

Paul W. Noble, MD
Chief

Paul W. Noble, MD



Department / Division:

Medicine / Pulmonary, Allergy and Critical Care

Physical Address:

106 Research Drive, 2nd Floor, Room 2079
Durham, NC 27705

Appointment Telephone:

(919) 668-7630

Office Telephone:

(919) 681-0355

Fax Telephone:

(919) 684-5266

Training:

- M.D., New York University, 1984

Residency:

- Internal Medicine, University of California, San Francisco, 1984-1988

Fellowship:

- Pulmonary Fellowship Program, University of Colorado, 1988-1991

Clinical Interests:

Pulmonary, allergy and critical care

Research Interests:

Research Interests

I have been focused on defining the mechanisms that contribute to chronic lung inflammation and fibroproliferation in the absence of infection.

1. Extracellular matrix and lung injury. My major research focus has been defining the role of the extracellular matrix glycosaminoglycan hyaluronan (HA) in lung inflammation. I was the first to show that HA could induce growth factors and identified a novel signaling pathway in macrophages. I showed that HA had to be modified by the inflammatory milieu to function as a signaling molecule. We then defined the role of the HA cell surface receptor CD44 in lung inflammation. CD44 is required to remove fragmented HA from injured lungs and prevent death from unremitting inflammation. We then showed that matrix could initiate innate immune responses when Toll-like receptors 2 and 4 were able to recognize fragmented HA in vivo. In addition we discovered that HA has different functions when interacting in a soluble form with macrophages or on the cell surface of lung epithelial cells where it is bound to TLR2 and TLR4. We were the first to show that cell surface HA on lung epithelial cells has a protective role against lung injury by interacting with TLR2 and TLR4 similar to how gut bacteria are protective against tissue injury. Our lab is using genetically modified mouse models in which hyaluronan synthases, hyaluronan degradation enzymes, and hyaluronan binding proteins have been knocked out or overexpressed.

2. Role of chemokines and chemokine receptors in lung injury and repair. I was also the first to describe a critical role for interferon-gamma produced by NK cells in limiting tissue fibrosis following non-infectious lung injury. We are working the immunoregulatory and molecular roles of CXCL10, CXCR3, CXCL12, and CCL2 in lung injury and repair.

3. Idiopathic Pulmonary Fibrosis.

Representative Publications:

Liang J, Jiang D, Griffith J, Yu S, Fan J, Zhao X, Bucala R, Noble PW. CD44 is a negative regulator of acute pulmonary inflammation and lipopolysaccharide-TLR signaling in mouse macrophages. *J Immunol.* 2007 Feb 15;178(4):2469-75. (2007)

[Abstract](#)

Jiang D, Liang J, Fan J, Yu S, Chen S, Luo Y, Prestwich GD, Mascarenhas MM, Garg HG, Quinn DA, Homer RJ, Goldstein DR, Bucala R, Lee PJ, Medzhitov R, Noble PW. Regulation of lung injury and repair by Toll-like receptors and hyaluronan. *Nat Med*. 2005 Nov; 11(11):1173-9. (2005) [Abstract](#)

Jiang D, Liang J, Hodge J, Lu B, Zhu Z, Yu S, Fan J, Gao Y, Yin Z, Homer R, Gerard C, Noble PW. Regulation of pulmonary fibrosis by chemokine receptor CXCR3. *J Clin Invest*. 2004 Jul; 114(2):291-9. (2004) [Abstract](#)

Raghu G, Brown KK, Bradford WZ, Starko K, Noble PW, Schwartz DA, King TE Jr, . A placebo-controlled trial of interferon gamma-1b in patients with idiopathic pulmonary fibrosis. *N Engl J Med*. 2004 Jan 8; 350(2):125-33. (2004) [Abstract](#)

Teder P, Vandivier RW, Jiang D, Liang J, Cohn L, Puré E, Henson PM, Noble PW. Resolution of lung inflammation by CD44. *Science*. 2002 Apr 5; 296(5565):155-8. (2002) [Abstract](#)

McKee CM, Penno MB, Cowman M, Burdick MD, Strieter RM, Bao C, Noble PW. Hyaluronan (HA) fragments induce chemokine gene expression in alveolar macrophages. The role of HA size and CD44. *J Clin Invest*. 1996 Nov 15; 98(10):2403-13. (1996) [Abstract](#)