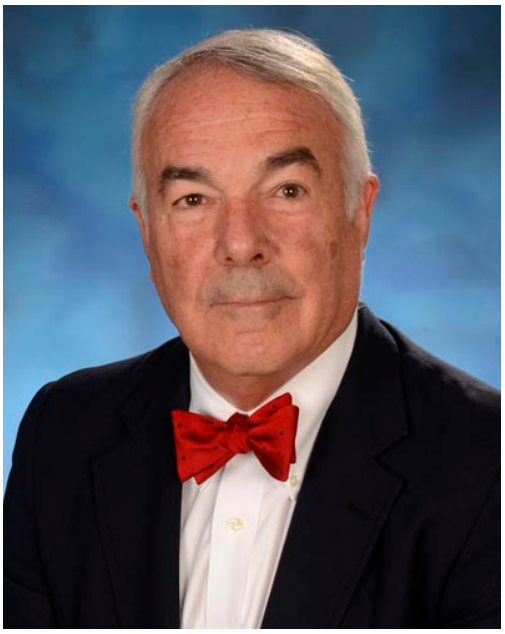
Glycobiology

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/

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publications: http://www.ncbi.nlm.nih.gov/sites/myncbi/alan.cross.1/bibliography/41139315/public/?sort=date&direction=ascending

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/

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:
Med School faculty page: http://www.medschool.umaryland.edu/profiles/Lillehoj-Erik/
PubMed publications:
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