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Education and Training

University of Michigan	BA	1969	English
University of Pittsburgh School of Medicine	MD	1973	Medicine

Montefiore Hospital Medical Center, Albert Einstein College	Residency	1976	Internal Medicine
University of New Mexico School of Medicine	Fellowship	1978	Infectious Disease

Biosketch

Over several decades, my research program had focused on mechanisms through which septic and proinflammatory processes lead to pulmonary leukostasis and acute pulmonary microvascular endothelial injury. Our studies identified protein tyrosine kinases and phosphatases and substrates for tyrosine phosphorylation that regulated the pulmonary microvascular endothelial paracellular pathway through which fluid, macromolecules, and cells move. We focused on tyrosine phosphorylation events that regulated the cell-cell adherens junctions or zonula adherens in response to both endogenous mediators, including the counter-adhesive proteins, SPARC and thrombospondin-1, and the cytokines, tumor necrosis factor α and interleukins 1 & 2, and exogenous factors such as bacterial lipopolysaccharide and staphylococcal enterotoxin B. More recently, we have begun to explore aspects of glycobiology, more specifically, sialic acid biology, with a focus on human sialidases in both human airway epithelia and human lung microvascular endothelia. Although far reaching advances in our understanding of lung cell biology have been made at the protein level, the regulatory role of glycans, and more specifically, sialylation, remains poorly understood. My laboratory has focused on the ability of host sialidase(s) to regulate the airway EC response to environmental cues and danger signals and to influence lung microvascular endothelial cell capillary-like tube formation or angiogenesis. Much information has been generated through studies of prokaryotic neurominidase/sialidase(s). Far less has been established for human sialidase biology in general, and almost nothing is known of these critical enzymes in human lung epithelia, endothelia, fibroblasts, and other cells. We now have established which sialidases are expressed in human airway epithelia and lung microvascular endothelia at the mRNA, protein, and catalytic levels, and have identified preformed pools of NEU1 and its chaperone/transport protein, PPCA, that associate with and desialyate surface receptors, including EGFR, the membrane-tethered mucin, MUC1, and CD31. We have established the ability of a NEU1-selective sialidase inhibitor, C9-BA-DANA, to inhibit NEU1 in multiple lung cells *in vitro* and murine lungs *in vivo.* Finally, we have found that NEU1 expression is increased in the lungs of patients with Idiopathic Pulmonary Fibrosis where it impairs epithelial wound healing and angiogenesis.

Research/Clinical Keywords

sialic acid, sialidases, neuraminidases, NEU1, sialylotransferases, lung, endothelium, epithelium, sepsis, acute lung injury

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* 287:8214-8231, 2012.

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, Puchè 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* 287:15966-15980, 2012.

3. Lee C, Liu A, Miranda-Ribera A, Hyun SW, Lillehoj EP, Cross AS, Passaniti A, **GOLDBLUM SE**. NEU1 Sialidase Regulates the Sialation State of CD31and Disrupts CD31-Driven Capillary-Like Tube Formation in Human Lung Microvascular Ednothelia. *J Biol Chem* 289:9121-9135, 2014.

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

5. Luzina IG, Lockatell V, Hyun SW, Kopach P, Kang PH, Noor Z, Liu A, Lillehoj EP, Lee C, <iranda-Ribera A, Todd NW, **GOLDBLUM SE**, Atmas SP. Elevated Expression of NEU1 Sialidase in Idiopathic Pulmonary Fibrosis Provokes Pulmonary Collagen Deposition, Lymphocytosis, and Fibrosis. *Am J Physiol Lung Cell Mol Physiol* 310:L940-L954, 2016.

6. Hyun SW, Liu A, Liu Z, Cross AS, Verceles AC, Magesh S, Kommagalla Y, Ando H, Luzina IG, Atamas SP, Piepenbrink KH, Sundberg EJ, Guang W, Ishida H, Lillehoj EP, and **GOLDBLUM SE**. The NEU1-selective Sialidase inhibitor, C9-buty1-amide-DANA, Blocks sialidase activity and NEU1-mediated bioactivities in human lung *in vitro* and murine lung *in vivo. Glycobiology* 8:834-849, 2016

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