BIOGRAPHICAL SKETCH

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NAME: East, Michael P.

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

POSITION TITLE: Research 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
Kennesaw State University, Kennesaw GA	B.S.	05/2007	Biochemistry
Emory University, Atlanta GA	Ph.D.	06/2014	Biochemistry
University of North Carolina, Chapel Hill NC	Postdoctoral	06/2019	Pharmacology

A. Personal Statement

My graduate and postdoctoral training has provided me with diverse training that encompasses both large scale systems biology approaches and very focused functional and biochemical characterization of understudied proteins. My graduate studies were primarily focused on biochemical and cell biology techniques characterizing understudied proteins with no known functions, ELMOD1-3. I integrated bioinformatics with bench science to define cellular functions of the ELMOD proteins and characterize their biochemical activity. As a member of the “Illuminating the Druggable Genome” (IDG) NIH initiative during my postdoctoral and current studies, my research focus has been to elucidate the functions of understudied protein kinases in the human genome. I have developed a diverse skillset to interrogate kinase function with an emphasis on genome engineering and transcriptional regulation using CRISPR technology, quantitative mass spectrometry using the Q-Exactive HF and Exploris 480, and next-generation sequencing for CRISPR screens, bulk and single-cell RNA sequencing, ATACseq, and ChIPseq. As a member of the IDG initiative which spans multiple labs at UNC and across the country and due to my proteomics and transcriptomics expertise, I also effectively communicate with other research groups daily to facilitate strong, active collaborations. I have developed and continue to develop both the skillset and support structure necessary to successfully accomplish my ultimate career goal of being a leading independent investigator in the fields of cellular signaling and cancer biology. I am highly motivated to contribute to our collective understanding of biology and to help guide and mentor my peers and emerging new scientists.

B. Positions and Honors

Positions and Employment

2019 – present Research Assistant Professor, Department of Pharmacology, University of North Carolina, Chapel Hill NC
2014 – 2019 Postdoctoral research associate (w/ Dr. Lee Graves and Dr. Gary Johnson), Department of Pharmacology, University of North Carolina, Chapel Hill NC

Other Experience and Professional Membership

2008 – 2012 Graduate Program Recruitment Committee, Emory University, Atlanta GA
2009 – 2012 Division Student Advisory Council Representative, Emory University, Atlanta GA
*Organized and hosted an annual student research symposia
2010 – 2011 Graduate Program Rotations Committee, Emory University, Atlanta GA

Honors

2018	Department of Pharmacology Postdoctoral Excellence Award, University of North Carolina, Chapel Hill NC
2007	University Regents' Scholar*, Kennesaw State University *Kennesaw State University's highest academic honor
2007	Outstanding Biochemistry Senior, Kennesaw State University
2007 – 2008	Phi Kappa Phi Graduate Fellowship
2008	Undergraduate Honors Program Award*, Kennesaw State University *This award is typically presented in the year following graduation.

C. Contribution to Science

1. Analysis of kinome dynamics in diverse biological inquiries.
I have made significant contributions to several research programs in the fields of cancer biology, drug resistance mechanism, virology, and small molecule inhibitor development. In my own unpublished work, I have explored the plasticity of the kinome in response to cellular perturbations and drug treatments and have defined mechanisms contributed to this plasticity. This work contributes to drug discovery efforts by identifying well characterized and understudied kinases that are differentially regulated in response to perturbations contributing to the drug tolerant phenotype and the development of drug resistance. I have also developed targeted methods for more accurate and comprehensive quantification of low abundance transcripts in single-cell RNAseq experiments and proteins using mass spectrometry that have transformed our ability to analyze kinase expression levels in these spheres.

