Allergy Research Laboratory

- 5 PIs
  - Alfred Doyle, Ph.D., Elizabeth Jacobsen, Ph.D., Hirohito Kita, M.D., Matt Rank, M.D., Ben Wright, M.D.
- ~4,000 sq. ft shared laboratory
  - Main laboratory, tissue culture, microscopy, mouse procedure, equipment
- A total of 17 members
  - Post-docs (4), students (4), technicians (4)
- From bench to bedside
  - Clinical studies and trials, animal models, basic immunology

Matthew Rank, M.D.

Ongoing Projects

- Asthma biologic use and outcomes
- Eosinophilic esophagitis and OIT GI effects (with Drs. Doyle and Wright)
- Chronic rhinosinusitis pathology and biomarkers (with Drs. Kita and Lal)
- Asthma biomarkers (with Drs. Jacobsen and Kita)
- Allergy-Immunology guideline development
- Aerobiology and air pollution (with Drs. Jacobsen, Kita, and Wright)
- Fiber for asthma (with Dr. Cope)
- COVID-19 clinical trials

Research Methods Expertise

- Clinical-translational research
- Systematic review and meta-analysis
- Guideline development
- Observational database research
- Survey research
- Clinical trials

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Current Grants

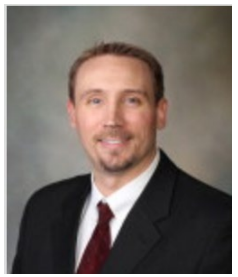
Asthma biologic step down (NHLBI)
PreCISE asthma trial (NHLBI)
ILC2s in CRS (NHBLI, PI Dr. Kita)
Fiber for asthma (Flinn Foundation, PI Dr. Cope)
Oral immunotherapy and EoE (Levin Family, PI Dr. Wright)
Colcorona (trial for COVID-19) (Montreal Heart Institute)

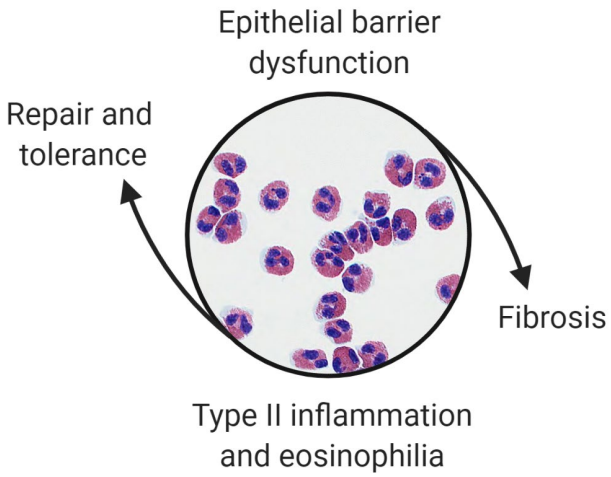
Recent Publications

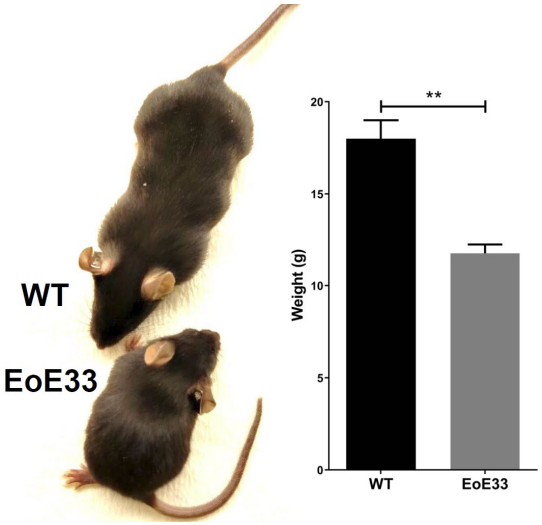
Wright BL, et al, Front Immunol 9:2624, 2018
Hines BT, et al, Ann Allergy 21(2):218-228, 2018
Yawn BP, et al, Ann Fam Med, 16(2), 2018
Rank MA, et al, Ann Allergy, 122(4):358-359, 2019
Doyle AD, et al, Eur Resp J, 53(5):1801291, 2019
Lal, D, et al J Allergy Clin Immunol, 143(6):2284-2287, 2019
Inselman, JW, et al, J Allergy Clin Immunol Pract 8(2):549-554, 2020
Shaker MS, et al, J Allergy Clin Immunol 145(4):1082-1123, 2020
Rank MA, et al, Gastroenterology 158(6):1789-1810, 2020

The Wright/Doyle Lab

Oral Immunotherapy (OIT)/ Eosinophilic Esophagitis (EoE)







Expression of secreted and active IL-33 *in vivo* results in failure to thrive.

