
BIOGRAPHICAL SKETCH

NAME Freeman, Bruce A.	POSITION TITLE Irwin Fridovich Professor and Chairman, Department of Pharmacology & Chemical Biology University of Pittsburgh School of Medicine		
eRA COMMONS USER NAME FREEMANBA			
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
University of California, Riverside	B.S.	1974	Biochemistry
University of California, Riverside	Ph.D.	1978	Biochemistry

A. Personal Statement

Bruce Freeman, Ph.D studies the cell and tissue production and actions of reactive species (free radical and oxidant inflammatory/signal transduction mediators), with the goal of understanding fundamental mechanisms of redox signaling and inflammatory tissue injury. His discoveries have revealed new therapeutic strategies for treating acute inflammation, respiratory disorders, diabetes, atherosclerosis, hypertension and other vascular diseases. Drug candidates stemming from this work have Investigative New Drug status from the FDA and are being evaluated in early stage human safety studies. In recent years, his laboratory revealed that a) nitric oxide signaling and pathogenic actions are modulated by a variety of redox reactions, b) nitric oxide and nitrite-dependent redox reactions of unsaturated fatty acids yield nitroalkene products that potently regulate the activity of key inflammatory-related enzymes and transcription factors. Current focus is directed towards understanding inflammatory events in asthma, hypertension and metabolic syndrome, where nitro- and keto-fatty acid-induced post-translational protein modification reactions are explored in the context of the regulation of cell and tissue inflammatory responses.

B. Positions and Honors

Positions and Employment

1982-1985	Assistant Professor, Dept. of Medicine, Duke University, Durham, NC
1985-1990	Associate Professor, Depts. of Anesthesiology and Biochemistry, UAB
1990-2005	Professor, Depts. of Anesthesiology, Biochemistry and Molecular Genetics, UAB
1993	Fulbright Research Scholar
1995-1996	President, Society for Free Radical Biology and Medicine
1996-2005	Director, Center for Free Radical Biology, University of Alabama at Birmingham
2003	Designated by ISI – Highly Cited Author in Biology and Medicine
2004	Invited Speaker, Nobel Conference 46
2005	Doctora Honoris Causa, Faculty of Medicine, University of the Republic, Montevideo, Uruguay
2005-2009	NIEHS Advisory Council
2006-Present	Chairman, Dept. Pharmacology & Chemical Biology, University of Pittsburgh School of Medicine
2012-2016	Lung Injury Repair and Remodeling Study Section

C. Selected Peer-reviewed Publications

1. Botti H, C Batthyany, A Trostchansky, R Radi, **BA Freeman** and H Rubbo. Peroxynitrite-mediated α -tocopherol oxidation in low-density lipoprotein: Free Rad Biol Med 36:152-162, 2004.
2. Castro L, JP Eiserich, S Sweeney, R Radi and **BA Freeman**. Cytochrome c: a catalyst and target of nitrite-hydrogen peroxide-dependent protein nitration. Arch Biochem Biophys 421:99-107, 2004.
3. Lang JD, Jr, M Figueroa, P Chumley, M Aslan, J Hurt, MM Tarpey, B Alvarez, R Radi and **BA Freeman**. Albumin and hydroxyethyl starch modulate oxidative inflammatory injury to vascular endothelium. Anesthesiology 100:51-58, 2004.
4. Schwartz JH, CA White and **BA Freeman**. Do we kNOw how HSP90 and eNOS mediate lung injury in

sickle cell disease? *Am J Physiol Lung Cell Mol Physiol* 286:L701-L704, 2004.

