

ILD/Fibrosis

Nevins Todd (ntodd@som.umaryland.edu): Dr Todd is a pulmonary physician with scientific research 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. I am the Director of the University of Maryland Pulmonary Fibrosis Foundation site and Director of the ILD Program at the University of Maryland.

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, Fischelevich 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
6. Kalchier-Dekel, Galvin JR, Burke AP, Atamas SP, Todd NW. Interstitial Lung Disease and Pulmonary Fibrosis: A Practical Approach for General Medicine Physicians with Focus on the Medical History. *J Clin Med* 2018, 7(12):1-27.
7. Amariei DA, Dodia N, Deepak J, Hines SE, Galvin JR, Atamas SP, Todd NW. Combined Emphysema and Pulmonary Fibrosis: Pulmonary Function Testing and a Pathophysiology Perspective. *Medicina* 2019, 55(9):580.
8. Luzina IG, Fischelevich R, Hampton BS, Courneya JP, Parisella FR, Lugkey KN, Baleno FX, Choi D, Kopach P, Lockatell V, Todd NW, Atamas SP. Full-length IL-33 regulates Smad3 phosphorylation and gene transcription in a distinctive AP2-dependent manner. *Cellular Immunology* 2020, 357:104203.
9. Graney BA, He C, Marll M, Matson S, Bianchi P, Cosgrove GP, Lee JS, PFF CCN Delphi Collaborators (Todd NW). Essential Components of an Interstitial Lung Disease Clinic: Results from a Delphi Survey and Patient Focus Group Analysis. *Chest* 2020, S0012-3692(20)34849-2.
10. Dodia N, Amarie D, Kenaa B, Corwin D, Chelala L, Britt EJ, Sachdeva A, Luzina IG, Hasday JD, Shah NG, Atamas SP, Franks TJ, Burke AP, Hines SE, Galvin JR, Todd NW. A Comprehensive Assessment of Environmental Exposures and the Medical History Guides Multidisciplinary Discussion in Interstitial Lung Disease. *Respiratory Medicine* 2021, 179:106333.

Links:

Med School faculty page: <https://www.medschool.umaryland.edu/profiles/Todd-Nevins/>

PubMed publications:

<https://www.ncbi.nlm.nih.gov/sites/myncbi/1VYDa8UwTBVQOP/bibliography/54623434/public/?sort=date&direction=ascending>

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. 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 currently has three areas of research: (1) the DoD-funded Cooling to Help Injured Lungs (CHILL) randomized clinical trial of mild hypothermia plus neuromuscular blockade vs. standard temperature management in patients with moderate to severe ARDS, a 14-center trial for which we serve as both the Data Coordinating Center and Clinical Coordinating Center; (2) expansion of our 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; and (3) the computer-assisted design of a novel class of substrate- and function-selective inhibitors of p38alpha for treatment of acute lung injury; one of these novel drugs has just completed Phase 1 studies and will begin Phase 2 studies in the near future. 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 p38 α -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](#).

7. Deredge, D., Wintrode, P., Tulapiurkar, M. E., Nagarsekar, A., Zhang, Y., Weber, D. J., Shapiro, P., and Hasday, J. D. (2019) A temperature-dependent conformational shift in p38 α MAP kinase substrate binding region associated with changes in substrate phosphorylation profile. *J. Biol. Chem.* 2019;294:1264-37. PubMed PMID 31073086.

