BIOGRAPHICAL SKETCH

NAME: **Andrew J. Gow**

eRA COMMONS USER NAME (credential, e.g., agency login): ANDREWGOW

POSITION TITLE: **Professor of Pharmacology and Toxicology**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Edinburgh University, U.K.	B.Sc.	06/1986	Biochemistry
Temple University	M.Ed.	05/1994	Exercise Science
Temple University	Ph.D.	05/1995	Exercise Physiology
University of Pennsylvania	Post-Doc	12/1996	Oxidative Stress

A. Personal Statement

Overall, my research focuses on how redox active molecules play a role in cellular signaling. I am particularly interested in how nitric oxide (NO) operates in both health and disease. Recently, I have been investigating how NO modifies other biomolecules, such as the pulmonary collectin SP-D, to generate novel signals. The lung represents an ideal organ system in which to on these experiments, as all three isoforms of NO Synthase (NOS) are expressed there, and NOS2 is critically important in regulating the cycle of inflammation and repair that occurs following lung injury. A significant component of this work is the assessment of inflammatory activation state. We have developed a series of techniques for assessing inflammation as it relates to oxidative stress signaling both in human and animal models. These studies are integrative projects requiring the use of techniques ranging from protein chemistry to organ-level physiology and require an extensive understanding of NO and its chemistry, as well as the cell biology of inflammation. I have conducted a range of studies examining NO, pulmonary collectins, and inflammatory lung disease using both animal models and human samples. NO is a critical factor in the regulation of inflammation, especially within the lung where the NOS2 isoform regulates both inflammation and resolution. I have investigated the role of NO in regulating inflammation in the lung with particular reference to the importance of cysteine residues in regulating NO effects. In this work I have used multiple injury models including vesicants, chlorine, ozone, and bleomycin. Strong collaborative relationships are necessary in modern biomedical science and in this regard I have been successful both within and beyond my institution.

Related Research Support - Ongoing

1 U01 OH012072-01 07/2021- 06/2024
Obstructive Sleep Apnea and WTC dust: Does Chronic Intermittent Hypoxia exacerbate WTC dust induced lung injury
Examination of the role of intermittent hypoxia on world trade center dust exposure induced lung injury.
Role: Co-PI

Government Contract with East Orange Veterans Administration 04/2019 – 09/2021
Inflammatory Mechanisms of post-deployment dyspnea
Assesses circulatory inflammatory status and its effects on V/Q mismatch and NO-mediated alterations in blood flow in veterans of the Southwestern Asian theater.
Role: PI

Related Research Support – Completed in the last three years

NIH R21ES029254 (No Cost Extension) 09/2018 – 08/2020
Ozone, Inflammation

Major Goals: Test the hypothesis that ozone exposure reduced microbial diversity increasing susceptibility to lung injury

NIH R01HL086621 07/2008 – 06/2019
NO-Modified Biomolecules and Pulmonary Signaling
Major Goals: The goal of this project is to investigate NO-modified biomolecules and their potential signaling mechanisms with particular reference to bleomycin-mediated lung injury.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2015-Present Professor of Pharmacology, Ernest Mario School of Pharmacy, Rutgers University, NJ
2006-2015 Assoc. Professor of Pharmacology, Ernest Mario School of Pharmacy, Rutgers University, NJ
2001-05 Research Assistant Professor, Department of Pediatrics, Children's Hospital of Philadelphia, PA
1998-01 Research Assistant Professor, Department of Pulmonary Medicine, Duke University, NC
1996-97 Research Associate, Institute for Environmental Medicine, University of Pennsylvania, PA
1994-95 Adjunct Assistant Professor, Manor Junior College, PA
1990-92 Research Assistant, Department of Molecular Biology, Princeton University, NJ

