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Novel study finds proton channels inhibit the release of histamine during allergic reactions

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Inhibiting the proton currents in basophils, a rare type of white blood cell, can stop the release of histamine and could provide a new target for allergy and asthma drugs according to a new study by researchers at Rush University Medical Center in Chicago and the Johns Hopkins Asthma and Allergy Center in Baltimore. The research is published in the August 5th issue the *Proceedings of the National Academy of Sciences*.

When allergens enter the body, they can be recognized by IgE antibodies bound to basophils, causing these white blood cells to release the inflammatory chemical histamine. Histamine causes several allergic symptoms, including airway constriction in the lungs, severe itching, hives and swelling, and is a major cause of asthma.

Basophils are among several cell types that express unique ion channels called voltage-gated proton channels. Ion channels open and close providing gates for ions, or charged electrical particles, to enter or leave cells. This in turn controls the function of the cell. Voltage-gated proton channels only allow protons to leave cells and seem to be designed to rapidly and efficiently force acid from cells.

Previously the function of the proton channels in basophils was unknown. Researchers at Rush have determined these channels are important in the process of histamine release.

"Our research shows that proton channels in basophils respond

vigorously to agents that elicit histamine release," said Thomas DeCoursey, PhD, professor of molecular biophysics and physiology at Rush. "We also determined that histamine was inhibited by zinc at concentrations that inhibit proton currents, consistent with the idea that proton channel activity is linked to basophil activation."

According to DeCoursey, this research points to a new target for drug developers. Prevent the channel from working and that would stop the release of histamine. Currently, the most potent inhibitor is zinc, but zinc is toxic in high concentrations and the body regulates zinc levels very closely. The goal is to develop a more selective inhibitor of the proton channel that would bind to it and prevent its activity without doing harm.

"It is exciting to discover a novel function for proton channels," said DeCoursey. "We believe this research could lead to new approaches to reduce the potentially deadly consequences of asthma and allergic reactions."

Source: Rush University