The Hsieh lab's major research interests are in mast cell development and function, allergic inflammation and its impact in allergic disorders and lung biology, and investigation into systemic mastocytosis and hypereosinophilic syndromes. To this end we have worked with students, internal medicine residents, postdoctoral fellows, and clinical fellows in Allergy and Immunology at the Cleveland Clinic on clinical, translational, and basic science projects in these various areas of study. With regards to clinical research, recent investigations have characterized disease variants in subjects with eosinophilic myocarditis, reported cases and outcomes in subjects with AERD (aspirin-exacerbated respiratory disease) with prominent eosinophilia, and explored outcomes, prognostic markers, and disease complications in subjects with cutaneous and systemic mastocytosis. Current studies focus on the role of tryptase, a protease uniquely situated to identify mast cell numbers or mast cell activation, in the identification and management of subjects with chronic urticaria, anaphylaxis, cardiovascular disorders, and mast cell-activation syndromes. With regards to translational
In terms of bench research, our work has focused on aspects of mast cell activation and now mast cell development as it relates to the local tissue mast cell activation and expansion found in airway inflammatory diseases such as asthma.

Novel gene mutations in mastocytosis subjects by SNP-array analysis.

In terms of bench research, our work has focused on aspects of mast cell activation and now mast cell development as it relates to the local tissue mast cell activation and expansion found in airway inflammatory diseases such as asthma. Our initial work identified interleukin-4 as a key regulator of mast cell leukotriene C4-synthase expression and explored the mechanisms by which IL-4 primes human mast cells for significant cysteinyl leukotriene generation. Subsequent studies involving human mast cell-airway epithelial cell co-culture identified epithelial cell-derived stem cell factor as key regulatory factor driving intra-epithelial mast cell survival and expansion and characterized soluble stem cell factor and soluble C-KIT levels in the bronchoalveolar lavage and serum of asthmatics and controls. Our current work explores the hypothesis that mast cells and endothelial cells may share a common progenitor and that these or other progenitors may traffic to and/or expand in the lung in asthmatic subject, where the ultimate lineage commitment of these progenitors may be directed by specific local tissue microenvironmental factors that are modulated by disease states. Using in vitro and animal models and blood and tissue samples derived from human subjects, including asthmatic subjects, we have identified 'committed' endothelial cell lineage progenitors that can transdifferentiate into mast or other cells both in vitro and in vivo. Active areas of study include identification of mast cell-specific transcription factors critical for the differentiation of mast cells from various precursors (including hematopoietic stem cells, induced pluripotent stem cells, mesenchymal stem cells, and endothelial progenitor cells), dissection of the putative role of pSTAT5 in mast cell lineage commitment, determination if endothelial to mast cell transdifferentiation is augmented in murine models of airway inflammation, and identification of epigenetic chromatin modifications in mast cell-specific genes, chromatin modification transcription factors, and 'stemness'-associated transcription factors in normal and diseased states.

Collaborated with investigators in Pathology and Laboratory Medicine to study the utility of pSTAT5 immunostaining in identifying abnormal tissue mast cells and have an open collaboration with investigators in the Taussig Cancer Center to identify novel gene mutations in mastocytosis subjects by SNP-array analysis.

Image 1: Primary human mast cells derived in vitro stained with toluidine blue (63X magnification). Mast cells are effector cells distributed ubiquitously throughout the body and play a role in physiologic and inflammatory responses. This lab is currently exploring the derivation and development of mast cells from a variety of progenitor cells from different tissues in the body.

Image 2: pSTAT5 expression in human mast cells after cytokine stimulation (40X magnification). A variety of cytokines may promote the development of mast cells by activating specific transcription factors crucial for mast cell lineage commitment.
Awards

Nagy, Laura

Laura Nagy, PhD was awarded $35,000 from 08/01/2010 - 12/31/10, "Liver Research Center," funded through the Cleveland Clinic.

Fiocchi, Claudio

Claudio Fiocchi, MD received the Crohn’s and Colitis Foundations of America’s (CCFA) 2010 Janowitz Lifetime Achievement Award in IBD. This award is presented annually by the CCFA to an inflammatory bowel disease research scientist who has demonstrated career-long dedication to the discovery and understanding of Crohn’s or ulcerative colitis.

Khatri, Sumita

Sumita Khatri, MD was awarded $138,185 (direct) from 8/24/10 - 12/12/11, “A multicentre, randomized, double-blind, placebo-controlled, parallel group, dose ranging study to determine the effect of mepolizumab on exacerbation rates in subjects with severe uncontrolled refractory asthma,” funded by GlaxoSmithKline, Inc.

Asosingh, Kewal

Kewal Asosingh, PhD was awarded $70,000 over four years from 1/1/2011-12/31/2014, “Angiogenesis and Inflammation in Asthma,” American Heart Association National Scientist Development Grant.

Dweik, Raed

Raed Dweik, MD was awarded $344,594 over two years from 8/16/2010-5/31/2012, “S-nitrosothiol Analyzer for the Clinical Diagnosis of Cardiovascular Disease Markers,” National Institute of Health Small Business Innovation Research (SBIR) sub-award with Accord Biomaterials, Inc.
Heng Duong and Ilka Decker are two of five Cleveland Clinic medical students who received the HHMI Medical Research Fellows award. The fellowship supports a year of full-time biomedical research training for medical, dental, and veterinary students. This year there were 74 recipients of the award nationwide out of an applicant pool of 274 students.