Other Experience and Professional Memberships

2009- Ad hoc reviewer for NIH study sections LIRR and SIEE, Free Rad. Biol. Med.
2003- Reviewer for NIH Study Section CDIN, Proc. Natl. Acad. Sci USA, J. Neurosci., Biochem., Nitric Oxide, Neurosci. Lett., Biochem. Pharmacol., Am. J. Resp. Med. Crit. Care, J. Pharm. Exp. Therap., Am. J. Physiol.
2002- Society for Pediatric Research, member
2001- Ad hoc reviewer for Eur. J.Neurosci., Biochim. et Biophys. Acta, Toxicol. & App. Pharm., J. Leuk. Biol., Neurosci., U.S. Civilian Research and Development Foundation
1999- Ad hoc reviewer for NIH Study Section BDCN-3, Free Radical Biology and Medicine, Veteran's Research Administration Affairs, Am. J. Physiol.
1997- Nitric Oxide Society, member
1996- Oxygen Society, member
1996- Royal Society of Chemistry, member
1993- American College of Sports Medicine, member

Honors

2023 Chair of the Gordon Conference for Nitric Oxide
2010-12 President of The International Nitric Oxide Society
2001 Florence R.C. Murray Fellowship
2000 Translational Medicine Award, Duke University
1998 Chartered Chemist, Royal Society of Chemistry
1997 Young Investigator Award, International Nitric Oxide Society
1996 Young Investigator Award, Oxygen Society
1995-97 NRSA from the NHLBI in Lung Cell and Molecular Biology
1993-95 Russell Conwell Research Fellowship

C. Contributions to Science

1. NO-modification of biological targets

I have contributed to reactive species biology since 1993, during my graduate studies examining the role of oxidants in ischemia/reperfusion injury and conditioning. During my postdoctoral training I became more focused on the role of NO in the post-translational modification of proteins and the resulting effects on cellular function. I have conducted seminal work on the two most widely recognized NO-mediated modifications *S*-nitrosylation of thiol residues and nitration of tyrosine. I have examined the molecular mechanisms of NO-modification of a wide range of proteins including hemoglobin, caspase-3, and Surfactant Protein-D. This work has helped establish S-nitrosylation as a fundamental signaling mechanism of NO. I have also examined other reactions of NO that are relevant in the biological milieu. These studies have revealed a number of other NO-based modifications of biomolecules, including both protein and lipid nitration, that have significant pathological consequences. I have been the PI on the majority of these studies; the earlier works were during my transition from postdoctoral fellow to research assistant professor.

a) **Gow A,** Duran D, Thom SR, Ischiropoulos H. Carbon dioxide enhancement of peroxynitrite-mediated protein tyrosine nitration. *Archives of Biochemistry & Biophysics.* 1996;333:42-8.
b) **Gow AJ,** Buerk DG, Ischiropoulos H. A novel reaction mechanism for the formation of S-nitrosothiol in vivo. *Journal of Biological Chemistry.* 1997;272:2841-5.
c) **Gow AJ,** Chen Q, Hess DT, Day BJ, Ischiropoulos H, Stamler JS. Basal and stimulated protein S-nitrosylation in multiple cell types and tissues. *Journal of Biological Chemistry.* 2002;277:9637-40.
d) Guo CJ, Schopfer FJ, Gonzales L, Wang P, Freeman BA, **Gow AJ**. Atypical PKCzeta transduces electrophilic fatty acid signaling in pulmonary epithelial cells. *Nitric Oxide.* 2011;25:366-72. PMC3766842

