Acute lung injury and ARDS

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:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Birukov-Konstantin/
PubMed publications: https://www.ncbi.nlm.nih.gov/pubmed/?term=birukov+k

Anna Birukova (abirukova@som.umaryland.edu):

Dr. Birukova's research addresses mechanisms of cytoskeletal regulation of lung inflammation and resolution of acute lung injury with focus on microtubule (MT)-associated signaling and endothelial barrier function. Her prior studies showed a link between MT disassembly, activation of small GTPase Rho, and leak in human lung endothelial cells (EC). Rho activation is triggered by the MT-bound Rho-specific guanine nucleotide exchange factor, GEF-H1. Cyclic-AMP suppresses Rho signaling and EC permeability by stabilizing MT. This MT-dependent pathway is activated by pathologic (high amplitude) cyclic stretch as well as vasoactive and pro-inflammatory agonists such as TGFβ and TNFα. Importantly for recovery from acute lung injury/ARDS, Dr. Birukova has discovered that stimulation of MT growth promotes restoration of peripheral cytoskeleton, cell junctions, and EC barrier integrity by facilitating activation of Rac GTPase. Dr. Birukova made the interesting and clinically relevant observation that unlike pathologic stress, physiologic cyclic stretch accelerates restoration of endothelial barrier function through Rap1 GTPase- and cingulin-dependent downregulation of RhoA signaling.

Highlighted Publications:

1. Tian X, Tian Y, Sarich N, Wu T, Birukova AA. Novel role of stathmin in microtubule-dependent control of endothelial permeability. *FASEB J,* 2012; 26(9): 3862-3874.

2. Tian Y, Gawlak G, Tian X, Shah A, Sarch N, Citi S, Birukova AA. Role of cingulin in agonist-induced vascular endothelial permeability. *J Biol Chem.* 2016; 291(45): 23681-23692.

3. Kratzer E, Tian Y, Sarich N, Wu T, Meliton A, Leff A, Birukova AA. ROS-mediated microtubule destabilization triggers GEF-H1-dependent endothelial permeability and inflammation in septic lung injury. *Am J Resp Cell Mol Biol,* 2012; 47(5): 688-697. PMCID:PMC3547103

4. Tian Y, Tian X, Gawlak G, O'Donnel JO, Sacks DB, Birukova AA. IQGAP1 regulates endothelial barrier function via EB1 - cortactin crosstalk. *Mol Cell Biol.* 2014; 34(18): 3546-3558.

5. Tian Y, Gawlak G, Shah AS, Higginbotham K, Tian X, Kawasaki Y, Akiyama T, Sacks DB, Birukova AA. HGF-induced Asef-IQGAP1 Complex Controls Cytoskeletal Remodeling and Endothelial Barrier. *J Biol Chem.* 2015 ;290(7): 4097-4109.

6. Tian X, Ohmura T, Shah AS, Son S, Tian Y, Birukova AA. Role of End Binding Protein-1 in endothelial permeability response to barrier-disruptive and barrier-enhancing agonists. *Cell Signal.* 2017; 29: 1-11.

Links:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Birukova-Anna/
PubMed publications: https://www.ncbi.nlm.nih.gov/pubmed/?term=birukova+anna

Simeon Goldblum (sgoldblu@som.umaryland.edu)**:**

Research in the Goldblum lab has focused on mechanisms through which septic and proinflammatory processes lead to pulmonary leukostasis and acute pulmonary microvascular endothelial injury and more recently glycobilogy. Mechanisms studied include (1) protein tyrosine kinases and phosphatases that regulate the cell-cell adherens junctions or zonula adherens in response to exogenous and endogenous mediators; (2) serine/threonine phosphorylation events that provoke reversible disassembly of the tight junction in response to *Vibrio cholera*-derived zonula occludins toxin (ZOT), and its human homologue, zonulin; and (3) the role of protein sialylation and the human sialidases in regulating the human airway epithelial

cell response to environmental cues and danger signals, including the role of the sialidase NEU1 in desialylating surface receptors, including MUC1.

