

BIOGRAPHICAL SKETCH

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NAME Daniel Stephen Lark		POSITION TITLE Research Fellow	
eRA COMMONS USER NAME (credential, e.g., agency login) LARKD24			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
University of Wisconsin - Milwaukee	B.S.	05/2008	Kinesiology
East Carolina University	M.S.	05/2010	Kinesiology
East Carolina University	Ph.D.	06/2014	Bioenergetics
Vanderbilt University Medical Center	Postdoc	Current	Molecular Physiology & Biophysics

A. Personal Statement

My ultimate career goal is to direct an academic research laboratory that conducts impactful basic and translational research that improves our understanding of human metabolic disease. Through this fellowship, I will achieve that goal by enhancing my technical skills, obtaining mentoring from senior investigators and establishing an independent line of inquiry. As an undergraduate and graduate student, my research interests were focused on the regulation of mitochondrial energetics and how redox biology contributes to metabolic disease. As a postdoctoral fellow, I have used my expertise in molecular metabolism to identify integrin-linked kinase as a new mechanism contributing to metabolic disease. In this fellowship, I will further define how integrin-linked kinase contributes to metabolic disease using novel *in vivo* physiological techniques and identify new and exciting research directions using unbiased "systems biology" approaches.

B. Positions and Honors

ACTIVITY/OCCUPATION	BEGINNING DATE (mm/yy)	ENDING DATE (mm/yy)	FIELD	INSTITUTION/COMPANY	SUPERVISOR/ EMPLOYER
Undergrad Research Assistant	12/2005	08/2008	Kinesiology	University of Wisconsin – Milwaukee	Ann C. Snyder, Ph.D.
Graduate Research Assistant	08/2008	06/2014	Kinesiology	East Carolina University	P. Darrell Neuffer, Ph.D.
Postdoctoral Fellow	07/2014	Present	Physiology	Vanderbilt University	David. H. Wasserman, Ph.D.

Academic and Professional Honors:

2008 UWM Chancellor's Undergraduate Research Award, University of Wisconsin – Milwaukee (2008)
2008 Victor A. Drill Award (runner-up) from the Society of Toxicology - Midwest Regional Chapter
2014 NIH/NIDDK Ruth L. Kirschstein National Research Service Award (NRSA) for "Research Training in Diabetes and Endocrinology" (T32DK007061)

Professional Affiliations:

American College of Sports Medicine (ACSM)
American Physiological Society (APS)
American Academy for the Advancement of Sciences (AAAS)

C. Contributions to Science:

1) Mechanisms linking mitochondrial energetics to metabolic disease. The vast majority of my research has focused on defining the role of mitochondrial biology in the etiology of disease. These projects have led to a number of important discoveries. As first author, I conceived and executed a recent project that revealed Protein Kinase A signaling as a major regulator of mitochondrial energetics. Through a fruitful international collaboration with Dr. Christopher Perry at York University, I designed and executed experiments to define the link between exercise and mitochondrial respiratory kinetics in human skeletal muscle. Through various internal collaborations, I have contributed to mitochondrial function studies focused on: 1) cardiovascular disease, 2) cancer chemotherapy and 3) defining new sites of mitochondrial oxidant production. **Most recently, I have received independent extramural funding to develop a novel system that can be used to quantify mitochondrial oxidative efficiency in real-time.**

Published Original Research:

- 1) **Lark DS**, Reese LR, Ryan TE, Torres MJ, Smith CD, Lin CT and Neuffer PD. Protein kinase A governs oxidative phosphorylation kinetics and oxidant emitting potential at complex I. *Frontiers in Physiology*, 2015 Nov 17;6:332. doi: 10.3389/fphys.2015.00332. eCollection 2015. PMID: Pending
- 2) **Lark DS**, Kang L, Lustig ME, Bonner JS, James FD, Neuffer PD, Wasserman DH. Enhanced Mitochondrial Superoxide Scavenging does not Improve Muscle Insulin Action in the High Fat-fed Mouse. *PLOS One* 2015 May 19;10(5):e0126732. PMID: Pending
- 3) Fisher-Wellman KH, Lin CT, Ryan TE, Reese LR, Gilliam LA, Cathey BL, **Lark DS**, Smith CD, Muoio DM and Neuffer PD. Pyruvate dehydrogenase complex and nicotinamide nucleotide transhydrogenase constitute an energy consuming redox circuit. *Biochem J*. 2015 Apr 15;467(2):271-80.
- 4) Anderson EJ, Thayne KA, Harris M, Shaikh SR, Darden T, **Lark DS**, Williams M, Chitwood WR, Kypson AP, Rodriguez E. Pre-operative fish oil therapy enhances mitochondrial fatty acid oxidation and redox balance in human atrial myocardium. *Antioxid Redox Signal*. 2014 Apr 10. PMID: PMC4142835
- 5) DeBalsi KL, Wong KE, Koves TR, Slentz DH, Seiler SE, Wittmann AH, Ilkayeva OR, Stevens RD, Perry CG, **Lark DS**, Hui ST, Szweda L, Neuffer PD, and Muoio DM. Targeted Metabolomics Connects TXNIP to Mitochondrial Fuel Selection and Regulation of Specific Oxidoreductase Enzymes in Skeletal Muscle. *J Biol Chem*. 2014 Mar 21; 289(12):8106-20. PMID: PMC3961642
- 6) Fisher-Wellman KH, Gilliam LA, Lin CT, Cathey BL, **Lark DS**, Neuffer PD. Mitochondrial glutathione depletion reveals a novel role for the pyruvate dehydrogenase complex as a key H₂O₂-emitting source under conditions of nutrient overload. *Free Radic Biol Med*. 2013 Sep 19. pii: S0891-5849(13)00611-4. PMID: PMC3965186
- 7) Perry CG, Kane DA, Herbst EA, Mukai K, **Lark DS**, Wright DC, Heigenhauser GJ, Neuffer PD, Spriet LL, Holloway GP. Mitochondrial creatine kinase activity and phosphate shuttling are acutely regulated by exercise in human skeletal muscle. *J Physiol*. 2012 Nov 1;590(Pt 21):5475-86. PMID: PMC3515832
- 8) Perry CG, Kane DA, Lin CT, Kozy R, Cathey BL, **Lark DS**, Kane CL, Brophy PM, Gavin TP, Anderson EJ, Neuffer PD. Inhibiting myosin-ATPase reveals a dynamic range of mitochondrial respiratory control in skeletal muscle. *Biochem J*. 2011 Jul 15;437(2):215-22. PMID: PMC3863643