Ongoing Projects

Clinical trial of milk OIT/dupilumab
Immunological mechanisms of EoE
Role of detergents/mucins in esophageal epithelial barrier function
Image analysis as a diagnostic tool for eosinophilic diseases

Current Grants/Applications

Levin Family Foundation – Define eosinophil-associated gastrointestinal complications associated with OIT
ADHS18-198880 Arizona Biomedical Research Consortium – The role of IgG4 in EoE
R37 AI71106-12 – characterize immune response to aeroallergens
FP00108639 – CEGIR Training Award for developing expertise in research and clinical care for eosinophilic gastrointestinal diseases
R21 AI132840-01A1 – Imaging tissue eosinophils
Mayo Foundation Funds – The role of IL-33 in airway remodeling
R01 NIAID (submitted) – The role of IL-33 in eosinophilic esophagitis
K23 NIAID (submitted) – Mechanisms of adverse GI events during OIT

Recent Publications

Wright BL, et al, J Allergy Clin Immunol Pract. 6:1799-1801, 2018.
Wright BL, et al, Front Immunol. 9:2624, 2018.
Doyle AD, et al, Eur Respir J. 53:1801291, 2019.
Lal D, Wright BL, et al, J Allergy Clin Immunol. 143:2284-2287, 2019.
Kurten RC, et al, Sci Rep. 17;9(1):6206, 2019.
Dellon ES, et al, Clin Transl Gastroenterol. 10(12):e00099, 2019.
Wright BL, Kita H, Mayo Clin Proc. 95(3):432-434, 2020.
Wright BL, Doyle AD, et al, Dig Dis Sci. Epub ahead of print, 2020.
Wright BL, et al, Clin Gastroenterol Hepatol. Epub ahead of print, 2020.

Jacobsen Lab

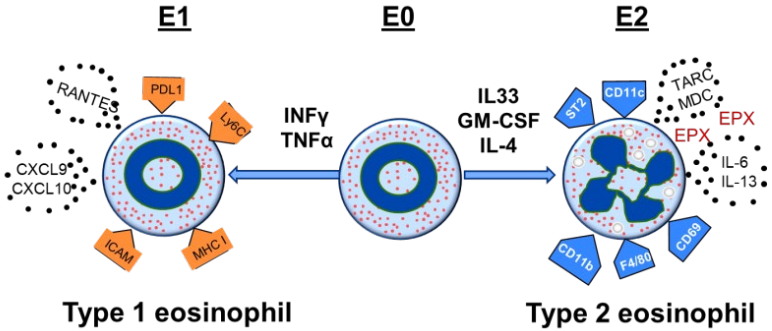
Eosinophil Biology

Jacobsen.Elizabeth@mayo.edu

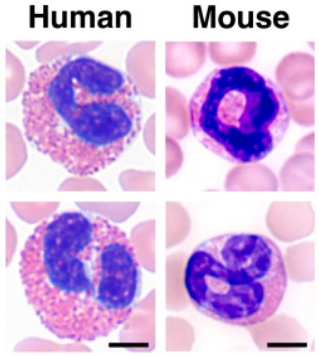
PubMed Search:
Jacobsen EA + Eosinophils

1. Defining Eosinophil Subtypes

(focus on immune subtypes)



RNAseq, protein assays, degranulation, flow cytometry, metabolics, histology….