Highlighted Publications:

1. Lillehoj EP, Hyun SW, Feng C, Zhang L, Liu A, Guang W, Nguyen C. Luzina IG, Atamas SP, Passaniti A, Twaddell WS, Puche AC, Wang LX, Cross AS, Goldblum SE. NEU1 Sialidase expressed in human airway epithelia regulates epidermal growth factor receptor (EGFR) and MUC1 signaling. *J Biol Chem* 2012; 287:8214-8231.

2. Cross AS, Hyun SW, Miranda-Ribera A, Feng C, Liu A, Nguyen C, Zhang L, Luzina IG, Atamas SP, Twaddell WS, Guang W, Lillehoj EP, Punche AC, Huang W, Wang LX, Passaniti A, Goldblum SE. NEU1 and NEU3 Sialidase Activity Expressed in Human Lung Microvascular Endothelia. NEU1 restrains endothelial cell migration whereas NEU3 does not. *J Biol Chem* 2012; 287:15966-15980.

3. Lee C, Liu A, Miranda-Ribera A, Hyun SW, Lillehoj EP, Cross AS, Passaniti A, Goldblum SE. NEU1 Sialidase Regulates the Sialylation State of CD31 abd Disrupts CD31-Driven Capillary-Like Tube Formation in Human Lung Microvascular Endothelia. *J Biol Chem* 2014; 289:9121-9135.

4. Lillehoj EP, Hyun SW, Liu A, Guang W, Verceles AC, Luzina IG, Atamas SP, Kim KC, Goldblum SE. NEU1 Sialidase Regulates Membrane-tethered Mucin (MUC1) Ectodomain Adhesiveness for *Pseudomonas aeruginosa* and Decoy Receptor Release. *J. Biol. Chem.* 2015; 290:18316-18331.

Links:

Med School faculty page: http://www.medschool.umaryland.edu/profiles/Goldblum-Simeon/

Bart Griffith (BGriffith@som.umaryland.edu):

Dr. Griffith's research focuses on development of an artificial lung and mechanical blood pumps, lung transplantion, and advanced treatment of ARDS with anti-inflammatory treatment, including stem cells and ECMO.

Highlighted Publications:

1. Wu ZJ, Gartner MS, Litwak KN, and **Griffith, BP**. Progress toward an ambulatory pump-lung. J Thorac Cardiovasc Surg 2005;130(4):973-8

2. **Griffith BP.** Children are not necessarily “small” adults: The growing field of miniaturized mechanical circulatory support. *Editorial Commentary* 2010 http://www.jhltonline.org

3. Iacono A, Groves S, Garcia J, **Griffith B**. Lung transplantation following 107 days of extracorporeal membrane oxygenation. Eur J Cardiothorac Surg 2010 Apr;37(4):969-71.

4. Garcia JP, Kon ZN, Evans C, Wu Z, Iacono AT, McCormick B and **Griffith BP**. Ambulatory veno-venous extracorporeal membrane oxygenation: Innovations and pitfalls. J Thorac Cardiovasc Surg 2011 Oct;142(4):755-61

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PubMed
publications: https://www.ncbi.nlm.nih.gov/sites/myncbi/bartley.griffith.1/bibliography/41145483/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. 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

Erik Lillehoj (elillehoj@peds.umaryland.edu)**:**

The Lillehoj laboratory focuses on the host response to lung infections caused by Pseudomonas aeruginosa, an opportunistic pathogen that impacts the morbidity and mortality of patients with a variety of respiratory diseases, including cystic fibrosis, ventilator-associated pneumonia, and chronic obstructive pulmonary disease. We have established that P. aeruginosa binds to airway epithelial cells through interaction of its flagellin with MUC1, a membrane-tethered mucin. More recently, using in vitro and in vivo model systems, we demonstrated that the P. aeruginosa flagellin-MUC1 interaction is regulated by neuraminidase-1 (NEU1), a host cell enzyme that desialylates MUC1. NEU1-mediated MUC1 desialylation not only renders it hyperadhesive for flagellin, but also increases its proteolytic shedding as a soluble decoy receptor that competitively inhibits P. aeruginosa adhesion to cell-associated MUC1. Our future goal is to develop the MUC1 decoy receptor as a novel therapeutic intervention for P. aeruginosa, and potentially other flagellated microbial pathogens, infecting the lungs.