a) **East MP**, Johnson GL. *Adaptive chromatin remodeling and transcriptional changes of the functional kinome in tumor cells in response to targeted kinase inhibition*. J Biol Chem. 2022 Feb;298(2):101525.
b) Angus SP, Stuhlmiller TJ, Mehta G, Bevill SM, Goulet DR, Olivares-Quintero JF, **East MP,** Tanioka M, Zawistowski JS, Singh D, Sciaky N, Chen X, He X, Rashid NU, Chollet-Hinton L, Fan C, Soloway MG, Spears PA, Jefferys S, Parker JS, Gallagher KK, Forero-Torres A, Krop IE, Thompson AM, Murthy R, Gatza ML, Perou CM, Earp HS, Carey LA, Johnson GL. FOXA1 and adaptive response determinants to HER2 targeted therapy in TBCRC 036. NPJ Breast Cancer. 2021 May 12;7(1):51.
c) Garcia-Recio S, Thennavan A, **East MP**, Parker JS, Cejalvo JM, Garay JP, Hollern DP, He X, Mott KR, Galván P, Fan C, Selitsky SR, Coffey AR, Marron D, Brasó-Maristany F, Burgues O, Albanell J, Rojo F, Lluch A, Martinez de Dueñas E, Rosen JM, Johnson GL, Carey LA, Prat A, Perou CM. *FGFR4 regulates tumor subtype differentiation in luminal breast cancer and metastatic disease*. J Clin Invest. 2020 Sep 1;130(9):4871-4887.
d) Collins KAL, Stuhlmiller TJ, Zawistowski JS, **East MP**, Pham TT, Hall CR, Goulet DR, Bevill SM, Angus SP, Velarde SH, Sciaky N, Oprea TI, Graves LM, Johnson GL, Gomez SM. *Proteomic analysis defines kinase taxonomies specific for subtypes of breast cancer*. Oncotarget. 2018 Mar 20;9(21):15480-15497.

2. Specificity profiling of novel chemical tools and probes targeting kinases using chemoproteomics.
Narrow spectrum specificity of chemical tools and probes is essential for their use in functional studies of their target kinases. I have adapted the chemoproteomics method of Multiplexed Inhibitor Bead enrichment of functional kinases from cell lysates coupled with mass spectrometry (MIB/MS) to profile the specificity of novel kinase inhibitors. This work informed the design of novel kinase inhibitors and offered a more physiologically relevant profile of compound specificity than other biochemical screening approaches as it uses native, endogenous kinases.

a) Kalogirou AS, **East MP**, Laitinen T, Torrice CD, Maffuid KA, Drewry DH, Koutentis PA, Johnson GL, Crona DJ, Asquith CRM. *Synthesis and Evaluation of Novel 1,2,6-Thiadiazinone Kinase Inhibitors as Potent Inhibitors of Solid Tumors.* Molecules. 2021 Sep 29;26(19).
b) Asquith CRM, Naegeli KM, **East MP**, Laitinen T, Havener TM, Wells CI, Johnson GL, Drewry DH, Zuercher WJ, Morris DC. *Design of a Cyclin G Associated Kinase (GAK)/Epidermal Growth Factor Receptor (EGFR) Inhibitor Set to Interrogate the Relationship of EGFR and GAK in Chordoma*. J Med Chem. 2019 May 9;62(9):4772-4778. doi: 10.1021/acs.jmedchem.9b00350.
c) Asquith CRM, Laitinen T, Bennett JM, Godoi PH, **East MP**, Tizzard GJ, Graves LM, Johnson GL, Dornsife RE, Wells CI, Elkins JM, Willson TM, Zuercher WJ. *Identification and Optimization of 4-Anilinoquinolines as*

Inhibitors of Cyclin G Associated Kinase. ChemMedChem. 2018 Jan 8;13(1):48-66. doi: 10.1002/cmdc.201700663.

d) Lipner MB, Peng XL, Jin C, Xu Y, Gao Y, **East MP**, Rashid NU, Moffitt RA, Herrera Loeza SG, Morrison AB, Golitz BT, Vaziri C, Graves LM, Johnson GL, Yeh JJ. *Irreversible JNK1-JUN inhibition by JNK-IN-8 sensitizes pancreatic cancer to 5-FU/FOLFOX chemotherapy*. JCI Insight. 2020 Apr 23;5(8).

