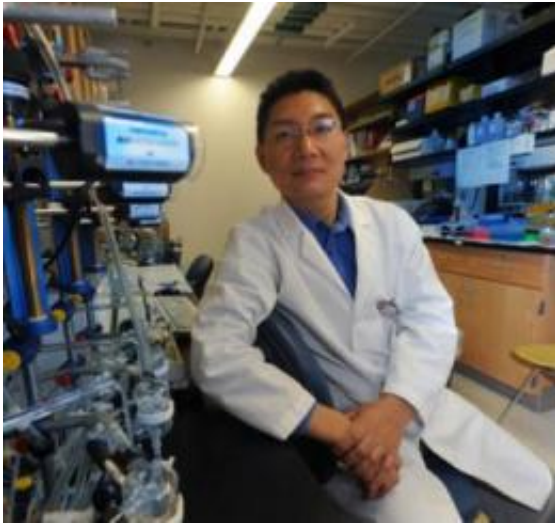


Protein is potential new treatment target for adult pulmonary hypertension

October 17 2011



Dr. Yunchao Su of Georgia's Health Sciences University has found the protein calpain holds promise for treating adult pulmonary hypertension. Credit: Phil Jones, GHSU photographer

A protein critical to development appears to have a grave impact on lungs exposed to smoking and air pollution, researchers report.

Blocking that protein, called calpain, in the lungs may prove an effective way to avoid narrow, scarred blood vessels and [pulmonary hypertension](#), said Dr. Yunchao Su, [pharmacologist](#) at Georgia Health Sciences University.

"Calpain enables the bad behavior that occurs in pulmonary hypertension," said Su, corresponding author of the study published in the [Journal of Clinical Investigation](#).

Pulmonary hypertension is an often progressive and deadly condition in which tiny blood vessels that permeate the lungs narrow, raising blood pressure and eventually enlarging the pumping chamber of the heart as it struggles to get blood inside the lungs.

Babies with [heart defects](#) can have it, but in adults it can result from chronic [obstructive lung disease](#), or COPD, primarily caused by smoking (emphysema is the most common form of COPD) or air pollutants, including second-hand smoke. Inflamed and poorly oxygenated lungs start producing growth factors and other measures to constrict blood vessels in an effort to restore balance between blood flow and [oxygen levels](#). This works in the short term, Su said, but a chronic stimulus such as smoking can make, ongoing constriction debilitating or deadly. Treatment improves symptoms such as shortness of breath, but the only cure is a heart-lung transplant.

Researchers found calpain gets activated by growth factors released by stressed lung tissue then multiplies the vascular remodeling by cleaving TGFbeta, another growth factor typically inactive in the lungs. Cleaving TGFbeta releases a strong, active form that increases [cell proliferation](#) and collagen production. A similar process helps heal a cut on the hand, but inside the blood vessel it's counterproductive, Su said.

Additionally, in animal models of pulmonary hypertension as well as lungs removed from patients getting a transplant, the researchers found elevated levels of calpain. When they blocked its action by giving an inhibitor or removing its gene, TGFbeta was not activated and vascular remodeling and scarring as well as the heart damage were prevented. "The pulmonary process was close to normal," Su said.

Next steps include seeing whether the calpain inhibitor can stop cell proliferation and collagen synthesis in lung cells removed during a biopsy. Toxicology studies also will be needed before looking toward clinical trials, Su said.

He noted that a calpain inhibitor is likely not feasible for children because of the protein's importance in development. He envisions an inhalable version of the inhibitor to minimize any side effects in adults.

Su's earlier studies helped define calpain's role in cell proliferation when he found that lung cells in culture healed just fine after being cut until he added the calpain inhibitor. The work was published in 2006 in the *The FASEB Journal*. Su suspected then that calpain also had a role in pulmonary hypertension.

Provided by Georgia Health Sciences University

Citation: Protein is potential new treatment target for adult pulmonary hypertension (2011, October 17) retrieved 28 April 2024 from <https://medicalxpress.com/news/2011-10-protein-potential-treatment-adult-pulmonary.html>

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