BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Cobine, Paul

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

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
The University of Queensland , Brisbane, Queensland	BS	03/1994	Microbiology
The University of Queensland, Brisbane, Queensland	PHD	03/2004	Microbiology
University of Utah, Salt Lake City, Utah	Postdoctoral Fellow	08/2008	Biochemistry

A. Personal Statement

My research is primarily focused on balancing metal requirements within cells and organelles. In particular, I use innovative approaches of basic science linking analytical measurement of metal elements to genetic and biochemical analysis of the genes, proteins and small molecules that mediate bioavailability. As a career goal I want to have a cooperative research group that provides our expertise with measurement and spectroscopic analysis to others using multiple prokaryotic and eukaryotic systems to enhance interdisciplinary training and research opportunities.

Mitochondrial copper homeostasis is required for maturation of cytochrome c oxidase and a fraction of the cellular superoxide dismutase. These two target enzymes are critical to normal physiology. However the transporters and molecules that control availability of copper in this organelle are unknown. Working in collaboration with Scot Leary and others we have contributed significant advances to our understanding of the assembly of cytochrome c oxidase and management of matrix copper. This experience has also provided significant challenges and our combined experience and unpublished results have uniquely positioned us to uncover the identity of the transporter proteins. I have extensive experience in biochemistry, yeast and bacterial genetics, spectroscopy, analytical chemistry, cell biology and natural products chemistry and my laboratory currently has active projects in multiple experimental systems including yeast, bacteria, cell culture, copepods and birds.

I have demonstrated a strong and continuing commitment to undergraduate teaching, training and outreach. I have provided basic training in undergraduate research program as a mentor for 160 students over the last 7 years. Many of these students come from our Biomedical Sciences major and they have used this experience to propel them to Medical and Graduate School. I have also mentored Regional High School students and Science Teachers for Auburn University Cellular and Molecular Bioscience program for Teaching Enhancement. This program provides the teacher with a scientific module that is taught in the classroom after completion of the program. I have been actively involved in outreach in Alabama, sponsoring High School student research for the Intel Science Fair and providing mentorship to high-needs regional school teachers for developing project based learning activities for improving Science Fair participation. This includes providing materials and advising students on scientific methods.

B. Positions and Honors

Positions and Employment

1994 - 1996 Research Assistant, The University of Queensland, Brisbane
1998 - 2000 Research Assistant, National Research Center for Environmental Toxicology, Brisbane
2008 - 2014 Assistant Professor, Auburn University, Auburn, AL
2014 - Associate Professor, Auburn University, Auburn, AL

Other Experience and Professional Memberships

2008 -	Member, American Society of Microbiology
2008 -	Member, American Society for Biochemistry and Molecular Biology
2008 -	Academic Editor, PLOS One
2008 -	Member, American Association for Advancement of Sciences
2018 -	Organizer, FASEB: Trace Elements in Biology and Medicine

Honors

2007 - 2008	UMDF Postdoctoral Fellowship, University of Utah
2010	Faculty Honoree, Camp War Eagle, Freshman Orientation Program, Auburn University
2014	Outstanding Faculty Advisor, College of Sciences and Mathematics, Auburn University
2016	Outstanding Faculty Outreach, College of Sciences and Mathematics, Auburn University
2017	Outstanding Teacher, College of Sciences and Mathematics, Auburn University
2018	Young Scholar Award, College of Science and Mathematics, Auburn University
2018	Faculty and Staff Award, Auburn University Parents Association

C. Contribution to Science

1. My work has contributed to the understanding of copper homeostasis in mitochondria. I discovered that copper was present in the mitochondrial matrix in a complex that is biologically inert and yet labile for exchange. This result was a shift from the prevailing paradigm that all intracellular copper in eukaryotes was protein bound. This discovery led to multiple hypotheses about the existence of inner membrane transporters and the control and distribution of mitochondrial copper. I also discovered and characterized the first mitochondrial copper transporter in Saccharomyces cerevisiae and have extended this work to demonstrate that copper is transported by SLC25A3 in mammals.

    a. Boulet A, Vest KE, Maynard MK, Gammon MG, Russell AC, Mathews AT, Cole SE, Zhu X, Phillips CB, Kwong JQ, Dodani SC, Leary SC, Cobine PA. The mammalian phosphate carrier SLC25A3 is a mitochondrial copper transporter required for cytochrome c oxidase biogenesis. J Biol Chem. 2018 Feb 9;293(6):1887-1896. PubMed PMID: 29237729; PubMed Central PMCID: PMC5808751.

    b. Vest KE, Wang J, Gammon MG, Maynard MK, White OL, Cobine JA, Mahone WK, Cobine PA. Overlap of copper and iron uptake systems in mitochondria in Saccharomyces cerevisiae. Open Biol. 2016 Jan;6(1):150223. PubMed PMID: 26763345; PubMed Central PMCID: PMC4736827.

    c. Vest KE, Leary SC, Winge DR, Cobine PA. Copper import into the mitochondrial matrix in Saccharomyces cerevisiae is mediated by Pic2, a mitochondrial carrier family protein. J Biol Chem. 2013 Aug 16;288(33):23884-92. PubMed PMID: 23846699; PubMed Central PMCID: PMC3745335.

    d. Cobine PA, Pierrel F, Bestwick ML, Winge DR. Mitochondrial matrix copper complex used in metallation of cytochrome oxidase and superoxide dismutase. J Biol Chem. 2006 Dec 1;281(48):36552-9. PubMed PMID: 17008312.

