Promising Allergy Gene Identified

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DENVER , CO — Researchers at National Jewish Medical and Research Center have identified a protein, known as Ndfip1, that protects mice from developing a severe and deadly allergic disease. The research, published online November 30, 2006, in the journal *Immunity*, suggests that Ndfip1 could be potential therapeutic target for allergic diseases, especially atopic dermatitis.

"Our findings are especially exciting because the *ndfip1* gene in humans resides within a section of DNA that is associated with allergies," said Paula Oliver, PhD, lead author on the paper and a postdoctoral researcher at National Jewish. "Ndfip1 helps keep activated T cells in check, preventing them from secreting chemicals known to promote allergic reactions."

Before Dr. Oliver began her research scientists knew almost nothing about Ndfip1, except that it binds to another protein, Nedd4, one of a family of proteins known as ubiquitin ligases. Ubiquitin ligases are known to regulate immune responses in a wide range of animals. Dr. Oliver and her colleagues created mice with a mutation that made the *ndfip1* gene nonfunctional. The mice with this mutation were born healthy, but within six weeks developed a severe allergic and inflammatory disease of the skin and lungs, and died prematurely.

"The mice just can't stop itching," said Dr. Oliver.

Through a complex and lengthy set of experiments, the researchers determined that Ndfip1 helps terminate a message to activated T cells telling them to produce the cytokine interleukin-4 (IL-4). Without Ndfip1, activated T cells produce IL-4, which helps drive allergic and inflammatory immune responses. IL-4 is known to play a leading role in atopic dermatitis, an allergic skin disease whose sufferers have dry, itchy skin.

"Ndfip1 may play an important role in human allergic diseases, especially atopic dermatitis," said Dr. Oliver.

Dr. Oliver's ongoing research seeks to better understand how Ndfip1 inhibits an allergic response, and to investigate several similar proteins for their potential role in immune dysfunction.

Dr. Oliver's paper will also appear in the December 19, 2006, printed issue of *Immunity*.

National Jewish Health is the leading respiratory hospital in the nation. Founded 125 years ago as a nonprofit hospital, National Jewish Health today is the only facility in the world dedicated exclusively to groundbreaking medical research and treatment of children and adults with respiratory, cardiac, immune and related disorders. Patients and families come to National Jewish Health from around the world to receive cutting-edge, comprehensive, coordinated care. To learn more, visit the media resources page.

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