Interstitial lung disease/Pulmonary fibrosis

Sergei Atamas (satamas@som.umaryland.edu):

Dr. Atamas's research focuses on the molecular and cellular mechanisms of pulmonary fibrosis and asthma, specifically the interplay between immune inflammation and fibrosis. The Atamas lab utilizes advanced methods of gene delivery in experimental animals in vivo (adenovirus- and lentivirus-mediated delivery of mouse and human genes), various genetically altered mouse models, cell culture-based molecular research that focuses on intracellular signaling pathways that regulate fibroblast differentiation, proliferation and production of extracellular matrix, and advanced methods of gene and protein expression. Prior work has focused on the cytokines an alternatively spliced variant of IL-4, CCL18/PARC, oncostatin M, CCL2/MCP-1, and IL-33, and the cell surface molecules CD40–CD40L and T cell-associated integrins. More recently, the focus of the Atamas lab has expanded to include intracellular/intranuclear regulators of inflammation and fibrosis, including IL-33 precursor, NEU1 sialidase, and sirtuins.

Highlighted Publications:

1. Luzina IG, Todd NW, Nacu N, Lockatell V, Choi J, Hummers LK, Atamas SP. Regulation of pulmonary inflammation and fibrosis through expression of integrins αVβ3 and αVβ5 on pulmonary T lymphocytes. Arthritis Rheum 2009, 60:1530-9

2. Luzina IG, Salcedo MV, Rojas-Peña ML, Wyman AE, Galvin JR, Sachdeva A, Clerman A, Kim J, Franks TJ, Britt EJ, Hasday JD, Pham SM, Burke AP, Todd NW, Atamas SP. Transcriptomic evidence of immune activation in macroscopically normal-appearing and scarred lung tissues in idiopathic pulmonary fibrosis. Cell Immunol. 2018, 325:1-13.

3. Luzina IG, Pickering EM, Kopach P, Kang PH, Lockatell V, Todd NW, Papadimitriou JC, McKenzie AN, Atamas SP*. Full-length IL-33 promotes inflammation but not Th2 response in vivo in an ST2-independent fashion. J Immunol. 2012, 189:403-10. **Faculty of 1000 Prime Recommended (Article Recommendation 717959565)*

4. Luzina IG, Kopach P, Lockatell V, Kang PH, Nagarsekar A, Burke AP, Hasday JD, Todd NW, Atamas SP. Interleukin-33 potentiates bleomycin-induced lung injury. Am J Respir Cell Mol Biol. 2013, 49:999-1008

5. Kopach P, Lockatell V, Pickering EM, Haskell RE, Anderson RD, Hasday JD, Todd NW, Luzina IG, Atamas SP. IFN-γ directly controls IL-33 protein level through a STAT1- and LMP2-dependent mechanism. J Biol Chem. 2014, 289:11829-43

6. Clerman A, Noor Z, Fishelevich R, Lockatell V, Hampton BS, Shah NG, Salcedo MV, Todd NW, Atamas SP*, Luzina IG. The full-length interleukin-33 (FLIL33)-importin-5 interaction does not regulate nuclear localization of FLIL33 but controls its intracellular degradation. J Biol Chem. 2017, 292:21653-61. *Senior co-author and corresponding author

Links:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Atamas-Sergei/
PubMed publications: https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/41582342/?sort=date&direction=descending
Google Scholar https://scholar.google.com/citations?user=C2LOTocAAAAJ

Konstantin Birukov (kbirukov@anes.umm.edu):

Dr. Birukov's research interests cover several areas including: a) signal transduction; b) cytoskeletal mechanisms of endothelial permeability and inflammation; c) control of endothelial function by mechanical forces; d) role of oxidized phospholipids in lung pathobiology. His laboratory uses advanced biophysical and imaging methods, endothelial cell culture models of mechanical stress, and animal models of lung injury to understand the autoregulatory cascades providing recovery and resolution of acute lung injury. He developed a new area of research addressing novel, barrier-protective and anti-inflammatory properties of oxidized phospholipids

and proposed a new group of synthetic phospholipase resistant lipid mediators for future treatment of lung injury, inflammation and vascular barrier dysfunction.

Highlighted Publications:

1. Birukova, A. A., Shah, A. S., Tian, Y., Gawlak, G., Sarich, N., & Birukov, K. G. (2016). Selective Role of Vinculin in Contractile Mechanisms of Endothelial Permeability. *Am J Respir Cell Mol Biol.* 55(4), 476-486. PMCID: PMC5070106

2. Ke Y, Oskolkova O, Sarich N, Tian Y, Sitikov A, Tulapurkar M, Son S, Birukova AA, Birukov KG (2017). Effects of prostaglandin lipid mediators on agonist-induced lung endothelial permeability and inflammation. *Am J Physiol Lung Cell Mol Physiol.* 313(4), L710-L721. PMID: 28663336.