5. White CR, DA Parks, RP Patel, J Shelton, MM Tarpey, **BA Freeman** and VM Darley-Usmar. L-Arginine inhibits xanthine oxidase-dependent endothelial dysfunction in hypercholesterolemia. *FEBS Letters* 561:94-98, 2004.
 6. Baker PRS, FJ Schopfer, S Sweeney and **BA Freeman**. Red cell membrane and plasma linoleic acid nitration products: Synthesis, clinical identification and quantitation. *Proc Nat Acad Sci*, 101:11577-11582, 2004. Commentary: B Kalyanaraman. Nitrated lipids: a class of cell-signaling molecules. *Proc Nat Acad Sci* 101:11577-11582, 2004.
 7. Alvarez B, V Demicheli, R Duran M Trujillo, C Cervenansky, **BA Freeman** and R Radi. Inactivation of human Cu, Zn superoxide dismutase by peroxynitrite and formation of histidinyl radical. *Free Rad Biol Med* 37:813-822, 2004.
 8. Baldus S, T Heitzer, JP Eiserich, D Lau, H Mollnau, M Ortak, S Petri B Goldmann, H-J Duchstein, J Berger, U Helmchen, **BA Freeman**, T Meinertz and T Munzel. Myeloperoxidase enhances nitric oxide catabolism during myocardial ischemia and reperfusion. *Free Rad Biol Med* 37:902-911, 2004.
 9. Kelley EE, A Trostchansky, H Rubbo, **BA Freeman**, R Radi and MM Tarpey. Binding of xanthine oxidase to glycosaminoglycans limits inhibition by oxypurinol. *J Biol Chem* 279:37231-37234, 2004.
 10. Lau D, H Mollnau, J Eiserich, **BA Freeman** and S Baldus. Myeloperoxidase serves as an autocrine and paracrine mediator of neutrophil activation by association with CD11b/CD18 integrins. *Proc Nat Acad Sci* 102:431-436, 2005.
 11. Lang JD, M Figueroa, KD Sanders, M Aslan, P Chumley, T Schoeb and **BA Freeman**. Hypercapnia amplifies pulmonary inflammation in an intact animal model of low tidal volume ventilation. *Am J Resp Crit Care Med* 171:147-157, 2005. Commentary: B. Kavanaugh. Therapeutic hypercapnia: careful science, better trials. *Am J Resp Crit Care Med* 171:96-97, 2005.
 12. Schopfer F, Y Lin, P Baker, T Cui, M Garcia-Barrio, J Zhang, K Chen, Y Chen and **BA Freeman**. Nitrolinoleic acid – an endogenous PPAR γ ligand. *Proc Nat Acad Sci* 102:2340-2345, 2005.
 13. Schopfer F, G Giles, PRS Baker, P Chumley, R Patel, N Hogg, B Branchaud, JR Lancaster and **BA Freeman**. Fatty acid transduction of nitric oxide signaling: Nitrolinoleate is a hydrophobically-stabilized nitric oxide donor. *J Biol Chem* 280:19289-19297, 2005.
 14. Gladwin MT, AN Schechter, DB Kim-Shapiro, RP Patel, N Hogg, S Shiva, RO Cannon, M Kelm, DA Wink, MG Espey, EH Oldfield, RM Pluta, **BA Freeman**, JR Lancaster, M Feelisch and JO Lundberg. The emerging biology of the nitrite anion. *Nature Chem Biol.* 1:308-314, 2005.
 15. Baker PRS, F Schopfer, Y Lin, T Cui, S Woodcock, C Batthyany, S Sweeney, MH Long, A Groeger, K Iles, LMS Baker, B Branchaud, Y Chen and **BA Freeman**. Fatty acid transduction of nitric oxide signaling: Multiple nitrated unsaturated fatty acid derivatives exist in human blood and urine and serve as endogenous PPAR γ ligands Clinical identification and PPAR signaling activity of nitrated fatty acids. *J Biol Chem* 280:42464-42475, 2005. Designated by editors as a “JBC Paper of the Week”.
 16. Baldus S, R Koster, P Chumley, T Heitzer, V Rudolph, MA Ostad, A Warnholtz, H-J Staude, F Thuneke, K Koss, J Berger, T Meinertz, **BA Freeman** and T Munzel. Oxypurinol improves coronary and peripheral endothelial function in patients with coronary artery disease. *Free Rad Biol Med* 39:1184-1190, 2005.
 17. Haegens A, A van der Bliet, KJ Butnor, N Heintz, D Taatjes, D Hemenway, P Vacek, **BA Freeman**, SL Hazen, ML Brennan and BT Mossman. Asbestos-induced lung inflammation and epithelial cell proliferation are altered in myeloperoxidase-null mice. *Cancer Research* 65(21): 9670-77, 2005.
-