3. Highlighting understudied kinases as important regulators of cellular signaling and potential targets for therapeutic intervention in human disease.

The vast majority of literature on kinase function in cell biology and human diseases focuses on a very small fraction of the kinome. This narrow focus also extends to pharmacological development of chemical probes and therapeutics in academia and industry. Understudied kinases are altered at similar rates as well-characterized kinases in human cancers and are implicated in a diverse array of other human diseases but are not being prioritized for development of small molecule probes or therapeutics. In a series of review articles, I have emphasized the importance of select understudied kinases in cell biology and disease to encourage development of small molecule inhibitors and further characterization of their cellular functions.

a) **East MP**, Laitinen T, Asquith CRM. *BCKDK: an emerging kinase target for metabolic diseases and cancer*. Nat Rev Drug Discov. 2021 Jul;20(7):498.
b) **East MP**, Asquith CRM. *CDC42BPA/MRCKα: a kinase target for brain, ovarian and skin cancers*. Nat Rev Drug Discov. 2021 Mar;20(3):167.
c) **East MP**, Laitinen T, Asquith CRM. *WNK kinases: an untapped opportunity to modulate ion transport*. Nat Rev Drug Discov. 2020 Dec;19(12):828.
d) **East MP**, Laitinen T, Asquith CRM. *PIP5K1A: a potential target for cancers with KRAS or TP53 mutations*. Nat Rev Drug Discov. 2020 Jul;19(7):436

4. Structural, phylogenetic, biochemical and functional characterization of the ELMO domain containing proteins, ELMOD1-3.

The focus of my graduate studies was to elucidate signal transduction pathways of monomeric regulatory GTP binding proteins of the Arf family. Historically, study of GTPase activating proteins (GAPs) have been instrumental in determining the functions and mechanisms of their substrate GTPases. Thus, I determined the phylogeny, GAP domain, and putative catalytic arginine residue of a novel family of Arf family GAPs, ELMOD1-3, and developed models for their cellular functions. The ELMODs were the first GAPs identified for any of the 22 mammalian Arf-like monomeric GTPases (Arls) and, prior to my work, there was virtually no functional information available for any of the three human ELMODs. Thus, my work offered initial functional characterization of an ancient family of proteins and linked novel ELMOD and Arf family biology to the Golgi apparatus, mitochondria, and lipid droplets.

a) **East, MP**, Bowzard, JB, Dacks, JB, and Kahn, RA,*ELMO domains, evolutionary and functional characterization of a novel GTPase-activating protein (GAP) domain for Arf protein family GTPases.* J Biol Chem, 2012. 287(47): p. 39538-53.
b) Turn RE, Hu Y, Dewees SI, Devi N, **East MP**, Hardin KR, Khatib T, Linnert J, Wolfrum U, Lim MJ, Casanova JE, Caspary T, Kahn RA. *The ARF GAPs ELMOD1 and ELMOD3 act at the Golgi and cilia to regulate ciliogenesis and ciliary protein traffic*. Mol Biol Cell. 2022 Feb 1;33(2):ar13.
c) Turn RE, **East MP**, Prekeris R, Kahn RA. *The ARF GAP ELMOD2 acts with different GTPases to regulate centrosomal microtubule nucleation and cytokinesis*. Mol Biol Cell. 2020 Aug 15;31(18):2070-2091.
d) Ivanova, A.A., **East, M.P.**, Yi, S.L., and Kahn, R.A., *Characterization of recombinant ELMOD (cell engulfment and motility domain) proteins as GTPase activating proteins (GAPs) for Arf family GTPases.* J Biol Chem, 2014. 289(16): p. 11111-21.

Complete List of Published Work in MyBibliography:
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