Highlighted Publications:

1. Lillehoj EP, Hyun SW, Feng C, Zhang L, Liu A, Guang W, Nguyen C, Luzina IG, Atamas SP, Passaniti A, Twaddell WS, Puché AC, Wang LX, Cross AS, Goldblum SE. NEU1 sialidase expressed in human airway epithelia regulates epidermal growth factor receptor (EGFR) and MUC1 protein signaling. J Biol Chem. 2012 Mar 9;287(11):8214-31. doi: 10.1074/jbc.M111.292888. Epub 2012 Jan 13. PMID: 22247545.

2. Lillehoj EP, Hyun SW, Feng C, Zhang L, Liu A, Guang W, Nguyen C, Sun W, Luzina IG, Webb TJ, Atamas SP, Passaniti A, Twaddell WS, Puché AC, Wang LX, Cross AS, Goldblum SE. Human airway epithelia express catalytically active NEU3 sialidase. Am J Physiol Lung Cell Mol Physiol. 2014 May 1;306(9):L876-86. doi: 10.1152/ajplung.00322.2013. Epub 2014 Mar 21. PMID: 24658138.

3. Lillehoj EP, Hyun SW, Liu A, Guang W, Verceles AC, Luzina IG, Atamas SP, Kim KC, Goldblum SE. NEU1 sialidase regulates membrane-tethered mucin (MUC1) ectodomain

adhesiveness for Pseudomonas aeruginosa and decoy receptor release. J Biol Chem. 2015 Jul 24;290(30):18316-31. doi: 10.1074/jbc.M115.657114. Epub 2015 May 11. PMID: 25963144.

4. Hyun SW, Liu A, Liu Z, Cross AS, Verceles AC, Magesh S, Kommagalla Y, Kona C, Ando H, Luzina IG, Atamas SP, Piepenbrink KH, Sundberg EJ, Guang W, Ishida H, Lillehoj EP, Goldblum SE. The NEU1-selective sialidase inhibitor, C9-butyl-amide-DANA, blocks sialidase activity and NEU1-mediated bioactivities in human lung in vitro and murine lung in vivo. Glycobiology. 2016 Aug;26(8):834-49. doi: 10.1093/glycob/cww060. Epub 2016 May 25. PMID: 27226251.

Links:
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PubMed publications:
https://www.ncbi.nlm.nih.gov/sites/myncbi/erik.lillehoj.2/bibliography/41157356/public/?sort=date&direction=descending

Nirav Shah (nshah@som.umaryland.edu):

Dr. Shah's research interests are in clinical studies of therapeutic hypothermia on lung injury and systemic inflammation and developing and evaluating medical education, including curriculum design and incorporation of new teaching methods such as flipped classroom, small group learning, and simulation into fellowship training.

Highlighted Publications:
1. Shah NG, Tulapurkar ME, Damarla M, Singh I, Goldblum S, Shapiro P, Hasday JD. "Febrile-range Hyperthermia Augments Reversible TNFa-induced Hyperpermeability in Human Lung Microvascular Endothelial Cells" *Int J Hyperthermia* 2012; 28(7):627-35.

2. Shah NG, Cowan M, Pickering E, Sareh H, Afshar M, Fox D, Marron J, Davis J, Herold K, Shanholtz C, Hasday JD. “Nonpharmacologic Approach to Minimizing Shivering During Surface Cooling: A Proof of Principle Study.” *Journal of Critical Care* 2012; 27(6):746e1-8.