18. Hsu HC, T Zhou, H Kim, S Barnes, P Yang, Q Wu, J Zhou, **BA Freeman**, M Luo and JD Mountz. Production of a novel class of polyreactive pathogenic autoantibodies in BXD2 mice causes glomerulonephritis and arthritis. *Arthritis Rheum* 54(1): 343-55, 2006.
 19. Wright MM, FJ Schopfer, PR Baker, V Vidyasagar, P Powell, P Chumley, KE Iles, **BA Freeman** and A Agarwal. Fatty acid transduction of nitric oxide signaling: nitrolinoleic acid potentially activates endothelial heme oxygenase 1 expression. *Proc Nat Acad Sci US* 103 (11): 4299-304, 2006.
 20. Batthyany C, FJ Schopfer, PR Baker, R Duran, LM Baker, Y Huang, C Cervenansky, BP Branchaud and **BA Freeman**. Reversible post-translational modification of proteins by nitrated fatty acids in vivo. *J Biol Chem* 281(29): 20450-20463, 2006.
 21. Cui T, F Schopfer, J Zhang, K Chen, T Ichigawa, PRS Baker, C Batthyany, BK Chacko, X Feng, R Patel, A Agarwal, **BA Freeman** and Y Chen. Nitrated fatty acids: Endogenous anti-inflammatory signaling mediators. *J Biol Chem* 281: 35686-35698, 2006.
 22. Baldus S, K Müllerleile, P Chumley, D Steven, V Rudolph, GK Lund, H-J Staude, A Stork, R Köster, J Kähler, C Weiss, T Münzel, T Meinertz, **BA Freeman** and T Heitzer. Inhibition of xanthine oxidase improves myocardial contractility in patients with ischemic cardiomyopathy. *Free Rad. Biol. & Medicine* 41: 1282–1288, 2006.
 23. Tórtora V, C Quijano, **BA Freeman**, R. Radi and L. Castro. Mitochondrial aconitase reaction with nitric oxide, S-nitrosoglutathione and peroxynitrite: Mechanisms and relative contributions to aconitase inactivation. *Free Rad. Biol & Medicine* 42:1075-1088, 2007.
 24. Villacorta L, J Zhang, MT Garcia-Barrio, X Chen, **BA Freeman**, YE Chen and T Cui. Nitro-linoleic acid inhibits vascular smooth muscle cell proliferation via the Keap1/Nrf2 signaling pathway. *Am J Physiol Heart Circ Physiol* 293:H770-H776, 2007.
 25. Baker LMS, PRS Baker, F Golin-Bisello, FJ Schopfer, M Fink, SR Woodcock, BP Branchaud, R Radi and **BA Freeman**. Nitro-fatty acid reaction with glutathione and cysteine: kinetic analysis of thiol alkylation by a Michael addition reaction. *J Biol Chem* 282:31085-31093, 2007.
 26. Turell L, H. Botti, S Carballal, G Ferrer-Sueta, JM Souza, R Duran, **BA Freeman**, R Radi and B Alvarez. Reactivity of sulfenic acid in human serum albumin. *Biochemistry* 47:358-367, 2008
 27. **Freeman BA**, PRS Baker, FJ Schopfer, SR Woodcock, A Napolitano and M d'Ischia. Nitro-fatty acid formation and signaling. *J. Biol. Chem.* 283:15515-15519, 2008.
 28. Li Y, J Zhang, FJ Schopfer, D Martynowski, MT Garcia-Barrio, A Kovach, K Suino-Powell, PRS Baker, **BA Freeman**, YE Chen and HE Xu. Molecular recognition of nitro-fatty acids by PPAR γ . *Nature Structural & Molecular Biology* 15:865-867, 2008.
 29. Rudolph V, TK Rudolph and **BA Freeman**. Copper trafficking and extracellular superoxide dismutase activity: Kinky hair, kinky vessels. *Hypertension* 52:811-812, 2008.
 30. Ichikawa T, J Zhang, K Chen, Y Liu, FJ Schopfer, PRS Baker, **BA Freeman**, YE Chen and T Cui. Nitroalkenes suppress lipopolysaccharide-induced signal transducer and activator of transcription signaling in macrophages: A critical role of mitogen-activated protein kinase phosphatase 1. *Endocrinology* 149:4086-4094, 2008.
 31. Rudolph V, TK Rudolph, FJ Schopfer, G. Bonacci, D Lau, K Szöcs, A Klinke, T Meinertz, **BA Freeman** and S Baldus. Bivalirudin decreases NO bioavailability by vascular immobilization of myeloperoxidase. *The Journal of Pharmacology and Experimental Therapeutics* 327:324-331, 2008.
 32. Kelly EE, CI Batthyany, NJ Hundley, SR Woodcock, G Bonacci, JM DelRio, FJ Schopfer, JR Lancaster, **BA Freeman** and MM Tarpey. Nitro-oleic acid, a novel and irreversible inhibitor of xanthine oxidoreductase. *Journal of Biological Chemistry* 283:36176-36184, 2008.
-

