

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Michael Leo Fitzgerald	POSITION TITLE Assistant Professor of Medicine		
eRA COMMONS USER NAME MLFITZGERALD			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Central Missouri State University, Warrensburg, Institute of Molecular Virology, St. Louis Univ., MO Colorado State Univ. Fort Collins, CO	B.Sc. Ph.D. Postdoc	1987 1993 1994-95	Biology, Chemistry Molecular and Cell Biol. Neurobiology
Harvard School of Public Health, Boston MA	Postdoc	1995-99	Cardiovascular Biology
Harvard Medical School, Boston MA	Postdoc	1999-2002	Lipid Metabolism

NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

8/02-3/06: Instructor of Medicine, Lipid Metabolism/Molecular Biology Dept. Mass. Gen. Hospital/Harvard Medical School

4/06-present: Assistant Professor of Medicine, Lipid Metabolism Unit /Center For Computational and Integrative Biology, Mass. Gen. Hospital/Harvard Medical School

Honors and Awards

Sigma Zeta Undergraduate Scholars Society, 1986, 1987
CMSU Scholarship Award, 1986
Undergraduate Grant, Missouri Academy of Sciences, 1987
Pre-doctoral Scholarship, Saint Louis University, NIH training grant, 1988, 1989
National Science Foundation, Retroviral Integration Grant Reviewer, 1994
Postdoctoral NIH Training Award, Division of Endocrinology, Mass General Hospital 7/99-7/00
Individual National Service Research Award, Division of Endocrinology, Mass General Hospital, 8/00-7/02
Membership in the American Society for Biochemistry and Molecular Biology, 2004-present
American Heart Association: Biotechnology Grant Review Committee Member, 2006-present
National Institute of Mental Health Special Emphasis Lipidomics Grant Review Committee Member 2007
Wellcome Trust Scientific Committee, Ad Hoc reviewer, 2008

B. Selected peer-reviewed publications (in chronological order).

- 1) Vora, A., **Fitzgerald, M.** and Grandgenett, D.(1990). Removal of 3'-OH-terminal nucleotides from blunt-ended long terminal repeat termini by the avian retrovirus integration protein. J. of Virol., 64, 5656-5659 PMID: 2214031
- 2) **Fitzgerald, M.**, Vora, A. and Grandgenett, D. (1991). Development of an acid-soluble assay for measuring retrovirus integrase 3'-OH terminal nuclease activity. Anal. Biochem., 196, 19-23. PMID: 1888032
- 3) **Fitzgerald, M.**, Vora, A., Zeh, B. and Grandgenett, D. (1992). Concerted integration of viral DNA termini by purified avian myeloblastosis virus integrase. J. of Virol., 66, 6257-6263 PMID: 1328665

