The general goal of the Dweik laboratory is the study of biomarkers in lung disease. Our translational research approach starts with clinically relevant questions generated at the bedside or clinic which we then take to the laboratory bench to understand the underlying basic pathobiology with the purpose of finding a relevant biomarker that we can take back to the bedside and/or clinic. Metin Aytekin is a postdoctoral fellow who is focusing on the role of hyaluronan in the pathobiology of pulmonary hypertension. Gustavo Heresi, a clinical pulmonary fellow, has been studying myeloperoxidase as a biomarker in pulmonary hypertension. Jennie Newman is our research assistant who collects and compiles clinical data in our comprehensive IRB-approved pulmonary hypertension registry that has data on over 1500 patients. Natalia Grob is a medical student studying biomarkers in exhaled breath and breath condensate in asthma. Our collaborators include Dr. Serpil Erzurum and Dr. Suzy Comhair (nitric oxide studies), Dr. Carol de la Motte and Dr. Vincent Hascall (hyaluronan studies), and Dr. Stanley Hazen (myeloperoxidase studies). While more recently we have focused on the roles of hyaluronan, myeloperoxidase and other systemic biomarkers in pulmonary hypertension, a long term emphasis in our laboratory has been the study of biomarkers in exhaled breath in a variety of lung diseases.
Human exhaled breath contains thousands of molecules in a combination that is unique to each and every one of us and that can tell a lot about our state of health. With modern technology, we can now identify more than 5000 unique substances in exhaled breath. These substances include elemental gases like nitric oxide and carbon monoxide and a multitude of volatile organic compounds. Exhaled breath also carries aerosolized droplets that have other compounds dissolved in them as well. We now have the ability to test for all of these components. Nitric oxide (NO) for example is formed in high concentrations in the upper respiratory tract (nasopharynx and paranasal sinuses). Our studies have also conclusively demonstrated that the lower respiratory tract is a significant source of NO in exhaled breath with major implications to lung physiology and perfusion coupling in the lung. Interestingly, exhaled NO levels are low in pulmonary hypertension patients and high in patients with asthma. Pulmonary hypertension (PH), a group of diseases characterized by high pulmonary artery pressures and pulmonary vascular resistance, can be either idiopathic (primary) or secondary to an identifiable underlying pulmonary, cardiac, or systemic disease. Idiopathic pulmonary arterial hypertension (IPAH) previously referred to as primary pulmonary hypertension (PPH) is a progressive disease that affects predominantly young and productive individuals, is more common in females, and has a mean survival between 2 to 3 years from the time of diagnosis. Dr. Dweik was a part of the team that initially described low levels of NO in the exhaled breath of patients with PPH. Although this is a far more complex issue than the simple lack of a vasodilator, replacement of NO seems to work well in treating the problem. Our laboratory continues to explore the role of NO in the pathobiology of PH especially as it relates to its effects on the lung matrix components like hyaluronan. Patients with asthma, on the other hand, have high levels of NO in their exhaled breath but the exact role of NO in asthma and airway reactivity remains elusive despite intense research in this area. Whether NO is beneficial through its bronchodilator and antioxidant effects or harmful by inducing inflammation remains unclear. Regardless of the role of NO in the pathobiology of asthma, exhaled NO has become accepted as a biomarker of airway inflammation in asthma with FDA approved devices currently in clinical use. In 2008 a multi-institutional team led by the Dweik laboratory has been awarded one of six Ohio Biomedical and Research Commercialization Partnership 3rd Frontier Grants. The award is for $3.8 million dollars and will support research performed here at the Cleveland Clinic, as well as collaborating institutions that include NASA Glenn Research Center, The Ohio State University, Case Western Reserve University, and Makel Engineering, Inc. to develop a nitric oxide sensor that will enable asthma patients to monitor their asthma. This multi-institutional cross-discipline collaboration that resulted in this award started in late 2007 at the First International Breath Analysis Summit that was organized by an international committee led by Dr. Dweik. This unique conference was held on the Cleveland Clinic campus and brought together more than 160 researchers, clinicians, scientists, and industry representatives from 22 countries and 18 states. Thus, the overall goal of our laboratory is to understand lung physiology and pathology through the study of systemic and exhaled biomarkers. While our current focus is on the pathobiology of pulmonary hypertension, our work also covers lung physiology as well as the full spectrum of lung diseases that involve the airway (asthma), parenchyma (berylliosis-CBD), and the pulmonary circulation (pulmonary hypertension) (see Ven diagram).
A multi-institutional team led by Dr. Raed Dweik has been awarded one of six Ohio Biomedical and Research Commercialization Partnership 3rd Frontier Grants. Dr. Serpil Erzurum is a collaborating investigator, and other Cleveland Clinic personnel include Daniel Laskowski, RPFT, Metin Aytekin, PhD, and Jennie Newman. The award is for $3.8 million dollars, which will support research performed here at the Cleveland Clinic, as well as collaborating institutions throughout Ohio.

The press release from the Ohio Department of Development describing Dr. Dweik’s project: “The Cleveland Clinic, in collaboration with NASA Glenn Research Center, The Ohio State University, Case Western Reserve University, and Makel Engineering, Inc., was recommended for nearly $3.8 million to develop a nitric oxide sensor that will enable asthma patients to monitor their asthma at home. The proposal aims to re-develop a sensor used in the aerospace industry, and the project’s emphasis will be on testing and commercializing sensors already produced in Ohio.”

Selection for one of these awards is an outstanding accomplishment. Forty-two proposals from excellent investigators and institutions from around Ohio were submitted for these prestigious awards.