2. Hemoglobins

A primary targets for NO in biological systems is the heme protein cofactor. This has led me to conduct a series of studies examining hemoglobins as model NO targets. This work has led me to study how globin structure influences heme reactivity and to study the possible redox reactions that can occur at the heme-iron. In particular, I have demonstrated that hemoglobin can operate as a preserver of NO-bioactivity through nitrosylation reactions, a consumer of NO by oxidation at bound oxygen, or as a reservoir by ligand binding. These reactions are critically dependent upon the relative concentrations of NO, oxygen, and hemoglobin, as well as the allosteric state of that globin. These fundamental biochemical reactions have provided novel paradigms for considering NO bioactivity in biological systems that contain hemoglobin, such as the blood. I have extended the principles from these studies to understand how the specific chaperone protein, alpha hemoglobin stability protein (AHSP), operates to reduce oxidative stress induced by free alpha globin chains. This work identified AHSP as capable of inducing a functional transition within the globin such that the heme iron was stabilized in a bis-histidyl ferric form. I performed most of this work solo, as a junior faculty, although my later work on hemoglobin was though collaborations, especially with Dr. Weiss.

a) **Gow AJ,** Luchsinger BP, Pawloski JR, Singel DJ, Stamler JS. The oxyhemoglobin reaction of nitric oxide. *ProcNatlAcadSciUSA.* 1999;96:9027-32.
b) **Gow AJ,** Stamler JS. Reactions between nitric oxide and haemoglobin under physiological conditions. *Nature.* 1998;391:169-73.
c) Helbo S, **Gow AJ,** Jamil A, Howes BD, Smulevich G, Fago A. Oxygen-linked S-nitrosation in fish myoglobins: a cysteine-specific tertiary allosteric effect. *PloS One.* 2014;9:e97012. PMC4039430
d) Zhou S, Olson JS, Fabian M, Weiss MJ, **Gow AJ**. Biochemical fates of {alpha} hemoglobin bound to {alpha} hemoglobin-stabilizing protein AHSP. *J Biol Chem.* 2006;281:32611-8.

3. Surfactant Protein-D

In 2004, as a relatively new faculty member at the University of Pennsylvania, I established a collaborative research relationship with Dr. Beers examining the role of NO in inflammatory signaling within the lung. Our initial work examined how loss of Surfactant Protein-D (SP-D) leads to an inflammatory response and how NO metabolism was involved in this signaling process. However, we extended this work to further examine how the disrupted NO metabolism associated with loss of SP-D led to an increased sensitivity to lung injury in a variety of models, including bleomycin injury. Also we noted that SP-D itself was a target for NO modification on the thiol residues of the N terminus. This modification appears to be an essential part of the inflammatory response to pulmonary insult. We have established that NO-modified SP-D is a potent-signaling molecule that can mediate both myeloid recruitment and activation. Many of these studies were NIH-sponsored, on which I was the senior investigator and project lead; they were also a productive collaboration with Dr. Atochina, who performed much of the hands-on work.

a) Atochina EN, Beers MF, Hawgood S, Poulain F, Davis C, Fusaro T, **Gow AJ**. Surfactant protein-D, a mediator of innate lung immunity, alters the products of nitric oxide metabolism. *Am J Resp Cell Molec Bio* 2004;30:271-9.
b) Atochina-Vasserman EN, Beers MF, Kadire H, Tomer Y, Inch A, Scott P, Guo CJ, **Gow AJ**. Selective inhibition of inducible NO synthase activity in vivo reverses inflammatory abnormalities in surfactant protein D-deficient mice. *J Immunol.* 2007;179:8090-7.
c) Atochina-Vasserman EN, **Gow AJ,** Abramova H, Guo CJ, Tomer Y, Preston AM, Beck JM, Beers MF. Immune reconstitution during Pneumocystis lung infection: disruption of surfactant component expression and function by S-nitrosylation. *J Immunol.* 2009;182:2277-87. PMC4016818

d) Knudsen L, Atochina-Vasserman EN, Guo CJ, Scott PA, Haenni B, Beers MF, Ochs M, **Gow AJ**. NOS2 is critical to the development of emphysema in Sftpd deficient mice but does not affect surfactant homeostasis. *PloS One.* 2014;9:e85722. PMC3897517

