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: Peter James Mullen

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

POSITION TITLE: Assistant 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)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Oxford, United Kingdom	M.Biochem.	07/2002	Biochemistry
University of Manchester, United Kingdom	M.Sc.	08/2005	Immunology
University of Basel, Switzerland	Ph.D.	12/2010	Cell Biology
University Health Network, Toronto, Canada	Postdoc	06/2017	Cell Biology
University of California, Los Angeles	Assistant Project Scientist	09/2021	Cell Biology

A. Personal Statement

I have spent 10 years studying the regulation and role of metabolism in tumor growth and virus infections. The overall goal of my recently established lab is to understand how whole-body metabolism alters respiratory virus replication, cancer treatment, and longevity. By elucidating disease-specific requirements for different nutrients, I aim to identify and develop novel treatment strategies. Relevant to the USC Norris Cancer Center, I have expertise in developing novel treatment strategies in multiple tumor types, modulating dietary nutrients in vivo, performing and analyzing LC-MS/MS based metabolomics, and analyzing scRNA-seq data. My lab is in the Department of Molecular Microbiology and Immunology at USC, which offers in-house facilities integral to the success of our research. We are committed to developing age-specific strategies against cancer and respiratory viruses.

B. Positions and Honors

Positions

2005 – 2007 Research Technician, University College London, United Kingdom
2021 – Present Assistant Professor, Keck School of Medicine, USC, Los Angeles, CA
2021 – Present Ad Hoc Reviewer for Nature Metabolism
2021 – Present Ad Hoc Reviewer for PLOS Neglected Tropical Diseases
2022 – Present Ad Hoc Reviewer for Cell Metabolism
2022 – Present Ad Hoc Reviewer for PLOS Pathogens
2022 – Present Ad Hoc Reviewer for Immunologic Research

Honors

2001 Erasmus Scholarship for Overseas Research, University of Oxford
2009 Seahorse Biosciences Travel Grant
2010 Basel Pharmaceutical Annual Research Meeting Poster Award
2011 Seahorse Biosciences Travel Grant
2012 Office of Research Trainees Travel Grant
2013 Seahorse Biosciences Travel Grant

2013 – 2014 Knudson Postdoctoral Fellowship
2015 Seahorse Biosciences Travel Grant

C. Contributions to Science

1. Uncovering metabolic vulnerabilities during SARS-CoV-2 infection. I led the virology research team in the Christofk lab at UCLA and established multidisciplinary collaborations to study the effects of SARS-CoV-2 infection in disease-relevant models such as human stem cell derived air liquid interface cultures. We showed that SARS-CoV-2 infection alters glucose and glutamine carbon entry into the mitochondria, increasing metabolites necessary for viral replication. We also showed that SARS-CoV-2 infection activates mTORC1 in multiple systems, and that FDA-approved mTORC1 inhibitors inhibit SARS-CoV-2 replication. This study gave me experience in working in BSL3 facilities and taught me how to culture air liquid interface cultures.

1. **Mullen PJ**, Garcia Jr G, Purkayastha A, Matulionis N, Schmid EW, Momcilovic M, Sen C, Langerman J, Ramaiah A, Shackelford DB, Damoiseaux R, French SW, Plath K, Gomperts BN, Arumugaswami V, Christofk HR. SARS-CoV-2 infection rewires host cell metabolism and is susceptible to mTORC1 inhibition. *Nature Communications.* 12(1):1876 (2021).
2. **Mullen PJ** and Christofk HR. The metabolic relationship between viral infection and cancer. *Annual Review of Cancer Biology.* 6:1-15 (2022).

2. Identifying growth-promoting nutrients in cancer. I co-led a project that described asparagine as the previously unknown sensor of mitochondrial electron transport chain activity to mTORC1. This identified asparagine as a limiting nutrient for cancer cell proliferation. We added therapeutic relevance by showing that combining dietary restriction of asparagine with electron transport chain inhibitors reduces the growth of multiple tumor types in vivo. In addition, I developed models to show that the extracellular matrix controls glucose uptake in vivo. This work also uncovered that RNA binding proteins can quickly alter metabolic pathway activity by degrading key regulators.