Diverse and Novel Functions of Eosinophils

Cancer
Indicator of risk
T cell recruitment/polarization
Fibrosis/ECM remodeling
Vascular remodeling

Eosinophilic Esophagitis (EoE)
Fibrosis/ECM remodeling
Epithelial damage and hyperplasia

Mammary Development
Terminal end budding and morphogenesis
ECM remodeling
Vascular remodeling

Metabolic Homeostasis
Type 2 Diabetes
Fat deposition
M2 recruitment/activation
Atherosclerosis
Fibrosis/ECM remodeling
Vascular remodeling
Smooth muscle proliferation
Bone Growth Kinetics

Reproductive Homeostasis
Preterm Labor/Endometriosis
Follicle release from ovaries
Estrus cycle
Cervix post-labor
ECM Remodeling
Vascular remodeling
Immune Modulation

Transplant Rejection
Indicator of risk
T cell recruitment/polarization
Fibrosis/ECM remodeling
Vascular remodeling

Demyelinating Diseases
Multiple sclerosis
Neuromyelitic Optica
T cell polarization
Nerve survival
Plasma B cell survival

Lung Diseases
Asthma
Idiopathic Pulmonary Fibrosis
Pulmonary Hypertension
Acute Lung Injury
COPD
T cell recruitment/polarization
Fibrosis/ECM remodeling
Vascular remodeling
Smooth muscle hyperplasia
Epithelial damage and hyperplasia
Nerve Function and Survival

Inflammatory Bowel Diseases (IBD)
Crohn's Disease/Ulcerative Colitis
T cell recruitment/polarization
Fibrosis/ECM remodeling
Vascular remodeling
Smooth muscle hyperplasia
Epithelial damage and hyperplasia
Nerve Function and Survival

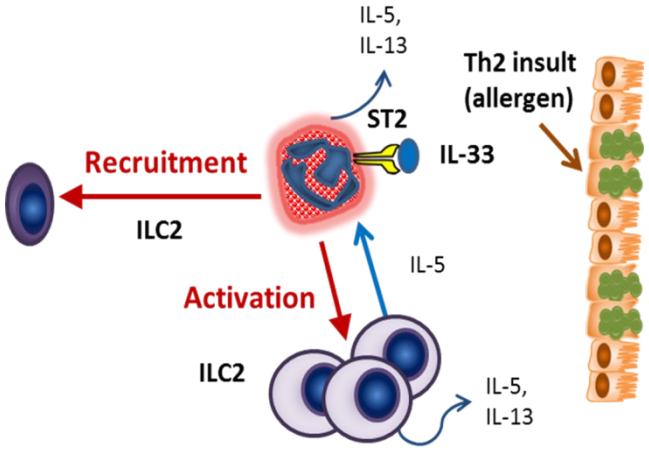
Innate/Adaptive Immunity
Host Defense
Cellular Immunity
Thymic T cell development
DC activation/recruitment
T cell polarization
Humoral Immunity
Plasma B cell survival

Duchenne Muscular Dystrophy
Fibrosis/ECM remodeling

Allergic/Chemical Contact Dermatitis
Neuron survival and growth
Fibrosis/ECM remodeling
Immune Modulation

2. Eosinophils and ILC2 Interactions

(focus on asthma)



3. Eosinophils in Lung Transplant

(with Dr. Krupnick, Vice Chief of Thoracic Surgey, UM)

OKWUDIRI ONYEMA ET AL.

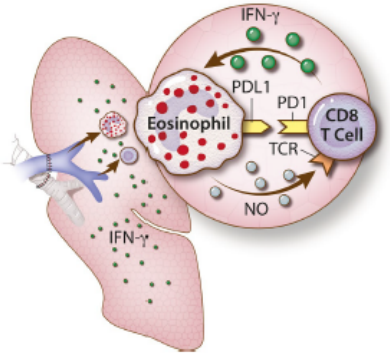


FIGURE 2 Mechanism of eosinophil-CD8$^+$ T cell tolerogenic feedback loops in the lung allograft. Effector CD8$^+$ T cells are the major culprits in allogeneic lung graft rejection. Naïve CD8$^+$ T cells become activated on experiencing alloantigen. This process is associated with TCR engagement and upregulation of differentiation associated molecules, such as PD-1, and the release of Th1-associated cytokines (IFN-γ and TNF-α). The Th1 cytokines released in the microenvironment milieu cause the polarization of eosinophils and their upregulation of PD-L1 and iNOS. PD-L1 binds to PD-1 to provide an immunologic synapse between eosinophil and CD8$^+$ T cells while iNOS catalyzes the synthesis of nitric oxide (NO) that inhibits TCR signaling in a feedback loop (reproduced from data described in [74,75,82]). IFN-γ, interferon γ; iNOS, inducible nitric oxide synthase; PD1, programed cell death protein-1; PDL1, programed death ligand-1; TCR, T cell receptor; TNF-α, tumor necrosis factor α