3. Ohmura T, Tian Y, Sarich N, Ke Y, Meliton A, Shah AS, Andreasson K, Birukov KG, Birukova AA (2017). Regulation of lung endothelial permeability and inflammatory responses by prostaglandin A2: role of EP4 receptor. *Mol Biol Cell*. 28(12), 1622-1635. PMID: 28428256.

4. Ke Y, Zebda N, Oskokova O, Afonyushkin T, Berdyshev E, Tian Y, Meng F, Sarich N, Bochkov VN, Wang JM, Birukova AA, Birukov KG (2017). Anti-Inflammatory Effects of OxPAPC Involve Endothelial Cell Mediated Generation of LXA4. *Circ Res* 121(3):244-257. PMID: 28522438.

5. Oskolkova O, Sarich N, Tian Y, Gawlak G, Meng F, Bochkov VN, Berdyshev E, Birukova AA, Birukov KG. (2018) Incorporation of iloprost in phospholipase-resistant phospholipid scaffold enhances its barrier protective effects on pulmonary endothelium. *Sci Rep.* 17;8(1):879. PMCID: PMC5772615

Links:
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PubMed publications: https://www.ncbi.nlm.nih.gov/pubmed/?term=birukov+k

Jeffrey Hasday (jhasday@som.umaryland.edu)**:**

The Hasday lab has focused on how febrile-range hyperthermia and hypothermia modify biological processes relevant to disease pathogenesis with emphasis on acute lung injury/ARDS and fibrosis. Using approaches that span structural biology, gene and protein expression, cell culture, animal models and human trials, the Hasday laboratory has shown that hyperthermia worsens and hypothermia improves lung injury by modifying endothelial permeability, neutrophil recruitment, epithelial injury, and cytokine and heat shock protein expression. Dr. Hasday is expanding on his open-label trial of therapeutic hypothermia in ARDS by currently conducting a randomized clinical trial of hypothermia vs. standard temperature management in patients with ARDS. The p38 MAP kinase pathway appears to be a major contributor to the temperature-dependence of endothelial barrier function and expression of pro- inflammatory cytokines. The Hasday laboratory is following up on exciting data showing that the structure and function of p38alpha, the proinflammatory p38 family member, but not p38beta is temperature-dependent in the 33° to 39°C range. Finally, the Hasday laboratory in collaboration with Dr. Paul Shapiro in the School of Pharmacy is designing novel p38alpha inhibitors that target the substrate binding domain rather than the catalytic domain of p38alpha. These novel compounds modify rather than inactivate its downstream signaling, are superior to conventional catalytic p38 inhibitors in preclinical testing, and are being developed into potential new drugs to treat ARDS and other inflammatory diseases. Dr. Hasday also directs the University of Maryland Cytokine Core Laboratory (www.cytokines.com).

Highlighted Publications:

1. Shah NG, Tulapurkar ME, Ramarathnam A, Brophy A, Martinez R 3rd, Hom K, Hodges, T, Samadani R, Singh IS, MacKerell AD Jr, Shapiro P, Hasday JD. Novel Noncatalytic Substrate-Selective p38α-Specific MAPK Inhibitors with Endothelial-Stabilizing and Anti-Inflammatory Activity. J Immunol. 2017; 198(8):3296-3306. Pubmed PMID: 28298524.

2. Slack DF, Corwin DS, Shah NG, Shanholtz CB, Verceles AC, Netzer G, Jones KM, Brown CH, Terrin ML, Hasday JD. Pilot Feasibility Study of Therapeutic Hypothermia for Moderate to

Severe Acute Respiratory Distress Syndrome. Crit Care Med. 2017 45:1152-59;PubMed PMID: 28406814.

3. Tulapurkar ME, Ramarathnam A, Hasday JD, Singh IS. Bacterial lipopolysaccharide augments febrile-range hyperthermia-induced heat shock protein 70 expression and extracellular release in human THP1 cells. PLoS One. 2015;10(2):e0118010. PubMed PMID: 25659128; PubMed Central PMCID: PMC4320107.

4. Gupta A, Cooper ZA, Tulapurkar ME, Potla R, Maity T, Hasday JD, Singh IS. Toll-like receptor agonists and febrile range hyperthermia synergize to induce heat shock protein 70 expression and extracellular release. J Biol Chem. 2013 Jan 25;288(4):2756-66. PubMed PMID: 23212905; PubMed Central PMCID: PMC3554941.

5. Tulapurkar ME, Almutairy EA, Shah NG, He JR, Puche AC, Shapiro P, Singh IS, Hasday JD. Febrile-range hyperthermia modifies endothelial and neutrophilic functions to promote extravasation. Am J Respir Cell Mol Biol. 2012 Jun;46(6):807-14. PubMed PMID: 22281986; PubMed Central PMCID: PMC3380289.