33. Woodcock SR and **BA Freeman**. A new hammer in the redox toolbox: High-purity peroxyxynitrite for cell signaling and toxicology studies. *Chem Res Toxicol* 21:2227-2228, 2008.
 34. Rudolph V, TK Rudolph and **BA Freeman**. Blood pressure regulation: Role for neutrophils? *Blood* 111:4840, 2008.
 35. Ferreira A, MI Ferrari, A Trostchansky, C Batthyany, JM Souza, MN Alvarez, GV Lopez, PRS Baker, FJ Schopfer, VB O'Donnell, **BA Freeman** and H Rubbo. Macrophage activation induces formation of the anti-inflammatory lipid cholesteryl-nitrolinoleate. *Biochem J* 417:223-234, 2009.
 36. Rudolph V, FJ Schopfer, NKH Khoo, TK Rudolph, MP Cole, SR Woodcock, G Bonacci, AL Groeger, F Golin-Bisello, C-S Chen, PRS Baker and **BA Freeman**. Nitro-fatty acid metabolome: Saturation, desaturation, β -oxidation, and protein adduction. *J. Biol. Chem.* 284:1461-1473, 2009.
 37. Villacorta L, FJ Schopfer, J Zhang, **BA Freeman** and YE Chen. PPAR γ and its ligands: Therapeutic implications in cardiovascular disease. *Clinical Science* 116:205-218, 2009.
 38. Iles KE, MM Wright, MP Cole, NE Welty, LB Ware, MA Matthay, FJ Schopfer, PRS Baker, A Agarwal and **BA Freeman**. Fatty acid transduction of nitric oxide signaling: Nitrolinoleic acid mediates protective effects through regulation of the ERK pathway. *Free Radical Biology & Medicine* 46:866-875, 2009.
 39. Schopfer FJ, C Batthyany, PRS Baker, G Bonacci, MP Cole, V Rudolph, AL Groeger, TK Rudolph, S Nadtochiy, PS Brookes and **BA Freeman**. Detection and quantification of protein adduction by electrophilic fatty acids: Mitochondrial generation of fatty acid nitroalkene derivatives. *Free Radical Biology & Medicine* 46:1250-1259, 2009.
 40. Nadtochiy SM, PRS Baker, **BA Freeman** and PS Brookes. Mitochondrial nitroalkene formation and mild uncoupling in ischaemic preconditioning: Implications for cardioprotection. *Cardiovascular Research* 82:333-340, 2009.
 41. Baker PRS, FJ Schopfer, VB O'Donnell and **BA Freeman**. Convergence of nitric oxide and lipid signaling: Anti-inflammatory nitro-fatty acids. *Free Radical Biology & Medicine* 46:989-1003, 2009.
 42. Cole MP and **BA Freeman**. Promotion of cardiovascular disease by exposure to the air pollutant ozone. *Am J Physiol Lung Cell Mol Physiol* 297:L205-208, 2009.
 43. Wright MM, J Kim, TD Hock, N Leitinger, **BA Freeman** and A Agarwal. Human heme oxygenase-1 induction by nitro-linoleic acid is mediated by cyclic AMP, AP-1, and E-box response element interactions. *Biochem J* 422:353-361, 2009.
 44. Rudolph V and **BA Freeman**. Cardiovascular consequences when nitric oxide and lipid signaling converge. *Circulation Research* 105:511-522, 2009.
 45. Rudolph TK and **BA Freeman**. Transduction of redox signaling by electrophile-protein reactions. *Science Signaling* 2(90 re7):1-12, 2009.
 46. Cole MP, TK Rudolph, NKH Khoo, UN Motanya, F Golin-Bisello, JW Wertz, FJ Schopfer, V Rudolph, SR Woodcock, S Bolisetty, MS Ali, J Zhang, YE Chen, A Agarwal, **BA Freeman** and PM Bauer. Nitro-fatty acid inhibition of neointima formation after endoluminal vessel injury. *Circulation Research* 105:965-972, 2009.
 47. Kansanen E, H-K Jyrkkänen, OL Volger, H Leinonen, AM Kivelä, S-K Häkkinen, SR Woodcock, FJ Schopfer, AJ Horrevoets, S Ylä-Herttuala, **BA Freeman** and A-L Levonen. Nrf-2 dependent and independent responses to nitro-fatty acids in human endothelial cells: Identification of heat shock response as the major pathway activated by nitro-oleic acid. *J Biol Chem* 284:33233-33241, 2009.
-