- 4) Grandgenett, D., Inman, R., Vora, A. and **Fitzgerald, M.** (1993). Comparison of DNA binding and integration half-site selection by avian myeloblastosis virus integrase. *J. of Virol.*, 67, 2628-2636 PMID: 8474165
- 5) **Fitzgerald, M.** and Grandgenett, D. (1994). Retroviral integration: in vitro host site selection by avian myeloblastosis virus integrase. *J. of Virol.*, 68, 4314-4321 PMID: 8207806
- 6) Vora, A., McCord, M., **Fitzgerald, M.**, Inman, R., Grandgenett, D. (1994) Efficient concerted integration of retrovirus-like DNA in vitro by avian myeloblastosis virus integrase. *Nucleic Acids Res.*, 22, 4454-4461 PMID: 7971276
- 7) Reed, GL., Houg, A., **Fitzgerald, ML.** (1999) Platelet secretory protein, a human unc-18c homologue that interacts with syntaxin 4 and is phosphorylated in activated cells: implication for triggered secretion in platelets. *Blood*, 93:2617-2626 PMID: 10194441
- 8) **Fitzgerald, ML.** and Reed, GL. (1999) Rab6 is phosphorylated in thrombin-activated platelets by a protein kinase C-dependent mechanism: effects on GTP/GDP binding and cellular distribution. *Biochemical Journal* 342:353-360 PMID: 10455022
- 9) **Fitzgerald, ML**, Moore, KJ, Freeman, M., and Reed, GL. (2000) Lipopolysaccharide induces Scavenger Receptor-A expression in mouse macrophages: a divergent regulatory mechanism relative to human macrophages. *J. of Immunology* 164(5):2692-700 PMID: 10679110
- 10) Moore KJ, Rosen ED, **Fitzgerald ML**, Randow F, Andersson LP, Altshuler D, Milstone DSPP, Mortensen RM, Spiegelman BM, Freeman, MW (2001) The role of PPAR-gamma in macrophage differentiation and cholesterol uptake. *Nature Medicine* 2001 Jan;7(1):41-7 PMID: 11135614
- 11) **Fitzgerald ML**, Mendez AJ, Moore KJ, Andersson LP, Panjeton HA, and MW Freeman. (2001) ABCA1 contains an N-terminal signal-anchor sequence that translocates the protein's first hydrophilic domain to the exoplasmic space *J. of Biol. Chem.* 276: 15137-15145 PMID: 11328826
- 12) **Fitzgerald ML**, Morris AL, Rhee JS, Andersson LP, MendezAJ, Freeman MW. Naturally Occurring Mutations in the Largest Extracellular Loops of ABCA1 Can Disrupt Its Direct Interaction with Apolipoprotein A-I. *J Biol Chem* 2002 Sep 6;277(36):33178-87 PMID: 12084722
- 13) Fukumoto H, Deng A, Irizarry MC, **Fitzgerald ML**, Rebeck GW. Induction of the cholesterol transporter ABCA1 in central nervous system cells by liver X receptor agonists increases secreted Abeta levels. *J Biol Chem.* 2002 Dec 13;277(50):48508-13. PMID: 12384498
- 14) **Fitzgerald ML**, Morris AL, Chorni A, Mendez AJ, Zannis VI, Freeman MW. ABCA1 and amphipathic apolipoproteins form high affinity molecular complexes required for cholesterol efflux. *J. of Lipid Research*, 2004 Feb;45(2):287-94. Epub 2003 PMID: 14617740
- 15). Chroni A, Liu T, **Fitzgerald ML**, Freeman MW, Zannis VI. Cross-Linking and Lipid Efflux Properties of APOA-I Mutants Suggest Direct Association between APOA-I Helices and ABCA1. *Biochemistry* (2004) Feb 24;43(7):2126-39. PMID: 14967052
- 16) Nieland TJ, Chroni A, **Fitzgerald ML**, Maliga Z, Zannis VI, Kirchhausen T, Krieger M. Cross-inhibition of SR-BI- and ABCA1-mediated cholesterol transport by the small molecules BLT-4 and glyburide. *J Lipid Res.* 2004 Jul;45(7):1256-65. Epub 2004 Apr 21 PMID: 15102890
- 17) **Fitzgerald ML**, Okuhira KI, Short GF 3rd, Manning JJ, Bell SA, Freeman M. ABCA1 contains a novel C-terminal VFNFA motif that is required for its cholesterol efflux and apoA-I binding activities. *J Biol Chem.* 2004 279:48477-485 PMID: 15347662
- 18) Fukuchi J, Hiipakka RA, Kokontis JM, Hsu S, Ko AL, **Fitzgerald ML**, Liao S. Androgenic suppression of ATP-binding cassette transporter A1 expression in LNCaP human prostate cancer cells. *Cancer Res.* 2004 Nov 1;64(21):7682-5. PMID: 15520169
- 19) Kim WS*, **Fitzgerald ML***, Kang K, Okuhira KI, Bell SA, Manning JJ, Koehn SL, Lu N, Moore KJ, Freeman MW. Abca7 null mice retain normal macrophage phosphatidylcholine and cholesterol efflux activity despite alterations in adipose mass and serum cholesterol levels. *J Biol Chem.* 2004 280:3989-89 PMID: 15550377
- 20) Okuhira KI*, **Fitzgerald ML***, Sarracino DA, Manning JJ, Bell SA, Goss JL, Freeman MW. Purification of ABCA1 and associated binding proteins reveals the importance of beta 1-syntrophin in cholesterol efflux. *J Biol Chem.* 2005, 79:48477-48485 PMID: 16192269 * Co-First Authors
- 21) Huang ZH, **Fitzgerald ML**, Mazzone T. Distinct Cellular Loci for the ABCA1-Dependent and ABCA1-Independent Lipid Efflux Mediated by Endogenous Apolipoprotein E Expression. *Arterioscler Thromb Vasc Biol.* 2006 Jan;26(1):157-62. Epub 2005 Oct 27 PMID: 16254198

Principal Investigator/Program Director (Last, First, Middle): PI Name Fitzgerald, Michael, Leo