4. Lung Inflammation and function

My SP-D research led to a greater understanding of the role of NO in inflammatory signling in the lung. Over the past several years I have extended this work to consider how NO is involved in a variety of injury models, and to examine how these inflammatory changes are related to lung function. We have examined both organ-level function and inflammatory activation as endpoints within injury models to characterize how inflammation, particularly macrophage activation, results in surface active dysfunction. We have also developed techniques to characterize macrophage phenotpye within both lung lining and tissue, and constructed lung functional models passed on pulmonary impedence spectra. We have utilized these studies to directly measure the effectiveness of a variety of pharmacological agents at reducing lung injury and inflammation at both the cellualr and functional level. I largely directed this work, though it has also featured collaboration with Dr. D.L. Laskin, an expert in exposure-based lung injury models, including ozone.

a) Wilkinson, ML, Abramova E, Guo C, Gow JG, Murray A, Koudelka A, Cechova V, Freeman BA, Gow AJ. Fatty acid nitroalkenes inhibit the inflammatory response to belomycin meidated lung injury. *Toxicol Applied Pharmacol.* 2020: in press (doi 10.1016/j.taap.2020.115236)
b) Atochina-Vasserman EN, Guo CJ, Abramova E, Golden TN, Sims M, James ML, Beers MF, **Gow AJ,** Krymskaya VP. Surfactant dysfunction and lung inflammation in the female mouse model of lymphangioleiomyomatosis (LAM). *Am J Resp Cell and Mol Biol.* 2014;53:96-104. PMC4566108
c) Massa CB, Scott P, Abramova E, Gardner C, Laskin DL, **Gow AJ**. Acute chlorine gas exposure produces transient inflammation and a progressive alteration in surfactant composition with accompanying mechanical dysfunction. *Toxicol Applied Pharmacol.* 2014;278:53-64. PMC4361901
d) Shi JD, Golden T, Guo CJ, Tu SP, Scott P, Lee MJ, Yang CS, **Gow AJ**. Tocopherol supplementation reduces NO production and pulmonary inflammatory response to bleomycin. *Nitric Oxide: Biol Chem.* 2013;34:27-36. PMC3769481

5. Biomarkers of inflammation and altered NO signaling

I have found in the course of investigating lung injury models that the cellular source and flux of NO production are critical to its action. In other words, NO is made in the right place at the right time and in the presence of the right targets. When it is not, pathology ensues. My work has become increasingly focused on macrophages as both generators and targets of NO. I have been involved in the development of appropriate models of lung function and disease to study NO regulation within the context of injury and inflammation. These studies have generally focused on the role of NOS2 in regulating the inflammatory response to injury.

a) Guo CJ, Atochina-Vasserman EN, Abramova E, Foley JP, Zaman A, Crouch E, Beers MF, Savani RC, **Gow AJ**. S-nitrosylation of surfactant protein-D controls inflammatory function. *PLoS Biol.* 2008;6: e266. PMC2581630
b) Groves AM, **Gow AJ,** Massa CB, Hall L, Laskin JD, Laskin DL. Age-related increases in ozone-induced injury and altered pulmonary mechanics in mice with progressive lung inflammation. *Am J Physiol Lung Cell Molec Physiol.* 2013;305:L555-68. PMC3798776
c) Guo CJ, Atochina-Vasserman E, Abramova H, George B, Manoj V, Scott P, **Gow A**. Role of NOS2 in pulmoanry injury and repair in response to bleomycin. *Free Radical Biol Med.* 2016;91:293-301. PMC5059840
d) Knudsen L, Atochina-Vasserman EN, Massa CB, Birkelbach B, Guo CJ, Scott P, Haenni B, Beers MF, Ochs M, **Gow AJ**. The role of inducible nitric oxide synthase for interstitial remodeling of alveolar septa in surfactant protein D-deficient mice. *Am J Physiol Lung Cell Mol Physiol*. 2015;309:L959-69. PMC4628984

My complete publications can be accessed on PubMed:
http://www.ncbi.nlm.nih.gov/sites/myncbi/andrew.gow.1/bibliography/40755282/public/?sort=date&direction=descending