do as well," Su said.

But he appears to have identified a break point in the destructive cycle. Su found that in the face of high oxygen levels, the enzyme that makes nitric oxide binds with the protein actin to produce more nitric oxide. So he developed a compound, peptide 326, that interferes with their binding and the excess peroxynitrite levels that typically follow. Su used the binding site itself as a cue for the peptide design after trying many existing compounds, including smoke, to break the bond.

Su's long term goal is for peptide 326, or something similar, to be used in patients likely after the first few days of oxygen therapy. Much as health care providers monitor blood oxygen long term to ensure sufficient levels, they could also monitor peroxynitrite levels. "It's only after several days of steady increases that the level becomes destructive," Su noted.

MCG scientists are already using peptide 326 in mice receiving [oxygen therapy](#).

Provided by Medical College of Georgia

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