6. Shah NG, Tulapurkar ME, Damarla M, Singh IS, Goldblum SE, Shapiro P, Hasday JD. Febrile-range hyperthermia augments reversible TNF-α-induced hyperpermeability in human microvascular lung endothelial cells. Int J Hyperthermia. 2012;28(7):627-35. PubMed PMID: 22834633.

Links:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Hasday-Jeffrey/
PubMed publications:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40776367/?sort=date&direction=ascending

Stella Hines (Shines@som.umaryland.edu):

Dr. Hines studies occupational & environmental lung disease with a particular focus on pulmonary physiology. She has a distinct interest in characterizing unique exposures in military populations, ranging from inhalational and systemic metal exposures, blast impact and other

airborne hazards in relation to measures of pulmonary physiology, including respiratory impedance. She also studies the use of different forms of respiratory protection among healthcare workers as protection from occupational hazards, with goals of improving preparedness for emerging infectious disease threats and strengthening the healthcare workforce infrastructure

Highlighted Publications:

1. Hines SE, Gucer P, Kligerman S, Breyer R, Centeno J, Gaitens J, Oliver M, Engelhardt S, Squibb K, McDiarmid M. Pulmonary Health Effects in Gulf War I Service Members Exposed to Depleted Uranium. Journal of Occupational and Environmental Medicine. 2013:55;937-944.
2. Hines SE, Barker EA, Robinson M, Knight V, Gaitens J, Sills M, Duvall K, Rose CS. Cross-Sectional Study of Respiratory Symptoms, Spirometry, and Immunologic Sensitivity in Epoxy Resin Workers. Clinical and Translational Science. 2015:8;722-28.
3. Hines SE, Mueller N, Oliver M, Gucer P, McDiarmid M. Qualitative Analysis of Origins and Evolution of an Elastomeric Respirator-based Hospital Respiratory Protection Program. Journal of the International Society for Respiratory Protection. 2017:34:95-111.
4. Hines et al. Impulse Oscillometry Measurement of Distal Airways Obstruction in Depleted Uranium Exposed Gulf War Veterans. American Journal of Industrial Medicine. Am J Ind Med. 2018 Feb 9. doi: 10.1002/ajim.22816. PMID: 29424024 DOI: 10.1002/ajim.22816
5. Kalchiem-Dekel, O. Hines SE. Forty years of reference values for respiratory system impedance in adults: 1977-2017. Respiratory Medicine. 2018;136:37-47.

Links:
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PubMed publications:

Nevins Todd (ntodd@som.umaryland.edu):

Dr. Todd is a physician-scientist with long-standing interest and experience in the diagnosis, clinical management, and clinical and molecular research in interstitial lung disease (ILD, pulmonary fibrosis). Over the past ten years, I have focused my basic, translational, and clinical research efforts on molecular abnormalities and clinical outcomes of patients with these pulmonary diseases. He is also the Director of the University of Maryland Pulmonary Fibrosis Foundation site.

Highlighted Publications:

1. Todd NW, Atamas SP, Luzina IG, Galvin JR. Permanent Alveolar Collapse is the Predominant Mechanism in Idiopathic Pulmonary Fibrosis. Expert Rev Respir Med 2015, 9:411-8.

2. Todd NW, Marciniak ET, Sachdeva A, Kligerman SJ, Galvin JR, Luzina IG, Atamas SP, Burke AP. Organizing Pneumonia/Non-specific Interstitial Pneumonia Overlap is associated with Unfavorable Lung Disease Progression. Respir Med.2015,109(11):1460-8.

3. Todd NW, Galvin JR, Sachdeva A, Luzina IG, Atamas SP, Burke AP. Microscopic Organizing Pneumonia and Cellular Nonspecific Interstitial Pneumonia are Widespread in Macroscopically Normal-Appearing Lung Tissue in Idiopathic Pulmonary Fibrosis. J Heart Lung Transplant 2016, 35(11):1367-1370.

4. Clerman A, Noor Z, Fishelevich R, Lockatell V, Hampton BS, Shah NG, Salcedo MV, Todd NW, Atamas SP, Luzina IG. The full-length interleukin-33 (FLIL33)-importin-5 interaction does not regulate nuclear localization of FLIL33 but controls its intracellular degradation. J Biol Chem 2017, 292(52):21653-21661.

5. Luzina IG, Salcedo MV, Rojas-Peña ML, Wyman AE, Galvin JR, Sachdeva A, Clerman A, Kim J, Franks TJ, Britt EJ, Hasday JD, Pham SM, Burke AP, Todd NW, Atamas SP. Transcriptomic evidence of immune activation in macroscopically normal-appearing and scarred lung tissues in idiopathic pulmonary fibrosis. Cell Immunol 2018, Jan 3 [Epub ahead of print]

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