3. Shah NG, Seam N, Woods C, Fessler H, Goyal M, McAreavey D, Lee B. “A Longitudinal Regional Educational Model for Pulmonary and Critical Care Fellows Emphasizing Small Group and Simulation-Based Learning.” *Annals ATS* 2016; 13(4):469-74.

4. Shah R, Holden V, Robinett K, Shah NG. “Endobronchial Blocker Placement.” https://www.thoracic.org/professionals/clinical-resources/video-lecture-series/bronchoscopy/endobronchial-blocker-placement.php

5. Shah NG, Marr B, Netzer G, Tisherman SA. “Multi-disciplinary, Inter-professional Communication Simulations for Training Critical Care Fellows in Delivering Bad News and Discussing Brain Death” ATS Poster Presentation May 2018.

Links:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Shah-Nirav/

Carl Shanholtz (Cshanhol@som.umaryland.edu):

Dr. Shanholtz has had a longstanding interest in improving management of critically ill patients and has a long and successful record of clinical research in critical illness in general, and acute respiratory distress syndrome specifically. Together Dr. Roy Brower, Dr. Shanholtz conducted the phase II clinical trial of low tidal volume ventilation in ARDS on which the ARDSNet ALVEOLI study was based and he has been site director for ARDSnet-I and II. Dr. Shanholtz also studies pain management/sedation pathways and pain assessment in critically ill patients, methods to reduce fluid administration to critically ill patients, and is a co-investigator on Dr. Hasday’s clinical trial of therapeutic hypothermia in ARDS patients.

Highlighted Publications:
1. Netzer G, Dowdy DW, Harrington T, Chandolu S, Dinglas VD, Shah NG, Colantuoni E, Mendez-Tellez PA, Shanholtz C, Hasday JD, Needham DM. Fever is associated with delayed ventilator liberation in acute lung injury. Ann Am Thorac Soc. 2013 Dec;10(6):608-15. PubMed PMID: 24024608; PubMed Central PMCID: PMC3960965.

2. Shah NG, Cowan MJ, Pickering E, Sareh H, Afshar M, Fox D, Marron J, Davis J, Herold K, Shanholtz CB, Hasday JD. Nonpharmacologic approach to minimizing shivering during surface cooling: a proof of principle study. J Crit Care. 2012 Dec;27(6):746.e1-8. PubMed PMID: 22762936; PubMed Central PMCID: PMC3494806.

3. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med. 2000 May 4;342(18):1301-8. PubMed PMID: 10793162.

4. Brower RG, Shanholtz CB, Fessler HE, Shade DM, White P Jr, Wiener CM, Teeter JG, Dodd-o JM, Almog Y, Piantadosi S. Prospective, randomized, controlled clinical trial comparing traditional versus reduced tidal volume ventilation in acute respiratory distress syndrome patients. Crit Care Med. 1999 Aug;27(8):1492-8. PubMed PMID: 10470755.

5. 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.

Links:

Med School faculty page: http://www.medschool.umaryland.edu/profiles/Shanholtz-Carl/
PubMed
publications: https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47839782/?sort=date&direction=ascending

Stefanie Vogel (svogel@som.umaryland.edu)**:**

Dr. Vogel's focuses on the innate immune response to infection, the mechanisms by which inflammatory responses are regulated, macrophage differentiation and disease outcome, and targeting TLR signaling pathways to blunt pathogen-mediated acute lung injury. Dr. Vogel's most recent work has identified novel strategies for treating influenza therapeutically by blocking Toll-like receptor 4 signaling, the role of metabolism in the differentiation of macrophages, the cross-talk between innate immune signaling pathways, and other related topics. Innate immune responses to respiratory infections

Highlighted Publications:

1. K. A. Shirey, W. Lai, A. J. Scott, M. Lipsky, P. Mistry, L. M. Pletneva, C. L. Karp, J. McAlees, T. L. Gioannini, J. Weiss, W. H. Chen, R, K. Ernst, D. P. Rossignol, F. Gusovsky, J. C. Blanco, and S. N. Vogel. The TLR4 antagonist, Eritoran, protects mice from lethal influenza infection. *Nature* 497:498-502 (2013) PMC3725830

2. K. A. Shirey, W. Lai, L. M. Pletneva, F. D. Finkelman, D. J. Feola, J. C. G. Blanco, and S. N. Vogel. Agents that increase alternatively activated macrophage differentiation blunt Respiratory Syncytial Virus-mediated lung pathology. *J. Leukoc. Biol.* 96: 951-955. PMC4226793. (2014). See accompanying editorial.