1. Krall AS*, **Mullen PJ***, Surjono F, Momcilovic M, Schmid EW, Halbrook CJ, Thambundit A, Mittelman SD, Lyssiotis CA, Shackelford DB, Knott SRV, Christofk HR. Asparagine signals mitochondrial respiration and can be targeted to impair tumour growth. *Cell Metabolism.* 33(5):1013-1026 (2021). *Co-first author.
2. Halbrook CJ, Thurston G, McCarthy A, Nelson BS, Sajjakulnukit P, Krall AS, **Mullen PJ**, Zhang L, Batra S, Viale A, Stanger BZ, Christofk HR, Zhang J, di Magliano MP, Jorgensen C, Lyssiotis CA. Clonal heterogeneity supports mitochondrial metabolism in pancreatic cancer. *bioRxiv.* doi: 10.1101/2020.05.15.098368 (2021).
3. Sullivan WJ, **Mullen PJ**, Schmid EW, Flores A, Momcilovic M, Sharpley MS, Jelinek D, Whiteley AE, Maxwell MB, Wilde BR, Banerjee U, Coller HA, Shackelford DB, Braas D, Ayer DE, de Aguiar Vallim TQ, Lowry WE, Christofk HR. Extracellular matrix remodeling regulates glucose metabolism through TXNIP destabilization. *Cell.* 175(1):117-132 (2018).

3. Determining that inhibiting the SREBP transcription factors is a viable therapeutic strategy in multiple tumor types. The SREBP transcription factors control the expression of genes involved in the synthesis of cholesterol and fatty acids. I co-discovered that targeting the SREBP transcription factors by RNAi potentiates the effects of statins in lung, breast and prostate cancer. We also discovered that the FDA-approved drug dipyridamole inhibits SREBP activation and synergizes with statins across multiple cancers, including leukemias, multiple myeloma and prostate cancer. These studies formed the basis for an ongoing clinical trial and could lead to a cost-effective strategy to target cancer and other metabolic diseases.

1. Pandyra AA, **Mullen PJ**, Kalkat M, Yu R, Pong JT, Li Z, Trudel S, Lang KS, Minden MD, Schimmer AD, Penn LZ. Immediate utility of two approved agents to target both the metabolic mevalonate pathway and its restorative feedback loop. *Cancer Research.* 74(17):4772-4782 (2014).
2. Pandyra AA, **Mullen PJ**, Goard CA, Ericson E, Sharma P, Kalkat M, Yu R, Pong JT, Brown KR, Hart T, Gebbia M, Lang KS, Giaever G, Nislow C, Moffat J, LZ Penn. Genome-wide RNAi analysis reveals that simultaneous inhibition of specific mevalonate pathway genes potentiates tumor cell death. *Oncotarget.* 6(29):26909-26921 (2015).
3. **Mullen PJ***, Yu R*, Longo J*, Archer MC, Penn LZ. The interplay between cell signaling and the mevalonate pathway in cancer. *Nature Reviews Cancer.* 16(11):718-731 (2016). *Co-first author.

4. Longo J, **Mullen PJ**, Yu R, van Leeuwen JE, Masoomian M, Woon DTS, Wang Y, Chen EX, Hamilton RJ, Sweet JM, van der Kwast TH, Fleshner NE, Penn LZ. An actionable sterol-regulated feedback loop modulates statin sensitivity in prostate cancer. *Molecular Metabolism.* 25:119-130 (2019).

4. Identifying mechanisms of side effects during metabolic therapy in normal tissues. As a graduate student I discovered that statins, the world's most commonly prescribed drugs, alter mitochondrial metabolism in skeletal muscle but not liver. I also showed that these defects could be prevented by increasing signaling through AKT. This discovery could lead to strategies to reduce the high incidence of skeletal myopathies and improve the quality of life in statin users. I also extended this work to cardiomyocytes and found that statins could also affect cardiac mitochondrial metabolism. This work has led to further research into how mitochondria can be impacted by drugs in normal tissues.

1. **Mullen PJ**, Lüscher B, Scharnagl H, Krähenbühl S, Brecht K. Effect of simvastatin on cholesterol metabolism in C2C12 myotubes and HepG2 cells, and consequences for statin-induced myopathy. *Biochemical Pharmacology.* 79(8):1200-1209 (2010).
2. **Mullen PJ**, Zahno A, Lindinger P, Maseneni S, Felser A, Krähenbühl S, Brecht K. Susceptibility to simvastatin-induced toxicity is partly determined by mitochondrial respiration and phosphorylation state of Akt. *Biochimica et Biophysica Acta.* 1813(12):2079-2087 (2011).
3. Bonificio A*, **Mullen PJ***, Mityko IS, Navegantes LC, Bouitbir J, Krahenbuhl S. Simvastatin induces mitochondrial dysfunction and increased atrogin-1 expression in H9c2 cardiomyocytes and mice in vivo. *Archives of Toxicology.* 90(1):203-215 (2016). *Co-first author.