diopathic Pulmonary fibrosis (IPF) is progressive scarring disorder of the lung of unknown etiology. Those afflicted have an average survival similar to that seen with many forms of cancer. Current treatment is focused on the amelioration of symptoms, without addressing the underlying problem or staying the inexorable progression of the disease. This disease affects over 100,000 patients/yr in the US alone.

The driving force behind our research program is to help patients with IPF by going beyond the boundaries of current basic and translational research into this devastating disorder. To this end, our basic research laboratory studies the pathways by which fibroblasts, the cells that form the scar in pulmonary fibrosis, are activated. We study the factors and processes that induce fibroblast migration, proliferation and transdifferentiation in the context of pulmonary fibrosis.

Specifically, we are interested in the ability of the naturally occurring proteins of the coagulation/fibrinolytic (blood clotting/dissolving) system’s capacity to modulate fibroblast...
pro-fibrotic processes. Most recently, we are investigating the signals that promote fibroblast migration in response to ligation of the urokinase receptor by its cognate ligand, the protease urokinase. In spreading primary human lung fibroblasts, u-PAR co-localizes with multiple integrins in protrusive structures (See Fig 1.). Furthermore, blockade of u-PAR-integrin interactions in live cells reduces their integrin-dependent spreading and migration. As urokinase receptor is a GPI-linked protein, with no cytoplasmic domain, we are currently investigating the significance of lipid-raft localization and partnering with integrins of u-PAR-dependent intracellular signaling. Such studies are done at multiple levels. First, we study fibroblast biology in vitro with both normal fibroblasts, those expressing u-PAR mutations, and pulmonary fibrosis patient-derived fibroblasts. Such studies may lead to the identification of novel u-PAR-integrin signaling pathways of direct relevance to pulmonary fibrosis. Second, we use a murine model of the human disease to determine the significance of our in vitro findings to the pathogenesis of the pulmonary fibrosis in vivo. Third, we measure related parameters in vivo comparing patients with pulmonary fibrosis to those with normal lungs. This hierarchical approach will hopefully lead to rapid translation of findings at the bench to patients with pulmonary fibrosis.

As far as translational research, the Clinic (Dr. Jeff Chapman – Director ILD program) is currently enrolling patients in a novel trial for the National Institutes of Health-based Idiopathic Pulmonary Fibrosis Clinical Research Network (IPFnet; www.ipfnet.org). The Cleveland Clinic is one of only 22 sites around the US selected to participate in this new trial of anti-coagulant therapy for IPF. In fact, work in my lab and others’, has provided me the honor of developing the first national clinical trial to use treatments directed toward the coagulation system in patients with pulmonary fibrosis for the IPFnet. Furthermore, our lab was recently awarded a new NIH grant to definitively determine if coagulation abnormalities, including genetic thrombophilic states, underly the pathogenesis, can predict prognosis, or predict treatment-response in IPF using the NIH-funded national trial IPF cohort. Our current lab group includes Dr. Lisa Dominak, Dr. Sailaja Paruchuri, Dr. Mircea Pavkov, Jennifer Leising and Amy Castilano. We have other open positions in our lab. Those interested in joining a dynamic lab effort with focus on cell-matrix interactions, and/or protease biology, and/or pulmonary fibrosis are encouraged to send their CV to Dr. Mitchell Olman (Olmanm@ccf.org).
Awards

Nagy, Laura
Laura Nagy, PhD received an award for $1,089,345 from 03/01/10-02/28/13, entitled, “Acceleration of Hepatic Fibrosis by Alcohol: Role of Adenosine.” Funded by the Department of Defense (DOD).

Fiocchi, Claudio
Claudio Fiocchi, MD received a competitive renewal for $1,668,602 over 5 years from 04/15/2010-03/31/2015 entitled, “Cell interactions in the inflamed intestinal mucosa”. Funded by the National Institute of Diabetes and Digestive and Kidney Diseases of NIH.

Erzurum, Serpil
Serpil Erzurum, MD received a sub award from Wake Forest University Health Sciences for $116,180 over 2 years for “Linking Genetics, Genomics and Phenomics to Better Understand Asthma Severity.” This is a NIH “Grand Opportunities Grant” (GO grant) funded by the American Recovery and Reinvestment Act (ARRA).

Asosingh, Kewal
Kewal Asosingh, PhD was awarded an Investigator Initiated Study from the Novartis Pharmaceuticals Corporation for $342,416 from 01/15/2010 - 02/15/2011 entitled “Angiogenic Biomarkers in Pulmonary Arterial Hypertension treated with Imatinib”.

Kasumov, Takhar
Takhar Kasumov, PhD received an award for $153,540.00 from 1/1/2010-12/31/10 entitled, “Enabling Studies of Protein Dynamics.” Funded by the National Center for Research Resources of NIH.
Awards Continued

Haus, Jacob

Jacob Haus, PhD received a Research Endowment for 10,000 entitled, “Effect of Exercise and Diet on Protein Glycation.” Funded by the American College of Sports Medicine.