3. K. A. Shirey, W. Lai, M. C. Patel, L. M. Pletneva, G. Pang, E. Kurt-Jones, M. Lipsky, T. Roger, T. Calandra, K. J. Tracey, Y. Al-Abed, A. G. Bowie, A. Fasano, C. A. Dinarello, F. Gusovsky, J. C. G. Blanco , S. N. Vogel. Novel strategies for targeting innate immune responses to influenza. *Mucosal Immunol*. 9: 1173-1182. (2016). PMC5125448

4. K. Richard, B. Mann, L. Stocker, A. Qin, E. M. Barry, R. K. Ernst, and S. N. Vogel. Monophosphoryl Lipid A enhances efficacy of a *Francisella tularensis* LVS-catanionic nanoparticle subunit vaccine against *F. tularensis* Schu S4 challenge by augmenting both humoral and cellular immunity. *Clin Vaccine Immunol*. 24: pii: 300574-16 (2017) PMC5339645

5. K. A. Shirey, W. Lai, L. M. Pletneva, C. L. Karp, S. Divanovic, J. C. G. Blanco, and S. N. Vogel. Role of the lipoxygenase pathway in RSV-induced alternatively activated macrophages leading to resolution of lung pathology. *Mucosal Immunol* 7: 549-557. (2013) PMC3965659.

6. A. A. Awomoyi, P. Rallabhandi, T. I. Pollin, E. Lorenz, M. B. Sztein, M. S. Boukhvalova, V. G. Hemming, J. C. G. Blanco, and S. N. Vogel. Association of TLR4 polymorphisms with symptomatic Respiratory Syncytial Virus infection in high-risk infants and young children. *J. Immunol*. 179: 3171-3177 (2007).

Links:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Vogel-Stefanie/
PubMed publications:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40447249/?sort=date&direction=ascending

Zeljko Vujaskovic (zvujaskovic@som.umaryland.edu)**:**

Dr. Vujaskovic's research has focused on identifying the underlying mechanisms associated with radiation-induced normal tissue injury, including lung, and development of radioprotectants/radiomitigators to prevent and/or mitigate the acute and chronic side effects of radiation exposure, including radiation pneumonitis. Dr. Vujaskovic has extensive experience developing small and large animal models of acute radiation sickness and testing mitigators and/or treatment options to improve survival and reduce the long-term consequences associated with acute radiation exposure.

Highlighted Publications:

1. Vujaskovic, Z.,Anscher, M. S., Feng, Q. F., Rabbani, Z. N., Amin, K., Samulski, T. S., Dewhirst, M. W., Haroon, Z. A. Radiation-induced hypoxia may perpetuate late normal tissue injury. International journal of radiation oncology, biology, physics. 50:851-855; 2001.
2. Kang, S. K., Rabbani, Z. N., Folz, R. J., Golson, M. L., Huang, H., Yu, D., Samulski, T. S., Dewhirst, M. W., Anscher, M. S., Vujaskovic, Z. Overexpression of extracellular superoxide dismutase protects mice from radiation-induced lung injury. International journal of radiation oncology, biology, physics. 57:1056-1066; 2003.
3. Vujaskovic, Z.,Batinic-Haberle, I., Rabbani, Z. N., Feng, Q. F., Kang, S. K., Spasojevic, I., Samulski, T. V., Fridovich, I., Dewhirst, M. W., Anscher, M. S. A small molecular weight catalytic metalloporphyrin antioxidant with superoxide dismutase (SOD) mimetic properties protects lungs from radiation-induced injury. Free radical biology & medicine. 33:857-863; 2002.
4. Jackson, I. L., Zhang, X., Hadley, C., Rabbani, Z. N., Zhang, Y., Marks, S., and Vujaskovic, Z. (2012). Temporal expression of hypoxia-regulated genes is associated with early changes in redox status in irradiated lung. *Free Radic Biol Med, 53*(2), 337-346.