48. Lundberg JO, MT Gladwin, A Ahluwalia, N Benjamin, NS Bryan, A Butler, P Cabrales, A Fago, M Feelisch, PC Ford, **BA Freeman** et al. Nitrate and nitrite in biology, nutrition and therapeutics. *Nature Chemical Biology* 5:865-869, 2009.
 49. Rudolph V, TK Rudolph, FJ Schopfer, G Bonacci, SR Woodcock, MP Cole, PRS Baker, R Ramani and **BA Freeman**. Endogenous generation and protective effects of nitro-fatty acids in a murine model of focal cardiac ischaemia and reperfusion. *Cardiovascular Research* 85:155-166, 2010.
 50. Khoo NKH, V Rudolph, MP Cole, F Golin-Bisello, FJ Schopfer, SR Woodcock, C Batthyany and **BA Freeman**. Activation of vascular endothelial nitric oxide synthase and heme oxygenase-1 expression by electrophilic nitro-fatty acids. *Free Radical Biology & Medicine* 48:230-239, 2010.
 51. Kelley EE, NK Khoo, NJ Hundley, UZ Malik, **BA Freeman** and MM Tarpey. Hydrogen peroxide is the major oxidant product of xanthine oxidase. *Free Radic Biol Med* 48:493-498, 2010.
 52. Borniquel S, EÅ Jansson, MP Cole, **BA Freeman** and JO Lundberg. Nitrated oleic acid up-regulates PPAR γ and attenuates experimental inflammatory bowel disease. *Free Radic Biol Med* 48:499-505, 2010.
 53. Groeger AL and **BA Freeman**. Signaling actions of electrophiles: Anti-inflammatory therapeutic candidates. *Molecular Interventions* 10:39-50, 2010.
 54. Rudolph V, RP Andrie, TK Rudolph, K Friedrichs, A Klinke, B Hirsch-Hoffmann, AP Schwoerer, D Lau, XM Fu, K Klingel, K Sydow, M Didie, A Seniuk, E-C von Leitner, K Szoecs, JW Schrickel, H Treede, U Wenzel, T Lewalter, G Nickenig, W-H Zimmermann, T Meinertz, RH Böger, H Reichensperner, **BA Freeman**, T Eschenhagen, H Ehmke, SL Hazen, S Willems and S Baldus. Myeloperoxidase acts as a profibrotic mediator of atrial fibrillation. *Nature Medicine* 16:470-474, 2010.
 55. Groeger AL, C Cipollina, MP Cole, SR Woodcock, G Bonacci, TK Rudolph, V Rudolph, **BA Freeman** and FJ Schopfer. Cyclooxygenase-2 generates anti-inflammatory mediators from omega-3 fatty acids. *Nature Chemical Biology* 6:433-441, 2010.
 56. Khoo NKH and **BA Freeman**. Electrophilic nitro-fatty acids: Anti-inflammatory mediators in the vascular compartment. *Current Opinion in Pharmacology* 10:179-184, 2010.
 57. Schopfer FJ, MP Cole, AL Groeger, C-S Chen, NKH Khoo, SR Woodcock, F Golin-Bisello, UN Motanya, Y Li, J Zhang, MT Garcia-Barrio, TK Rudolph, V Rudolph, G Bonacci, PRS Baker, HE Xu, CI Batthyany, YE Chen, TM Hallis and **BA Freeman**. Covalent peroxisome proliferator-activated receptor γ adduction by nitro-fatty acids: Selective ligand activity and anti-diabetic signaling actions. *Journal of Biological Chemistry* 285:12321-12333, 2010.
 58. Sculptoreanu A, FA Kullman, DE Artim, FA Bazley, F Schopfer, S Woodcock, **BA Freeman** and WC de Groat. Nitro-oleic acid inhibits firing and activates TRPV1- and TRPA1-mediated inward currents in dorsal root ganglion neurons from adult male rats. *Journal of Pharmacology and Experimental Therapeutics* 333:883-895, 2010.
 59. Koenitzer JR and **BA Freeman**. Redox signaling in inflammation: Interactions of endogenous electrophiles and mitochondria in cardiovascular disease. *Annals of the New York Academy of Sciences* 1203:45-52, 2010.
 60. Rudolph TK, V Rudolph, MM Edreira, MP Cole, G Bonacci, FJ Schopfer, SR Woodcock, A Franek, M Pekarova, NKH Khoo, AH Hasty, S Baldus and **BA Freeman**. Nitro-fatty acids reduce atherosclerosis in apolipoprotein E-deficient mice. *Arterioscler Thromb Vasc Biol* 30:938-945, 2010.
 61. Zhang J, L Villacorta, L Chang, Z Fan, M Hamblin, T Zhu, CS Chen, MP Cole, FJ Schopfer, CX Deng, MT Garcia-Barrio, Y-H Feng, **BA Freeman** and YE Chen. Nitro-oleic acid inhibits angiotensin II-induced hypertension. *Circ Res* 107:540-548, 2010.
-