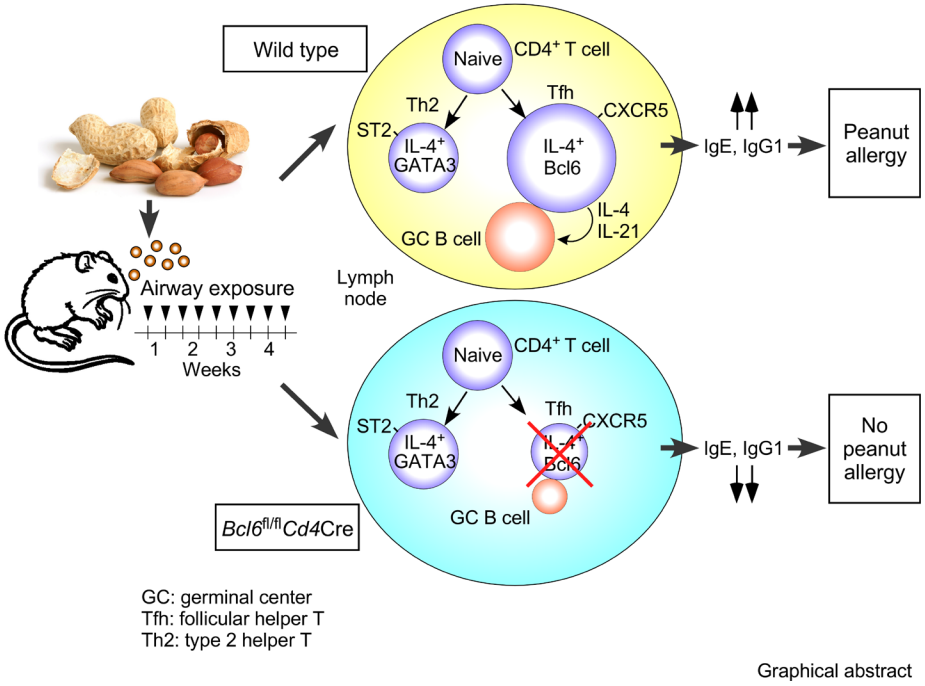
The Kita Lab (Hirohito Kita, M.D.)

Immunological mechanisms of asthma and allergic diseases

Ongoing Projects

- Immunobiology of group 2 innate lymphoid cells (ILC2s)
- Cellular mechanisms involved in development of asthma, hay fever and peanut allergy
- Roles of follicular helper T (Tfh) cells in regulation of IgE antibody production
- Immune function of airway epithelia cells
- Regulatory mechanisms involved in production and secretion of IL-33
- Immunological mechanisms of asthma and chronic rhinosinusitis in humans

Airway exposure initiates peanut allergy through follicular helper T cells in mice



Graphical abstract

From Dolence et al, JACI 2018

Current Grants

R37 AI71106 – Mechanisms Allergen-induced Type 2 Immunity
R01 HL117823 – ILC2s and asthma
R01 AI128729 – Mechanisms of IL-33 secretion in allergic diseases

Recent Publications

Kobayashi T, J Allergy Clin Immunol. 139:300-13, 2017.
Chen CC, J Allergy Clin Immunol. 140:1351-63, 2017.
Uchida M, Allergy 72:1521-31, 2017.
Drake LY, Immunol Rev 278:173-84, 2017.
Bartemes KR, J Immunol, 200:229-36, 2018.
Bartemes KR, J Allergy Clin Immunol 142:353-63, 2018.
Dolence JJ. J Allergy Clin Immunol 142:1144-58, 2018.
Drake LY. J Immunol, 203:1952-60, 2019.
Bacharier LB. J Allergy Clin Immunol 144:906-19, 2019.
Write BL. Mayo Clin Proc 95:43-4, 2020.
Krempski JW. J Immunol 204:3086-96, 2020.