Manuscripts Submitted, In Revision or In Preparation:

- 1) Gilliam LA, **Lark DS**, Reese LR, Torres MJ, Ryan TE, Lin CT, Cathey BL, and Neuffer PD. Targeted overexpression of mitochondrial catalase protects against cancer chemotherapy-induced skeletal muscle dysfunction. (*submitted to AJP-Endo*)
- 2) **Lark DS**, Lin CT, Ryan TE, Anderson EJ and Neuffer PD. Demand-driven enhancement of oxidative phosphorylation efficiency in permeabilized myofibers. (*in preparation*)
- 3) Perry CG, **Lark DS**, Kane DA, Lin CT, Cathey BL, and Neuffer PD. Acute influence of dietary fat versus carbohydrate intake on skeletal muscle mitochondrial H₂O₂ emission, cellular redox state, and insulin sensitivity. (*in preparation*)

Published Reviews:

- 1) **Lark DS**, Fisher-Wellman KH and Neuffer PD. High-fat load: Mechanism(s) of insulin resistance in skeletal muscle. *Int J Obes Suppl.* 2012 Dec; 2(Suppl 2):S31-36. PMID: PMC4457392

Selected Abstracts:

- 1) **Lark DS**, Ryan TE, Torres MJ, Lin CT, Anderson EJ and Neuffer PD. Demand-driven enhancement of mitochondrial oxidative phosphorylation efficiency in permeabilized myofibers. *Diabetes Day at Vanderbilt University Medical Center, Nashville TN, 10/14 and Tennessee Physiological Society Meeting, Nashville TN 01/15*
- 2) Brown D, Moukdar F, Sullivan EM, Sloan RC, Alleman RJ, Patel HD, **Lark DS**, Neuffer PD and Shaikh SR. The mitochondria-targeting peptide Bendavia restores mitochondrial function in diabetic hearts by normalizing cardiolipin content. *European Society of Cardiology, 9/14.*
- 3) Reese LR, **Lark DS** and Neuffer PD. 2-Hydroxyestradiol as a pro-oxidant regulator of muscle mitochondrial function. *Metabolic Origins of Disease, Orlando FL, 4/14 and Advances in Skeletal Muscle Biology and Disease, Gainesville FL, 04/14*
- 4) Gilliam LA, **Lark DS**, Fisher-Wellman KH, Torres MJ, Reese LR, Cather BL and Neuffer PD. Cancer chemotherapy impairs mitochondrial function in non-tumor-bearing tissue. *Metabolic Origins of Disease, Orlando FL, 4/14 and Advances in Skeletal Muscle Biology and Disease, Gainesville FL, 04/14*
- 5) Anderson EJ, Thayne KA, Harris M, Shaikh SR, Darden T, **Lark DS**, Williams M, Chitwood WR, Kypson AP and Rodriguez E. Pre-operative fish oil therapy enhances mitochondrial fatty acid oxidation and redox balance in human atrial myocardium. *Society for Heart and Vascular Metabolism, Cambridge MD, 9/13*
- 6) **Lark DS**, Neuffer PD and Anderson ET. Glycolytic skeletal myofibers display higher ATP/O ratios than cardiac myofibers due to adenylate kinase: Preliminary findings using a novel oxi-fluorometer apparatus. *APS Integrative Biology of Exercise, Westminster CO, 10/12*
- 7) **Lark DS**, Gopalakrishnan S, Wilson RW, Sandoval CL, Eells JT and Snyder AC. Effect of photobiomodulation on glutathione redox status of gastrocnemius muscle in an animal model of diabetes. *Experimental Biology, San Diego CA, 04/08 and Midwest Regional Chapter of the Society of Toxicology Spring Meeting, 05/08.*

2) Integrin-linked kinase and the etiology of metabolic syndrome.