62. Tsujita T, L Li, H Nakajima, N Iwamoto, Y Nakajima-Takagi, K Ohashi, K Kawakami, Y Kumagai, **BA Freeman**, M Yamamoto and M Kobayashi. Nitro-fatty acids and cyclopentenone prostaglandins share strategies to activate the Keap1-Nrf2 system: A study using green fluorescent protein transgenic zebrafish. *Genes to Cells* 16:46-57, 2011.
 63. Bonacci G, FJ Schopfer, CI Batthyany, TK Rudolph, V Rudolph, NKH Khoo and **BA Freeman**. Electrophilic fatty acids regulate matrix metalloproteinase activity and expression. *Journal of Biological Chemistry* 286:16074-16081, 2011.
 64. Kansanen E, G Bonacci, FJ Schopfer, SM Kuosmanen, KI Tong, H Leinonen, SR Woodcock, M Yamamoto, C Carlberg, S Ylä-Herttua, **BA Freeman** and A-L Levonen. Electrophilic nitro-fatty acids activate NRF2 by a KEAP1 cysteine 151-independent mechanism. *Journal of Biological Chemistry* 286:14019-14027, 2011.
 65. Malik UZ, NJ Hundley, G Romero, R Radi, **BA Freeman**, MM Tarpey and EE Kelley. Febuxostat inhibition of endothelial-bound XO: Implications for targeting vascular ROS production. *Free Radical Biology and Medicine* 51:179-184, 2011.
 66. Bonacci G, EK Ascianto, SR Woodcock, SR Salvatore, **BA Freeman** and FJ Schopfer. Gas-phase fragmentation analysis of nitro-fatty acids. *J Am Soc Mass Spectrom* 22:1534-1551, 2011.
 67. Artim DE, F Bazely, SL Daugherty, A Sculptoreanu, KB Koronowski, FJ Schopfer, SR Woodcock, **BA Freeman** and WC de Groat. Nitro-oleic acid targets transient receptor potential (TRP) channels in capsaicin sensitive afferent nerves of rat urinary bladder. *Exp Neurol* 232:90-99, 2011.
 68. Guo CJ, FJ Schopfer, L Gonzales, P Wang, **BA Freeman** and AJ Gow. Atypical PKC ζ transduces electrophilic fatty acid signaling in pulmonary epithelial cells. *Nitric Oxide* 25:366-372, 2011.
 69. Alastalo TP, M Li, V de Jesus Perez, D Pham, H Sawada, JK Wang, M Koskenvuo, L Wang, **BA Freeman**, HY Chang and M Rabinovitch. Disruption of PPAR γ / β -catenin-mediated regulation of apelin impairs BMP-induced mouse and human pulmonary arterial EC survival. *J Clin Invest* 121:3735-3746, 2011.
 70. Al Ghoul I, NKH Khoo, UG Knaus, KK Griendling, RM Touyz, VJ Thannickal, A Barchowsky, WM Nauseef, EE Kelley, PM Bauer, V Darley-Usmar, S Shiva, E Cifuentes-Pagano, **BA Freeman**, MT Gladwin and PJ Pagano. Oxidases and peroxidases in cardiovascular and lung disease: New concepts in reactive oxygen species signaling. *Free Radic Biol Med* 51:1271-1288, 2011.
 71. Shores DR, DG Binion, **BA Freeman** and PRS Baker. New insights into the role of fatty acids in the pathogenesis and resolution of inflammatory bowel disease. *Inflamm Bowel Dis* 17:2192-2204, 2011.
 72. Fukuto JM, SJ Carrington, DJ Tantillo, JG Harrison, LJ Ignarro, **BA Freeman**, A Chen and DA Wink. Small molecule signaling agents: The integrated chemistry and biochemistry of nitrogen oxides, oxides of carbon, dioxygen, hydrogen sulfide and their derived species. *Chemical Research in Toxicology* 25:769-793, 2012.
 73. Khoo NK, N Cantu-Medellin, JE Devlin, CM St. Croix, SC Watkins, AM Fleming, HC Champion, RP Mason, **BA Freeman** and EE Kelley. Obesity-induced tissue free radical generation: An in vivo immuno-spin trapping study. *Free Radic Biol Med* 52:2312-2319, 2012.
 74. Nishida M, T Sawa, N Kitajima, K Ono, H Inoue, H Ihara, H Motohashi, M Yamamoto, M Suematsu, H. Kurose, A van der Vliet, **BA Freeman**, T Shibata, K Uchida, Y Kumagai and T Akaike. Hydrogen sulfide anion regulates redox signaling via electrophile sulfhydration. *Nature Chemical Biology* 8:714-724, 2012.
 75. Rothstein SN, JE Kay, FJ Schopfer, **BA Freeman** and SR Little. A retrospective mathematical analysis of controlled release design and experimentation. *Molecular Pharmaceutics* 9:3003-3011, 2012.
-

