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IFM Therapeutics announces discovery of new immune system triggers

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IFM THERAPEUTICS

IFM Therapeutics (IFM), a privately held biopharmaceutical company focused on developing therapies that modulate novel targets in the innate immune system has announced the discovery of new immune system triggers that are associated with certain inflammatory diseases. The study, published in the Journal of Immunology, was co-authored by IFM co-founder Eicke Latz, M.D., Ph.D., along with colleagues Bernardo Franklin, M.D., Ph.D. and Juan Francisco Rodriguez-Alcázar of the Institute of Innate Immunity at the University of Bonn.

Charcot-Leyden Crystals (CLCs) are protein crystals that appear and persist in the tissues of patients with conditions such as asthma, allergic reactions, and fungal and parasitic diseases. Collectively, these are known as Eosinophilic diseases because of the marked increase of eosinophils, a part of the immune system consisting of a variety of white blood cells.

Following immune stimulus, eosinophils degranulate, releasing an array of cytotoxic proteins. One of these proteins, Galectin-10, crystallizes to form CLCs. Higher levels of CLCs correlate with higher eosinophil activity, which is believed to contribute to disease severity.

In this study, Dr. Latz's team demonstrates that CLCs are engulfed by human macrophages *in vitro,* resulting in the release of the pro-inflammatory cytokine IL-1?. Additionally, CLCs were shown to promote inflammation *in vivo,* as evidenced by an increased tissue presence of IL-1?. Importantly, chemical inhibition and small interfering RNA (siRNA) knock-down of NLRP3 in primary human macrophages reduced IL-1B production in response to CLCs, suggesting that the inflammatory response occurs via the NLRP3 inflammasome pathway.

"CLCs have been observed in patients for over 150 years. However, until recently, they were believed to be inert by-products of eosinophil activity with no immune activation," says Eicke Latz, M.D., Ph.D. "This study suggests that degradation of eosinophils leaves behind remnants that sustain immune activity. At a fundamental level, this supports the hypothesis that NLRP3 inhibition may be a therapeutically relevant approach for eosinophilic disorders, such as asthma and allergic disease."

NLRP3 (NOD-, LRR- and pyrin domain-containing 3) is an intracellular innate immune signaling receptor that allows immune cells to detect the presence of foreign or endogenous molecules that signal infection or tissue damage. Abnormal activation of the NLRP3 inflammasome typically occurs without the presence of a foreign pathogen, and is known to cause negative downstream effects.

"The work of our scientific founders, including Dr. Eicke Latz, further underscores the strong scientific rationale for targeting NLRP3 to treat chronic inflammation," said Martin Seidel, Ph.D., executive vice president of R&D at IFM. "By building on our vast knowledge of innate immune system pathways and their links to inflammatory processes, we are better equipped to lead the development of therapies for patients with serious inflammatory diseases."