Lung infections

Nicholas Carbonetti (ncarbone@umaryland.edu)**:**

Dr. Carbonetti studies the pathogenesis of infection and disease caused by *Bordetella pertussis*, the agent of the respiratory disease pertussis (whooping cough). His lab uses a combination of animal models and in vitro approaches to investigate this host-pathogen interaction, with an emphasis on the host response. Current projects include: (i) investigation of the role of type I interferons in lung inflammatory pathology; (ii) determining the mechanism of action and therapeutic potential of sphingosine-1-phosphate receptor-targeted drugs in reducing pertussis-induced lung pathogenesis; and (iii) investigation of pertussis pathogenesis in neonatal mouse models and age-dependent protective host responses.

Highlighted Publications:

1. Scanlon, KM, Snyder, YG, Skerry, C, Carbonetti, NH (2017) Fatal pertussis in the neonatal mouse model is associated with pertussis toxin-mediated pathology beyond the airways. *Infection and Immunity* 85(11): e00355-17

2. Skerry, C, Scanlon, KM, Ardanuy, JG, Roberts, D, Zhang, L, Rosen, H, Carbonetti, NH (2017) Reduction of pertussis inflammatory pathology by therapeutic treatment with sphingosine-1-phosphate receptor ligands by a pertussis toxin-insensitive mechanism. *Journal of Infectious Diseases* 215:278-286

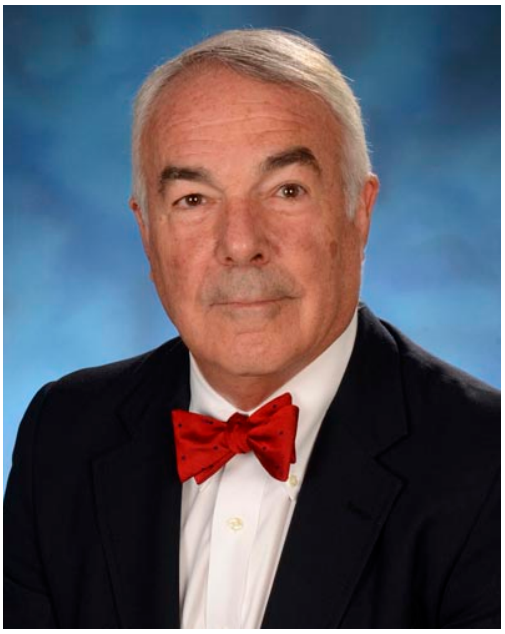
3. Scanlon, KM, Skerry, C, Carbonetti, NH (2015) Novel therapies for the treatment of whooping cough. *Pathogens and Disease* 73:ftv074

4. Scanlon, KM, Gau, Y, Skerry, C, Soleimani, M, Wall, SM, Carbonetti, NH (2014) The epithelial anion transporter pendrin contributes to inflammatory lung pathology in *Bordetella pertussis* infection. *Infection & Immunity* 82:4212-4221

5. Connelly, C, Sun, Y, Carbonetti, NH (2012) Pertussis toxin exacerbates and prolongs airway inflammatory responses during *Bordetella pertussis* infection. *Infection & Immunity* 80:4317-4332

Links:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Carbonetti-Nicholas/
PubMed Publications:
https://www.ncbi.nlm.nih.gov/sites/myncbi/nicholas.carbonetti.1/bibliography/41153362/public/?sort=date&direction=ascending

Alan Cross (across@som.umaryland.edu)**:**



Dr. Cross' research focuses on the study of sepsis, including: (1) development of vaccines to prevent sepsis including development of multivalent vaccines for *P. aeruginosa, Klebsiella* and *E. coli* that progressed to phase 1 testing in human subjects; (2) study of glycobiology and sialic acid turnover as a druggable mechanism in innate host response and sepsis; (3) mechanisms of anthrax infection; (4) targeting the CD28/B7 axis to treat sepsis; and (5) mechanisms of Gram-negative bacterial sepsis.

Highlighted Publications:
1. Cross AS, Karreman HJ, Zhang L, Rosenberg Z, Opal SM, Lees A. Immunization of cows with novel core glycolipid vaccine induces anti-endotoxin antibodies in bovine colostrum. Vaccine 2014; 32(46):6107-14. PMID: 25242628.

2. Feng C, Stamatos NM, Dragan A, Medvedev A, Whitford M, Zhang L, Song C, Rallabhandi, P, Nhu Q, Vogel SN, Geddes C, Cross AS. Sialyl residues modulate LPS-mediated signaling through the Toll-like receptor 4 complex. PLoS One 2012;7:e32359

3. Feng C, Zhang L, Almulki L, Faez S, Whitford M, Hafezi-Moghadam A, Cross AS. Endogenous PMN sialidase activity exposes activation epitope on CD11b/CD18 which enhances its binding interaction with ICAM-1. J. Leukoc. Biol. 2011;90:313-321

4. Ramachandran G, Tulapurkar ME2, Harris KM, Arad G, Shirvan A, Shemesh R, DeTolla LJ, Benazzi C, Opal SM, Kaempfer R, Cross AS. A peptide antagonist of CD28 signaling attenuates toxic shock and necrotizing soft tissue infection induced by Streptococcus pyogenes J. Infect Dis. 2013;207:1869-77. Epub 2013Mar14. PMID23493729

Links: Faculty webpage: http://www.medschool.umaryland.edu/profiles/Cross-Alan/
PubMed
publications: http://www.ncbi.nlm.nih.gov/sites/myncbi/alan.cross.1/bibliography/41139315/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