2. SCO proteins serve an unexpected dual function in eukaryotic cells: providing copper to cytochrome c oxidase and regulating cellular copper homoeostasis. I have contributed to the the developing model that SCO proteins are central to a signaling cascade that from mitochondria that control the abundance and localization of the high affinity copper import system and the copper export system.

    a. Baker ZN, Jett K, Boulet A, Hossain A, Cobine PA, Kim BE, El Zawily AM, Lee L, Tibbits GF, Petris MJ, Leary SC. The mitochondrial metallochaperone SCO1 maintains CTR1 at the plasma membrane to preserve copper homeostasis in the murine heart. Hum Mol Genet. 2017 Dec 1;26(23):4617-4628. PubMed PMID: 28973536; PubMed Central PMCID: PMC5886179.

    b. Hlynialuk CJ, Ling B, Baker ZN, Cobine PA, Yu LD, Boulet A, Wai T, Hossain A, El Zawily AM, McFie PJ, Stone SJ, Diaz F, Moraes CT, Viswanathan D, Petris MJ, Leary SC. The Mitochondrial Metallochaperone SCO1 Is Required to Sustain Expression of the High-Affinity Copper Transporter CTR1 and Preserve Copper Homeostasis. Cell Rep. 2015 Feb 12;PubMed PMID: 25683716.

c. Leary SC, Cobine PA, Nishimura T, Verdijk RM, de Krijger R, de Coo R, Tarnopolsky MA, Winge DR, Shoubridge EA. COX19 mediates the transduction of a mitochondrial redox signal from SCO1 that regulates ATP7A-mediated cellular copper efflux. Mol Biol Cell. 2013 Mar;24(6):683-91. PubMed PMID: 23345593; PubMed Central PMCID: PMC3596241.

d. Leary SC, Cobine PA, Kaufman BA, Guercin GH, Mattman A, Palaty J, Lockitch G, Winge DR, Rustin P, Horvath R, Shoubridge EA. The human cytochrome c oxidase assembly factors SCO1 and SCO2 have regulatory roles in the maintenance of cellular copper homeostasis. Cell Metab. 2007 Jan;5(1):9-20. PubMed PMID: 17189203.

3. I have made a series of contributions to the in vitro and in vivo characterization of the copper transfer pathway in the intermembrane space. Using protein chemistry, yeast genetics and cell culture we have characterized the copper binding functions of Sco1, Sco2 and Cox17. In addition I was a part of the studies to define the copper binding function of Cox19. These studies established the framework to test the function disease causing mutation in human Sco1 and led to the discovery that the common Sco1 (P174L) mutation that cause neonatal liver failure was due to decreased interaction in the copper delivery pathway.

   a. Horng YC, Cobine PA, Maxfield AB, Carr HS, Winge DR. Specific copper transfer from the Cox17 metallochaperone to both Sco1 and Cox11 in the assembly of yeast cytochrome C oxidase. J Biol Chem. 2004 Aug 20;279(34):35334-40. PubMed PMID: 15199057.

   b. Horng YC, Leary SC, Cobine PA, Young FB, George GN, Shoubridge EA, Winge DR. Human Sco1 and Sco2 function as copper-binding proteins. J Biol Chem. 2005 Oct 7;280(40):34113-22. PubMed PMID: 16091356.

   c. Cobine PA, Pierrel F, Leary SC, Sasarman F, Horng YC, Shoubridge EA, Winge DR. The P174L mutation in human Sco1 severely compromises Cox17-dependent metallation but does not impair copper binding. J Biol Chem. 2006 May 5;281(18):12270-6. PubMed PMID: 16520371.

   d. Rigby K, Zhang L, Cobine PA, George GN, Winge DR. characterization of the cytochrome c oxidase assembly factor Cox19 of Saccharomyces cerevisiae. J Biol Chem. 2007 Apr 6;282(14):10233-42. PubMed PMID: 17237235.

4. Xylella fastidiosa is a plant pathogen that causes billions of dollars worth of damage each year worldwide. The bacterium inhabits the xylem of the host plants and causes disease via biofilm formation. I have contributed to this field by demonstrating the role of metal elements in this plant disease. In collaboration we have demonstrated a clear role for calcium in regulating virulence factors in the bacterium and shown that ionic remodeling of the plant host in response to infection can be directly correlated to disease symptoms. Therefore we have expanded the concept of nutritional immunity to include response to this xylem limited pathogen.

   a. Chen H, Kandel PP, Cruz LF, Cobine PA, De La Fuente L. The Major Outer Membrane Protein MopB Is Required for Twitching Movement and Affects Biofilm Formation and Virulence in Two Xylella fastidiosa strains. Mol Plant Microbe Interact. 2017 Nov;30(11):896-905. PubMed PMID: 28800709.

   b. Kandel PP, Almeida RPP, Cobine PA, De La Fuente L. Natural Competence Rates Are Variable Among Xylella fastidiosa Strains and Homologous Recombination Occurs In Vitro Between Subspecies fastidiosa and multiplex. Mol Plant Microbe Interact. 2017 Jul;30(7):589-600. PubMed PMID: 28459171.

   c. Cruz LF, Parker JK, Cobine PA, De La Fuente L. Calcium-Enhanced Twitching Motility in Xylella fastidiosa Is Linked to a Single PilY1 Homolog. Appl Environ Microbiol. 2014 Dec;80(23):7176-85. PubMed PMID: 25217013; PubMed Central PMCID: PMC4249194.

   d. Oliver JE, Sefick SA, Parker JK, Arnold T, Cobine PA, De La Fuente L. Ionome changes in Xylella fastidiosa-infected Nicotiana tabacum correlate with virulence and discriminate between subspecies of bacterial isolates. Mol Plant Microbe Interact. 2014 Oct;27(10):1048-58. PubMed PMID: 24983508.