76. Bonacci G, PRS Baker, SR Salvatore, D Shores, NKH Khoo, JR Koenitzer, DA Vitturi, SR Woodcock, F Golin-Bisello, MP Cole, S Watkins, C St. Croix, CI Batthyany, **BA Freeman** and FJ Schopfer. Conjugated linoleic acid is a preferential substrate for fatty acid nitration. *Journal of Biological Chemistry* 287:44071-44082, 2012.
77. Hammond VJ, AH Morgan, S Lauder, CP Thomas, S Brown, **BA Freeman**, CM Lloyd, J Davies, A Bush, AL Levonen, E Kansanen, L Villacorta, YE Chen, N Porter, YM Garcia-Diaz, FJ Schopfer and VB O'Donnell. Novel keto-phospholipids are generated by monocytes and macrophages, detected in cystic fibrosis, and activate peroxisome proliferator-activated receptor- γ . *J Biol Chem* 287:41651-41666, 2012.
78. Villacorta L, L Chang, SR Salvatore, T Ichikawa, J Zhang, D Petrovic-Djergovic, L Jia, H Carlsen, FJ Schopfer, **BA Freeman** and YE Chen. Electrophilic nitro-fatty acids inhibit vascular inflammation by disrupting LPS-dependent TLR4 signaling in lipid rafts. *Cardiovasc Res* 98:116-124, 2013.
79. Fajt ML, SL Gelhaus, **B Freeman**, CE Uvalle, JB Trudeau, F Holguin and SE Wenzel. Prostaglandin D2 pathway upregulation: Relation to asthma severity, control, and TH2 inflammation. *J Allergy Clin Immunol* 131:1504-1512, 2013.
80. Perez-Rosello T, CT Anderson, FJ Schopfer, YJ Zhao, D Gilad, SR Salvatore, **BA Freeman**, M Hershinkel, E Aizenman and T Tzounopoulos. Synaptic Zn²⁺ inhibits neurotransmitter release by promoting endocannabinoid synthesis. *Journal of Neuroscience* 33:9259-9272, 2013.
81. Gil M, M Graña, FJ Schopfer, T Wagner, A Denicola, **BA Freeman**, PM Alzari, C Batthyány and R Durán. Inhibition of Mycobacterium tuberculosis PknG by non-catalytic rubredoxin domain specific modification: Reaction of an electrophilic nitro-fatty acid with the Fe-S center. *Free Radical Biology and Medicine* 65:150-161, 2013.
82. Salvatore SR, DA Vitturi, PRS Baker, G Bonacci, JR Koenitzer, SR Woodcock, **BA Freeman** and FJ Schopfer. Characterization and quantification of endogenous fatty acid nitroalkene metabolites in human urine. *Journal of Lipid Research* 54:1998-2009, 2013.
83. Vitturi DA, C-S Chen, SR Woodcock, SR Salvatore, G Bonacci, JR Koenitzer, NA Stewart, N Wakabayashi, TW Kensler, **BA Freeman** and FJ Schopfer. Modulation of nitro-fatty acid signaling: Prostaglandin reductase-1 is a nitroalkene reductase. *J Biol Chem* 288:25626-25637, 2013.
84. Zhang X, KB Koronowski, L Lu, **BA Freeman**, S Woodcock and WC deGroat. Nitro-oleic acid desensitizes TRPA1 and TRPV1 agonist responses in adult rat DRG neurons. *Experimental Neurology* 251:12-21, 2014.
85. Turell L, H Botti, L Bonilla, MJ Torres, F Schopfer, **BA Freeman**, L Armas, A Ricciardi, B Alvarez and R Radi. HPLC separation of human serum albumin isoforms based on their isoelectric points. *Journal of Chromatography B* 944:144-151, 2014.
86. Woodcock SR, SR Salvatore, G Bonacci, FJ Schopfer and **BA Freeman**. Biomimetic nitration of conjugated linoleic acid: Formation and characterization of naturally occurring conjugated nitrodienes. *J Org Chem* 79:25-33, 2014.
87. Fazzari M, A Trostchansky, FJ Schopfer, SR Salvatore, B Sánchez-Calvo, D Vitturi, R Valderrama, JB Barroso, R Radi and **BA Freeman**. Olives and olive oil are sources of electrophilic fatty acid nitroalkenes. *PLOS ONE* 9:e84884, 2014.
88. Kelley EE, J Baust, G Bonacci, F Golin-Bisello, JE Devlin, CM St. Croix, SC Watkins, S Gor, N Cantu-Medellin, ER Weidert, JC Frisbee, MT Gladwin, HC Champion, **BA Freeman** and NKH Khoo. Fatty acid nitroalkenes ameliorate glucose intolerance and pulmonary hypertension in high-fat diet-induced obesity. *Cardiovascular Research* 101:352-363, 2014.
-

