La Jolla Institute FOR ALLERGY AND IMMUNOLOGY | Life Without Disease.

News Release

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LA JOLLA INSTITUTE SCIENTIST IDENTIFIES PIVOTAL CELLULAR PROTEIN UNDERLYING ECZEMA

Discovery opens new therapeutic avenue for chronic skin condition affecting millions

SAN DIEGO – (January 9th, 2014) Researchers from the La Jolla Institute for Allergy and Immunology have revealed a critical player in the cellular interactions leading to eczema – a chronic inflammatory skin condition affecting more than 14 million U.S. children and adults.

In a study published today, Toshiaki Kawakami, M.D., Ph.D., and his research team provide information which supports – for the first time in humans – the long-held theory that mast cells are a key culprit in causing eczema, also known as atopic dermatitis. Further, the team showed that a cellular protein, known as STAT5, plays a pivotal role by triggering major increases in mast cells in the skin of some eczema sufferers. The discovery opens the door to creating new therapies to prevent or better treat eczema based on blocking STAT5 in mast cells.

The team conducted its studies using skin samples from eczema patients. "We found that the number of mast cells, which we have previously shown to be important in mouse atopic dermatitis, is increased in human patients," says Kawakami. "We also showed that these mast cells contain high levels of the active form of STAT5."

Kawakami says the researchers also tested their theory on STAT5's importance in mice. "When STAT5 is knocked out in the mast cells (of specially engineered mice), the mice become resistant to atopic dermatitis," says Kawakami. "This indicates that STAT5 regulatory mechanisms in mast cells are important for the pathogenesis of this disease."

The findings were published online in *Cell Reports* in a paper entitled "Critical role for mast-cell Stat5 activity in skin inflammation." The study was supported in part by the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health, under contract number N01 AI40030.

Eczema is a condition in which the skin becomes inflamed or irritated and is marked by redness, itchiness and dry, cracked skin. The exact cause of eczema is unknown, but it's thought to be linked to an overactive response by the body's immune system to allergens and irritants, similar to other allergic diseases such as asthma and food allergy. Eczema is more common in children than adults, since it sometimes resolves with age. About 10.7 percent of U.S. children and 3 percent of adults are estimated to be affected.

Kawakami says this finding is a continuation of his nearly 10-year effort to pinpoint the cascade of key cellular actions involved in eczema. Initially working in mice, his latest study enabled human confirmation of his key findings. "We now know that, in eczema, the mechanisms we found in mice are also operative in human disease," says Kawakami. Along with showing that mast cells and STAT5 drive the eczema process in humans, this study also found an enzyme -- Phospholipase C-beta3 (PLC-β3) – that can block the activation. PLC-β3 has a calming effort on STAT5 and can prevent it from driving up the mast cell numbers, explains Kawakami. "The mast cell numbers are inversely correlated with PLC-β3 levels," he says. "The more PLC-β3, the fewer the mast cells."

Mast cells have long been known to be central players in causing allergies. However until recently their role in eczema was strongly suspected, but not clear. In July of 2013, Kawakami published a study demonstrating the mast cell's importance in mouse models of eczema, followed by his current paper showing it in human skin samples.

His paper also included a genetic analysis, which showed that the four genes involved in mouse atopic dermatitis, including the genes for STAT5 and PLC-β3, are also contributors to human atopic dermatitis.

Other researchers in a multinational team contributed to this study, including those from Johns Hopkins University; University of California San Diego; National Research Institute for Child Health and Development (Tokyo); RIKEN Center for Integrative Medical Sciences (IMS-RCAI); Saga Medical University; Brigham and Women's Hospital, and University of Technology Dresden.

About La Jolla Institute

Founded in 1988, La Jolla Institute for Allergy and Immunology is a nonprofit, independent biomedical research institute focused on improving human health through increased understanding of the immune system. Its scientists carry out research seeking new knowledge leading to the prevention of disease through vaccines and the treatment and cure of infectious diseases, cancer, inflammatory, and autoimmune diseases such as rheumatoid arthritis, type 1 (juvenile) diabetes, Crohn's disease and asthma. La Jolla Institute's research staff includes more than 150 Ph.D.s and M.D.s. To learn more about the Institute's work, visit www.lji.org.

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