### Howard Hughes Award

**Fred Hsieh, M.D.**

Fred Hsieh has been awarded a ‘Howard Hughes Physician Scientist Award’. This is the first HHMI individual award ever at LRI. One of the long-term goals of the Howard Hughes Medical Institute (HHMI) is to increase the number of researchers who translate basic science discoveries into improved treatments for patients. To that end, in 2008 the HHMI awarded 19 physicians at 14 academic medical centers in the United States an HHMI Early Career Physician-Scientist Award, providing $375,000 over five years to help physician-scientists develop their individual research programs. This is the third year of the HHMI Early Career Physician-Scientist Award, and a total of 53 researchers have received a grant through this program.
Raed A. Dweik, MD, Director of the Pulmonary Vascular Program in the Respiratory Institute and Department of Pathobiology received two teaching awards from the Internal Medicine residents for the academic year 2007-08: “Teacher of the Year” and “Best Teacher at Senior Morning Report”. Each one of these awards is given annually to one staff member selected from all staff physicians in medicine and all medical subspecialties and the recipient is nominated by the Internal Medicine residents. Dr. Dweik has now received the Teacher of Year Award 5 times, including 4 of the last 5 years. In 2007, Dr. Dweik was also selected as the “Staff Teacher of the Year” by the Pulmonary Fellows and received the “Scholarship in Teaching Award” from Case Western Reserve University.

**Key Speaker, Dennis Steuhr, Ph.D.**

Dennis will be a key speaker at this international meeting. The 9th UK Nitric Oxide Forum Meeting will be held on Friday 22 August 2008 at Guy’s Campus, King’s College London, with the following Invited Keynote Lectures:

- Prof Victor Darley-Usmar (Univ. Alabama School of Medicine, USA) ‘Mitochondria: Nitric Oxide Signals to the Powerhouse’
- Prof Dennis Stuehr (Lerner Research Institute, USA) “Keep your friends close, and your enemies closer: How might NO control the biological functions of the NO synthases?”

**AHA grant, Ashis Biswas, Ph.D.**

Ashis Biswas, Ph.D. (postdoctoral fellow in Dr. Dennis Stuehr’s lab) was recently awarded an AHA Postdoctoral fellowship. He had submitted the grant entitled “What is the molecular basis for the low activity of endothelial NO synthase?” to the American Heart Association (AHA) [Great River Affiliate]. This post-doctoral award is for two years ($88,000.00).

**ATS grant, Kewal Asosingh, Ph.D.**

Kewal Asosingh, Ph.D. from Dr. Erzurum’s Lab. was recently awarded an ATS grant. “Role of Pulmonary Vascular Wall Resident Endothelial Progenitors and Circulating Bone Marrow-Derived Angiogenic Precursors in Idiopathic Pulmonary Arterial Hypertension”

Over the last several years, letter-of-intent submissions to the program have grown exponentially. The Committee ranked these applications according to scientific merit and awarded grants to these 17 researchers.

**National AHA grant Metin Aytekin, Ph.D.**

Metin Aytekin, Ph.D. postdoctoral fellow in Dr. Raed Dweik’s lab was recently awarded an American Heart Association (AHA) Postdoctoral fellowship grant. He had submitted the grant entitled “Hyaluronan in Idiopathic Pulmonary Hypertension”. This post-doctoral award is for two years.
New Employees

Angie Steitz
Financial Analyst
Admin office

Lori Mavrakis,
Sr. Technologist.
Comhair Lab.

Sougata Sinha Ray, P.h.D
Postdoctoral Fellow
Steur Lab.

Not pictured

Nivedita Clark,
Technician
Dodig Lab.

Eleni Stylianou, P.h.D.
Staff Scientist

Nancy Rebert, Sr.
Technologist
Achkar Lab.

Deepa Grandon George, M.D.
Fellow Erzurum Lab.

Susan Marczewski,
Clinical Research Nurse
Dasarathy Lab.

Special Awards Given by the CCF Dept of Pathobiology

Northeastern Ohio Science and Engineering Fair Held at CSU, March 10-13, 2008

Aiste Degesys
Beaumont School
Health-Medicine, grades 11-12
"Why sleeping beauty does not snore"

Geraldine Ranasinghe
Laurel School
Biology, grades 9-10
"Identifying the zfp28 gene in the human genome"

Peter Delaney
St Dominic Elementary School
Health-Medicine, grades 7-8
"A comparison of childhood allergies in 4 countries"

New Publications


Serpil C. Erzurum, M.D. (Chair of Pathobiology) hosted our second annual Pathobiology Department Research Day & Picnic on Tuesday, June 3rd, to end our educational seminar series. This academic year (Sept 2007- June 2008), Pathobiology hosted 32 internal seminars and external Visiting Professors. On June 3rd, over 30 posters and a GCRC video presentation were presented by our own labs and highlighted from various research projects presented through the 2007-2008 academic year at several meetings.

Mission:

The mission of the Department of Pathobiology is the discovery of mechanisms and origin of human disease, and the use of that knowledge for the development of basic and applied strategies for detection, prevention and control of disease.

The Cleveland Clinic Foundation has a long and distinguished history in research. Most of the 127 research laboratories are housed in the state-of-the-art Lerner Building. The scientists who conduct research in the LRI welcome applications from qualified individuals who wish to further their scientific careers by participating in and contributing to leading edge biomedical research.

What is it?

Can you tell what this photo is? Complete the form below and place it in the what is it? box by the pathobiology Administration office. One winner drawn from all correct entries will receive a Starbucks Gift card. Good luck!

Contact information

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