Heng Duong is working in Dr. Serpil Erzurum’s lab under the mentorship of Drs. Kewal Asosingh and Serpil Erzurum. His project is entitled “An in vivo model to investigate the role of pulmonary arterial endothelial cells in pulmonary arterial hypertension”. The project seeks to elucidate the mechanism of dysregulated angiogenesis seen in pulmonary arterial hypertension (PAH), a poorly understood disease that leads to right heart failure and death. The roles of dysfunctional pulmonary artery endothelial cells (PAEC) and bone marrow-derived endothelial precursor cells in generating the vascular lesions of PAH will be investigated using xenograft of human PAEC into NOD SCID mice, thus allowing for in vivo study of PAEC biology.

Ilka Decker is working under the mentorship of Drs. Sudakshina Ghosh and Serpil Erzurum. Her project focuses on understanding the role of iron metabolism in pulmonary arterial hypertension (PAH). In clinical studies, Dr. Erzurum’s lab has shown that PAH patients have a functional iron deficiency that correlates with disease severity. Ilka is using pulmonary arterial smooth muscle cells to investigate the relationship between cellular oxygen sensing and iron metabolism and to elicit its impact on disease pathogenesis.

**Featured Stories**

**Achkar, J.P.**
Jean Paul Achkar, MD, Gastroenterology and Hepatology, comments on a study that shows patients with inflammatory bowel disease who are vitamin D deficient have a significantly increased risk for osteoporosis, osteopenia and abnormal bone density levels. Read the story on Medscape.

**McDonald, C.**
Christine McDonald, PhD, Pathobiology, and colleagues identified a common pathway altered by genetic variants in two genes known to be independently involved in CD risk, ATG16L1 and NOD2. [Homer et al. Gastroenterology 2010 Nov; 139:1630-41, 1641.e1-2; Impact Factor 12.899]

**Mattox, E.**
Emmea Mattox successfully completed the required course of study Investigational Product Monitoring: Intermediate, November 18, 2010.

**Erzurum, S.**
Serpil Erzurum, MD, Pathobiology, Respiratory Institute, comments on the new surgery to treat asthma. Read the story from The Wall Street Journal.
Presentations/Speakers

Fiocchi, Claudio

Claudio Fiocchi, MD, invited speaker, 9th Annual Broad Medical Research Investigator Meeting, "Stepping Away from the Trees to Look at the IBD Forest: the "omes" are here to stay," Los Angeles, CA, February 11, 2011.

Claudio Fiocchi, MD, invited speaker, Belgian Week of Gastroenterology, "Fibrosis in Crohn’s Disease, the Overlooked Villain," Liege, Belgium, February 17, 2011.

Erzurum, Serpil


Stuehr, Dennis


Boards/Committees

Dweik, Raed

Raed Dweik, MD was elected to be a member on the Board of Governors on January 1, 2011.
New Publications


Holiday Party
New Employees

Sabina Chandiramani
Research Student
Dweik Lab

Holly Cline, BS,
Research Technician
Nagy Lab

Manoa Hui, BA,
Coordinator

Brian Southern, MD,
Visiting Scientist,
Olman Lab

Sorana Pisano, BS,
Research Technician
Nagy Lab

Liping Tian, BS
Research Senior
Technologist
Dweik Lab

Manoj Veleeparambil PhD
Postdoctoral Fellow
Haque Lab

Not pictured:

Mary Beth Spitznagel, PhD,
Visiting Scientist
Kirwan Lab

James Kasper, PhD,
Postdoctoral Fellow
Nagy Lab

Promotions

Berk, Pamela, BS
Research Administrative Coordinator to Assistant Administrator

Han, Yingchun, MD

Homer, Craig, M.Sc.

Mavrakis, Lori, BM

From Senior Technologists to Lead Technologists
High Fives for the Quarter

NC2-22

Joe Cody
Reason for Recognition: Always helpful.

Carol de la Motte
Reason for Recognition: Terrific person and always so supportive.

Amrita Kabi
Reason for Recognition: For all the help setting up experiments in the weekend.

Lori Mavrakis
Reason for Recognition: For helping to fix the developer.

Lori Mavrakis
Reason for Recognition: For helping with tissue during Christmas/New Year.

Jin Rho
Reason for Recognition: Jin is always friendly, smiling, and eager to help when I have questions.

Jin Rho
Reason for Recognition: Taking the extra step when asked for help!

Benjamin Savasky
Reason for Recognition: Always flexible with time and planning.

Benjamin Savasky
Reason for Recognition: Always helpful.

Sean Kessler
Reason for Recognition: For always giving me the right answer!

Amy Richmond
Reason for Recognition: Always looking at the positive.

Judy
Reason for Recognition: Thanks for doing a good job!

NE4-40

Joyce Nolan
Reason for Recognition: For willfully and graciously helping out in the admin office.

Lourdes Gruca, Carole Bennett and Clarita Dueñas
Reason for Recognition: Great Meeting! Thanks.

Michele Pritchard
Reason for Recognition: Her outstanding commitment and dedication to the lab!

Yu Yang and Chengyang Zhao
Reason for Recognition: For conscientiously turning in the envelope money!!

Becky Sebastian
Reason for Recognition: Thanks for training us with image 4000R system. It’s very nice to meet you!

Susamma Abraham
Reason for Recognition: Being patient with me and helping whenever possible.

Contact information

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To learn more, visit our department on the web:
http://www.lerner.ccf.org/pathobio