D. Research Support

Ongoing Research Support

- R37HL058115 - NIH/NHLBI
Redox Transduction of Nitric Oxide Signaling
The major goals of this project are to define redox reactions between nitric oxide and both the lipids and lipophilic antioxidants of vascular cell membranes and serum lipoproteins.
Freeman (PI) 01/15/98 – 05/31/18
- R01HL064937 - NIH/NHLBI
Redox-Derived Pulmonary Anti-Inflammatory Signaling Mediators
This project will define how the oxidative reactions occurring during inflammatory lung injury lead to the formation of oxidizing and nitrating species that regulate pulmonary inflammatory signaling and metabolism.
Freeman (PI) 06/01/11 – 03/31/16
- R01 HL105114 – NIH – Subcontract with Univ. of MI
Nitro-fatty Acids and Nrf2 in Obesity-related Vascular Remodeling
1) Define a key role of Nrf2 in nitroalkene derivatives of LNO₂- and OA-NO₂-induced VSMC fate *in vitro*; 2) Define the mechanism of the nitroalkene-mediated Nrf2 activation in VSMCs; 3) Determine the nitroalkene-operated Nrf2 signaling in obesity-induced vascular remodeling after vascular injury.
Chen (PI) 07/01/10 - 06/30/15
- P01HL103455 – NIH/NHLBI
Vascular Subphenotypes of Lung Disease (Project 3)
The overarching translational goal of this program is to define common mechanistic and therapeutic pathways for treating PAH in the context of major lung and systemic diseases, such as obesity, COPD and HIV.
Gladwin (PI) 06/01/2011-04/30/2016
-