As a postdoctoral fellow, I have embarked on a new and exciting research direction to define how integrins regulate muscle insulin action. Thus far I have contributed to a paper currently in revision at Diabetes and have, as first author, began preparing an additional manuscript for submission. The landmark discovery of this research direction thus far is that integrin-linked kinase is a potent regulator of fatty acid metabolism, a major factor in the etiology of metabolic disease. One of my primary career development goals is to merge this line of inquiry with my expertise in mitochondrial energetics, effectively linking extracellular matrix biology to mitochondrial metabolism.

Manuscripts Submitted, In Revision or In Preparation:

- 1) Kang L, **Lark DS**, Pozzi A, Zent R and Wasserman DH. Integrin-Linked Kinase in Muscle is Necessary for the Development of Insulin Resistance in Diet-Induced Obese Mice. (*in revision at Diabetes*)
- 2) **Lark DS**, Trefts E, Kang L, James M, James FD, Pozzi A, Zent R and Wasserman DH. Integrin-linked kinase enhances skeletal muscle fatty acid metabolism *in vivo*. (*in preparation*)

Selected Abstracts:

- 1) **Lark DS**, Trefts E, James M, Pozzi A, Zent R and Wasserman DH. Integrin-linked Kinase enhances skeletal muscle fatty acid metabolism *in vivo*. *Diabetes Day at Vanderbilt University Medical Center, 12/15.*

Current Extramural Support:

NIH/NIDDK T32 Institutional Training Grant (DK007061)
"Research Training in Diabetes and Endocrinology"

September 2014 – September 2016

Role: Postdoctoral Fellow Trainee

Description: DK007061 is the longest tenured T32 training grant in the history of NIDDK, a demonstration of the exceptional training that aspiring academic scientists receive through the Vanderbilt Diabetes and

Research Training Center. As a Postdoctoral Trainee supported by DK007061, I receive salary support and modest funds for travel and research supplies. As a trainee thus far, I have engaged in numerous activities relevant to my training, including attending Endocrinology Grand Rounds, presenting my research at local and national conferences and being competitively selected to the Vanderbilt Program in Molecular Medicine.

NIH/NIDDK MMPC MICROMouse Grant (15GRU2558) *November 2015 – November 2016*
 “A Novel Toolkit for Measuring Mitochondrial Energetics in Mouse Muscle”

Role: Principal Investigator (20% effort)

Description: As principal investigator, I am responsible for all aspects of executing the award, including: managing the award budget, designing and executing experiments and writing manuscripts and progress reports. The goals of this one-year research grant (\$43,570 in total direct costs) are to: 1) develop and validate of an assay to measure mitochondrial oxidative efficiency in permeabilized mouse myofibers and 2) determine whether mitochondrial oxidants contribute to acute lipid-induced muscle insulin resistance and metabolic inefficiency *in vivo*.

D. Scholastic Performance.

YEAR	COURSE TITLE	GRADE	YEAR	COURSE TITLE	GRADE
East Carolina University			2012	Practical Problems in Biometry	A
2008	Theory and Techniques in Bioenergetics	B	UW – Parkside		
2008	Physiology of Exercise	A	2002	Nature of Life	B-
2008	Research Techniques in Exercise	A	UW – Fond du Lac		
2009	General Chemistry II	B	2003	College Algebra	B
2009	Nutrition and Exercise	A	2004	Concepts of Biology	A-
2009	Cardiopulmonary Physiology	B	2004	Human Anatomy	C
2009	Biostatistics	B	2005	Human Physiology	B
2009	Organic Chemistry I	B	2005	Introductory Psychology	B-
2009	Organic Chemistry Laboratory I	A	UW – Milwaukee		
2009	Bioenergetics I	A	2005	Applied Human Anatomy	A-
2009	Muscle Physiology	B	2005	Stats in Health Professions	B
2010	Animal Research Methods	A	2005	Health Aspects of Exercise/Nutrition	A-
2010	Bioenergetics II	B	2006	Physiological Psychology	A-
2010	Intro to Research	A	2006	Ethics and Values in Health Professions	B
2010	Ethics and Research	B	2006	Exercise Physiology	B
2010	Graduate Organ Systems Physiology	B	2006	Program Development in Exercise	A-
2011	Graduate Neuroscience	B	2007	Qual Analysis of Human Movement	B+
2011	Physiological Proteogenomics	A	2007	Exercise Testing	B
2011	Advanced Topics: Glucose Trafficking	A	2007	Principles of Motor Learning	B
2011	Advanced Topics: Redox Biology and Diabetes	A	2007	General Chemistry I	B
			2008	Kinesiology Internship/Seminar	A