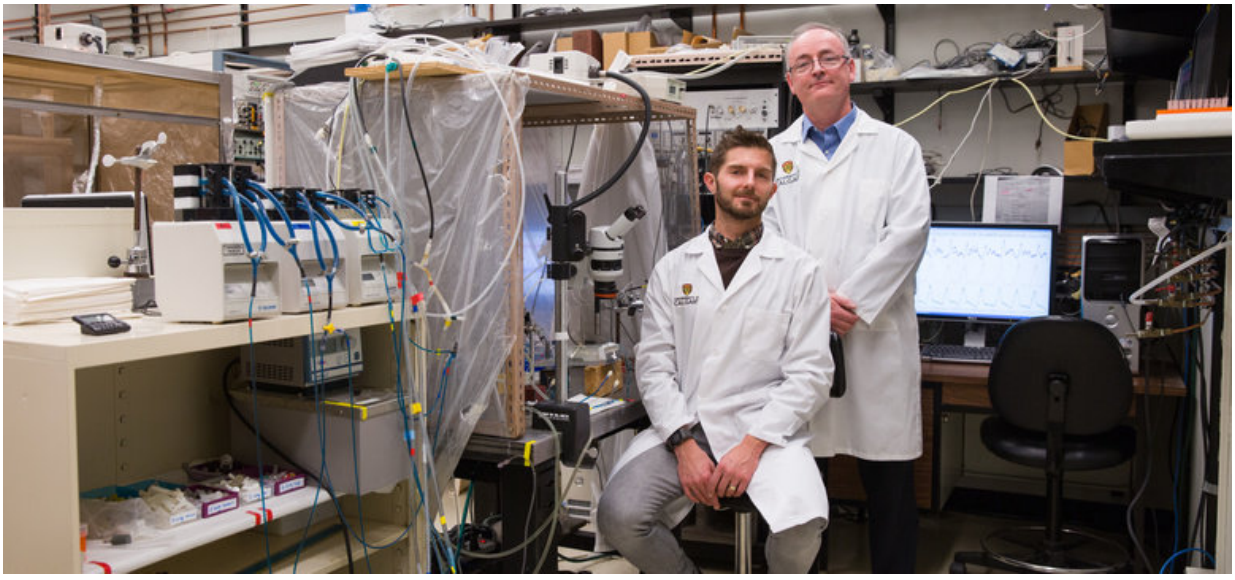
Scientists discover a new way to eliminate allergen-induced asthma attacks

October 9 2018, by Kelly Johnston



University of Calgary researchers Nick Jendzjowsky, left, first author on the study, and Richard Wilson describe the results of the study as 'immediate and dramatic.' . Credit: Riley Brandt, University of Calgary

Around the globe, an estimated 235 million people suffer from asthma. Most people are able to manage their symptoms and live healthy, active lives. However, for some, current treatments are not effective. Managing symptoms can be difficult because triggers are lurking everywhere.

"At one point, we had to remove all the carpets from our home. Dust

mites can trigger an attack. I've had to leave restaurants in the middle of a meal because someone's perfume is too strong. Smells can trigger an attack. Sometimes I feel like I can't leave my house," says Carolyn whose asthma is triggered by allergies. "When I do have an attack, I feel like someone is sitting on my chest, and I'm trying to breath around the weight. It's horrible, my whole body can start to shake and I can feel my lungs filling with mucus."

In asthmatics, the lining of the airways becomes inflamed and swollen. During an asthma attack, air passages in the lungs narrow and mucus production increases. To open the airways, asthmatics inhale medication to relax the airways and reduce lung inflammation. A difficult task, when you are struggling to take a breath and not always effective. Asthma attacks result in over 70,000 emergency room visits and 250 deaths in Canada each year.

University of Calgary scientists with the Alberta Children's Hospital Research Institute and Hotchkiss Brain Institute at the Cumming School of Medicine have discovered another way to help asthmatics breathe more easily by targeting treatment at the nervous system. A recent study performed on rats shows the carotid bodies, tiny collections of neurons on each side of the neck, may be responsible for causing lung airway narrowing during an allergen-induced asthma attack.

"This idea is going to come out of left field for some people. It's a completely new way to think about how the body responds during an asthma attack," says Dr. Richard Wilson, Ph.D., professor in the Department of Physiology and Pharmacology. "We've been able to show why the carotid bodies react during an asthma attack, how they make the attack worse and perhaps most importantly, how to block them to prevent an attack."

The carotid bodies signal the brain for many reasons—the main one is to

breathe. Cells in the carotid bodies detect oxygen and tell the brain when the oxygen is too low. In response, breathing increases.

Certain chemicals in the blood can also stimulate the carotid bodies. During an asthma attack, a naturally occurring chemical called lysophosphatidic acid, or LPA, increases in the lungs and in the blood stream. The team discovered that these higher levels of LPA stimulate the carotid bodies, and in response, the carotid bodies increase lung resistance so that the body cannot breathe as efficiently.

"We didn't expect this result. It's counterintuitive," says Dr. Nick Jendzjowsky, Ph.D., a post-doc fellow and first author on the study. "Normally, the carotid bodies increase lung resistance to keep the airways open so that the airways don't collapse when breathing increases to inhale more oxygen. But, asthmatics have compromised airways that are full of inflammation; the increased resistance caused by the carotid bodies makes it harder for asthmatics to breathe."

The researchers then decided to block the receptors in the carotid bodies from being able to detect the increased levels of LPA during an asthma attack.

"The results were immediate and dramatic. When we blocked the receptors, the carotid bodies were unable to create resistance in the lungs and the asthma attack was eliminated," says Wilson, a member of the Hotchkiss Brain Institute and Alberta Children's Hospital Research Institute at the CSM. "This was a eureka moment for us. The findings indicate that instead of targeting medications to the airways during an asthma attack, we can stop airway narrowing by blocking LPA activation of the carotid bodies."

"This could open the door for a new treatment for asthma," adds Jendzjowsky. "Instead of inhaling medication into the lungs, medicine

could be delivered via a pill or injection. During a severe asthmatic attack for example, we could use a similar approach to how EpiPens are used now in response to insect stings."

Moving from research in animals to humans involves a number of steps, but the scientists are hopeful that these promising results, published in *Nature Communications*, will encourage further studies to investigate the link they have discovered between acute asthma attacks and the response of the carotid body.

More information: Nicholas G. Jendzjowsky et al, Preventing acute asthmatic symptoms by targeting a neuronal mechanism involving carotid body lysophosphatidic acid receptors, *Nature Communications* (2018). DOI: 10.1038/s41467-018-06189-y

Provided by University of Calgary