- 22) **Fitzgerald ML**, Xavier R, Haley KJ, Welti R, Goss JL, Brown CE, Zhuang DZ, Bell SA, Lu N, McKee M, Seed B, Freeman MW. ABCA3 inactivation in mice causes respiratory failure, loss of pulmonary surfactant and depletion of lung phosphatidylglycerol. *J Lipid Res.* 2007, 48:621-632. PMID: 17142808
- 23) Tamehiro N, Zhou S, Okuhira K, Benita Y, Brown CE, Zhuang DZ, Latz E, Hornemann T, von Eckardstein A, Xavier RJ, Freeman MW, **Fitzgerald ML**. SPTLC1 Binds ABCA1 to Negatively Regulate Trafficking and Cholesterol Efflux Activity of the Transporter. *Biochemistry*, 2008 Jun 10; 47(23):6138-47. Epub 2008 May 17. PMID: 18484747
- 24) Zuo, Z., Zhuang, D., Han, R., Isaac, G., Manning, J., McKee, M., Welti, R., Brissette, J., **Fitzgerald, ML**, and Freeman, MW. ABCA12 maintains the epidermal lipid permeability barrier by facilitating formation of ceramide linoleic esters. *J Biol Chem.* 2008 Dec 26; 283(52):36624-35. Epub 2008 Oct 27 PMID: 18957418
- 25) Tamehiro N, Mujawar Z, Zhou S, Zhuang DZ, Hornemann T, von Eckardstein A, **Fitzgerald ML**. Cell polarity factor Par3 binds SPTLC1 and modulates monocyte serine palmitoyltransferase activity and chemotaxis. *J Biol Chem.* 2009 Jul 10. [Epub ahead of print] PMID: 19592499

Reviews

- 1) Reed, GL, **Fitzgerald, ML**., Polgar, J. (2000)Molecular mechanisms of platelet exocytosis: insights into the "secrete" life of thrombocytes. *Blood.* Nov 15;96(10):3334-42 PMID: 11071625
- 2) Moore, KJ, **Fitzgerald, ML**, Freeman, MW. Peroxisome proliferator-activated receptors in macrophage biology: anti-inflammatory modulators? *Curr. Opin. Lipidology*, 2001 Oct;12(5):519-27. PMID: 11561171
- 3) **Fitzgerald, ML**, Moore, KJ, Freeman, MW. Nuclear hormone receptors and cholesterol trafficking: the orphans find a new home. *J. Mol. Medicine*, 2002 May;80(5):271-81 PMID: 12021839

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

Grant # RO1 HL074136-01A1 (PI Fitzgerald, Michael, L.)
NIH/NHLBI: 8/1/05-7/31/10

“ABCA1 cholesterol efflux and protein-protein interactions”

This grant has developed a proteomic approach to analyze ABCA1 protein-protein interactions that control the efflux activity of the transporter. Mass spectrometry screens have identified candidate interacting proteins that bind the C-terminus of the transporter affecting its distribution and efflux activity. The mechanistic details of these interactions are being further characterized and follow up screens are being conducted.

Grant in Aid # 09GRNT2260352 (PI, Fitzgerald, Michael L.)
American Heart Association 7/1/2009-6/30/2012

“Analysis of an ABCA1/SPTLC1 Protein Complex That Negatively Regulates Cholesterol Efflux”

This grant explores how SPTLC1 interacts with ABCA1 versus its binding of the SPTLC2 subunit of the serine palmitoyltransferase holoenzyme. Additionally, in vivo experiments will be conducted to test whether the ability of the SPT inhibitor myriocin to inhibit atherosclerosis in mice correlates with its ability to disrupt the ABCA1/SPTLC1 protein complex.

Grant #1R24RR020345 (PI Freeman, Mason, W)

Principal Investigator/Program Director (Last, First, Middle): PI Name Fitzgerald, Michael, Leo

NIH/NCRR: 7/1/06-5/31/10

“Analysis of ABCA Transporter Function in Homologous Recombinant Mice”

This animal resource grant provides funds for the generation and initial phenotype analysis of mice lacking poorly characterized ABCA transporters whose mutation in humans are associated with significant genetic diseases. As part of this funding mechanism the animals and other research reagents: antibodies; cDNA clones are made readily available to the research community.

Role: Co-investigator

Foundation for Ichthyosis Research Grant Award: 9/1/08-8/31/10

“Analysis of a Mouse Gene Deletion Model for the Lamellar/Harlequin Ichthyosis ABCA12 Transporter”

This award funds work to phenotype a Abca12 null mouse model we have developed that recapitulates the severe HI phenotype, which is associated with a disruption of the skin’s lipid permeability barrier

Role: Co-investigator

Completed

National Research Service Award HL10398 (Fitzgerald, Michael, L.) NIH/NHLBI

Dates 7/1/00-7/31/02

The overall goals of this project were to

I. Determine whether PDZ-domain proteins bind ABCA1, and if so whether such binding is important for the apoA1-efflux of intracellular cholesterol-ester stores

II. Determine the cellular localization of ABCA1 during apoA1 cholesterol-efflux with respect to phosphorylation status and interactions with PDZ-proteins.

Role: Principal Investigator