Chiang, Dian

Dian Chiang, MD in Dr. Laura Nagy’s lab was awarded the Dean Thiel Postdoctoral Research Fellowship Award beginning July 1, 2010 from the American Liver Foundation (AFL).

Awarded Best Doctors, March 2010 issue in Cleveland Magazine

Achkar, JP

Culver, Daniel

Dweik, Raed

Hsieh, Fred

McCullough, Arthur

McCurry, Kenneth
Presentations/Speakers

Claudio Fiocchi, MD, invited speaker of the XX Jornada de Gastroenterologia da Santa Casa do Rio de Janeiro conference in Rio de Janeiro, Brazil, March 2010.

Claudio Fiocchi, MD, invited speaker of the 5th International Meeting on Inflammatory Bowel Diseases in Capri, Italy, April 2010.

New Publications

Asosingh, Kewal

Comhair, Suzy


Dweik, Raed


Erzurum, Serpil


Fiocchi, Claudio


Hsieh, Fred

Kalhan, Satish

Kirwan, John


McCullough, Arthur

Nagy, Laura


Olman, Mitchell

Stuehr, Dennis


Swaisgood, Carmen
The ATS International Conference is one of the largest gatherings of pulmonary, critical care and sleep clinicians and researchers in the world. More than 14,000 people from 90 countries attended last year’s Conference. The annual International Conference was held in New Orleans and offered many sessions and several speakers on important scientific and clinical advances in pulmonary, critical care, and sleep medicine. Many topics were covered including adult and pediatric respiratory medicine, asthma, COPD, lung cancer, obstructive sleep apnea, pulmonary hypertension, cystic fibrosis, ARDS, and sarcoidosis. A major strength of the International Conference is the ability of clinicians and researchers to interact and to exchange ideas. The Conference is also an excellent opportunity to become involved with other ATS programs and activities.
New Employees

Allison Bode
Research Student
Erzurum Lab

Ciaran Fealy, BS
Research Scholar
Kirwan Lab

Sailaja Paruchuri, PhD
Research Associate
Olman Lab

Amanda Metzger, PhD
Research Technologist
Olman Lab

Amrita Kabi, PhD
Post-doctoral Fellow
McDonald Lab

Claudio Fiocchi, MD became an Honorary Foreign Member of the National Academy of Medicine of Brazil. The Brazilian National Academy of Medicine was founded in 1829 and is the oldest academy in Latin America. It has only 100 national members and few foreign members.

Outstanding Biotechnology Science Student Award
Allison Bode worked as student-technician for 8 weeks (April - May) with Dr. Kewal Asosingh. Her project involved enumeration of circulating proangiogenic progenitors in peripheral and pulmonary artery blood obtained from patients with cardiovascular disorders, undergoing right heart catheterization (in collaboration with Dr. Wilson Tang, Cardiovascular Medicine). She graduated on May 15th this year from Lakeland College as Associate of Applied Science in Biotechnology Science and has been selected for the Outstanding Biotechnology Science Student Award 2010. Allison will continue with her education to obtain a Bachelor’s degree in biology while working part-time in our department.
The Annual Pathobiology poster day was held on Tuesday, June 8, 2010. There were more than 30 posters presented by graduate students, medical fellows, post-doctoral fellows, technologists, research associates and junior faculty in the department. The posters were well attended, in part as department members searched for answers to this years “data scavenger hunt”. Posters were judged by faculty, post-docs, graduate students and technologists and 5 presenters were given Best Poster prizes.

**Poster winners:**
Lisa Dominak, PhD, Post-doctoral Fellow, Olman Lab
Hui Tang, PhD, Post-doctoral Fellow, Nagy lab
Amy Richmond, Lead Technologist, McDonald lab
Becky Sebastian, Lead Technologist, Nagy lab
Iva Dostanic-Larson, Medical Student, Erzurum Lab

**Scavenger Hunt Winners:**
Amy Richmond
Mahfuzul Haque
Charlotte Bhasin

*Thanks to everyone for making this a very exciting poster day event!*
Summer Students

Alecia Blaszczak,
Summer Student,
Kirwan Lab

Amanda Scelsi,
Summer Student,
Kirwan Lab

Jonathan Lang,
Summer Student,
Hsieh Lab

Amir Al-Dabagh,
Medical Student,
Culver Lab

Mark Barnes,
Graduate Student,
Nagy Lab

Maria Chan,
Summer Student,
Erzurum Lab

James Barton,
Summer Student,
Kirwan Lab

Not-pictured Summer Students
Joshua Asamo, Culver Lab
Aditi Gupta, Kalhan Lab
Amanda Hardy, Olman Lab
Nick Kar, Stuehr Lab
Anam Khan, Erzurum Lab
Roxanne Krylaikais, Comhair Lab
Kristen Krymowski, de la Motte Lab
Robert Malinak, Pritchard Lab
Jaime Newman, Dweik Lab
Corey Sheerer, Kirwan Lab
Molly Singer, de la Motte Lab
Rashmi Singh, Erzurum Lab
Ryan Verbic, de la Motte Lab
Sylvia Williams, Nagy Lab

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Contents by Nicole FENNELL e-mail: fenneln@ccf.org

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