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>

Konstantin Birukov (kbirukov@som.umaryland.edu): Dr. Birukov's research is aimed at better understanding of molecular events driving onset and resolution of acute lung injury and development of new therapies to mitigate pathologic signaling leading to ARDS. The studies cover several areas, including: a) role of circulating danger associated molecular patterns (DAMPs) as biomarkers and pathogenic factors augmenting ARDS; b) synergy between mechanical stretch, tissue stiffness and bacterial pathogens in propagation of lung injury and inflammation; c) control of endothelial function by mechanical forces; d) role of oxidized phospholipids in lung pathobiology and development of new phospholipid-based therapeutics. 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. Everitt ML, Boegner DJ, Birukov KG, White IM. Sample-to-answer diagnostic system for the detection of circulating histones in whole blood. *ACS Sens.* 2021
2. Wyman AE, Nguyen TTT, Karki P, Tulapurkar ME, Zhang CO, Kim J, Feng TG, Dabo AJ, Todd NW, Luzina IG, Geraghty P, Foronjy RF, Hasday JD, Birukova AA, Atamas SP, Birukov KG. Sirt7 deficiency suppresses inflammation, induces EndoMT, and increases vascular permeability in primary pulmonary endothelial cells. *Sci Rep.* 2020;10:12497
3. Kim J, Nguyen TTT, Li Y, Zhang CO, Cha B, Ke Y, Mazzeffi MA, Tanaka KA, Birukova AA, Birukov KG. Contrasting effects of stored allogeneic red blood cells and their supernatants on permeability and inflammatory responses in human pulmonary endothelial cells. *Am J Physiol Lung Cell Mol Physiol.* 2020;318:L533-L548
4. Karki P, Birukov KG, Birukova AA. Extracellular histones in lung dysfunction: A new biomarker and therapeutic target? *Pulm Circ.* 2020;10:2045894020965357
5. Karki P, Birukov KG. Oxidized phospholipids in healthy and diseased lung endothelium. *Cells.* 2020;9
6. Ke Y, Karki P, Kim J, Son S, Berdyshev E, Bochkov VN, Birukova AA, Birukov KG. Elevated truncated oxidized phospholipids as a factor exacerbating ALI in the aging lungs. *FASEB J.* 2019;33:3887-3900
7. Fang Y, Wu D, Birukov KG. Mechanosensing and mechanoregulation of endothelial cell functions. *Compr Physiol.* 2019;9:873-904
8. Karki P, Meliton A, Shah A, Tian Y, Ohmura T, Sarich N, Birukova AA, Birukov KG. Role of truncated oxidized phospholipids in acute endothelial barrier dysfunction caused by particulate matter. *PLoS One.* 2018;13:e0206251

Links:

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

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**, Barnes, AH, Brown, C, Gucer, P, Oliver, MS, Gaitens, JM, Condon, M, McDiarmid, M. Impulse Oscillometry Measurement of Distal Airways Obstruction in Depleted Uranium Exposed Gulf War Veterans. *American Journal of Industrial Medicine*. 2018;61:308-316.
2. **Hines, SE**, Brown, C, Oliver, M, Gucer, P, Frisch, M, Hogan, R, Roth, T, Chang, J, McDiarmid, M. User acceptance of reusable respirators in healthcare. *American Journal of Infection Control*. 2019;47:648-655.
3. **Hines, SE**, Brown, C, Oliver, M, Gucer, P, Frisch, M, Hogan, R, Roth, T, Chang, J, McDiarmid, M. Cleaning and Disinfection Perceptions and Use Practices Among Elastomeric Respirator Users in Healthcare. *Workplace Health and Safety*, 2020;68(12):572-582.
4. Glick, DR, Brown, CH, Li, L, Weiler-Lisowski, B, Gaitens, JM, McDiarmid, M, **Hines, SE**. Longitudinal Evaluation of Lung Function in Gulf War I Veterans Exposed to Depleted Uranium. *Journal of Occupational and Environmental Medicine*, 2020;62:1059-1062.
5. Dement J, Cloeren M, Ringen K, Quinn, P, Chen A, Cranford K, Haas S, **Hines SE**. COPD Risk among Older Construction Workers – Updated Analyses 2020. *American Journal of Industrial Medicine*. 2021; Mar 16; doi: 10.1002/ajim.23244.

Links:

Med School faculty page: <https://www.medschool.umaryland.edu/profiles/Hines-Stella/>

PubMed publications: <https://www.ncbi.nlm.nih.gov/myncbi/stella.hines.1/bibliography/public/>