5. Gauter-Fleckenstein, B., Reboucas, J. S…Vujaskovic, Z. (2014). Robust rat pulmonary radioprotection by a lipophilic Mn N-alkylpyridylporphyrin, MnTnHex-2-PyP(5+). *Redox Biol, 2*, 400-410.

Links:
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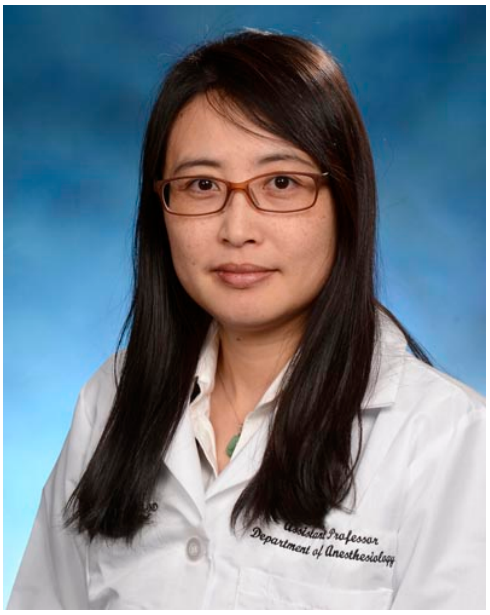
http://www.ncbi.nlm.nih.gov/sites/myncbi/14mhPZ6KDvk5F/bibliograpahy/48455065/public/?sort=date&direction=ascending

Lin Zou (lzou@som.umaryland.edu):



My research interest has been inflammation and organ injury in sepsis, specifically the role of innate immune signaling, such as Toll-like receptors (TLRs) and complement, in the

development of cardiac and renal injury during sepsis. More recently, we demonstrated that extracellular RNAs/miRNAs are released during tissue ischemia or polymicrobial sepsis and are capable of activating TLR7-dependent cytokine/complement production in cardiac cells and macrophages. We are currently extending this work by studying the role of extracellular miRNA in sepsis induced acute lung injury.

Highlighted Publications:

1. Zou, L., Feng, Y., Chen, Y-J., Si, R., Shen, S., Zhou, Q., Ichinose, F., Scherrer-Crosbie, M., Chao, W. Toll-like receptor 2 plays a critical role in cardiac dysfunction during polymicrobial sepsis. Critical Care Med. 2010; 38:1335-1342. PMID: 20228680

2. Zou, L., Feng, Y., Li, Y., Zhang, M., Chen, C., Cai, JY., Gong, Y., Wang, L., Thurman, JM., Wu, XB., Atkinson, JP., Chao, W. Complement factor B is the downstream effector of TLRs and plays an important role in a mouse model of severe sepsis. J Immunol. 2013; 191:5625-5635.

3. Li D, Zou L, Feng Y, Xu G, Gong Y, Zhao G, Ouyang W, Thurman JM, Chao W. Complement factor B production in renal tubular cells and its role in sodium transporter expression during polymicrobial sepsis. Crit Care Med. 2016; 44 (5): e289-99.

4. Feng Y, Chen H, Cai J, Zou L, Yan D, Xu G, Li D, Chao W. Cardiac RNA induces inflammatory responses in cardiomyocytes and immune cells via Toll-like receptor 7 signaling. J Biol Chem. 2015; 290: 26688-98

Links:

Med School faculty page: http://www.medschool.umaryland.edu/profiles/Zou-Lin/

PubMed publications: https://www.ncbi.nlm.nih.gov/sites/myncbi/lin.zou.1/bibliography/40653615/public/?sort=date&direction=descending