

YOU ARE INVITED TO ATTEND THE
DEFENSE OF THE DOCTORAL
DISSERTATION

“CHARACTERIZING THE LOCAL AND SYSTEMIC ADAPTIVE
IMMUNE RESPONSES TO PROTEASE ALLERGENS”

By

Jihad El-Fenej

Infection, Immunity and Inflammation Program

M.S. Biology, 2017, St-Joseph’s University, Philadelphia, PA

B.S. Biology, 2015, Temple University, Philadelphia, PA

Thesis Advisor: Yosuke Kumamoto, PhD

Assistant Professor

Department of Pathology, Immunology and Laboratory Medicine

Wednesday, April 2nd, 2025

Cancer Center, G1196

11:00 A.M.

Join Zoom presentation

<https://rutgers.zoom.us/j/96299531250?pwd=gZMbM2B7IAKkMJ45IrVmOFwGrwP6Fv.1>

Meeting ID: 962 9953 1250

Password: 093999

ABSTRACT

Many environmental allergens are known to possess protease activity, but the outcome of the hosts adaptive immune response to protease allergens remains incompletely understood. Papain is a cysteine protease found in papaya latex and is commonly used as an experimental allergen. Papain induces potent type 2 inflammation upon primary exposure in the skin and lungs in mice, leading to the development of type 2 adaptive immunity including differentiation of papain-specific Th2 cells and B cells producing anti-papain antibodies. However, surprisingly little is known about how papain-specific adaptive immunity modulates host responses to papain upon re-exposure. We found that intraplantar injection of papain in naive mice induced acute edematous inflammation in the footpad that resolved within 24 hours. In contrast, re-exposure of these mice to papain in a different paw led to an attenuation of acute edema but paradoxically prolonged footpad inflammation lasting up to three days at the site of re-exposure. The challenged mice also exhibited hypothermia, indicating a systemic response to a local challenge. Notably, the proteolytic activity of papain is required to drive local edema, whereas papain-specific antibodies are responsible for the modulation of the local response and hypothermia in a mast cell-dependent manner. Inactivated papain was capable of inducing hypothermia without causing local edema in papain-immunized mice. However, when remotely administered, it attenuated acute edema but protracted inflammation in the footpad that was induced by a structurally unrelated protease. These data demonstrate that the pre-existing adaptive immunity to allergens can modulate protease-induced local inflammation in an antigen-nonspecific manner.