

Michael V. Keebler

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Nationality: American

Summary

I am a highly motivated, independent scientist with research interests in cancer biology, stem cell biology, calcium signaling, auditory neuroscience and data science. I have technical expertise in the areas of molecular biology, cell culture, biochemistry, cell physiology, high-resolution microscopy and computational biology. I also have excellent presentation skills and enjoy sharing knowledge with others. I think that collaboration yields the best science and I enjoy being part of a team. My ambition is to contribute towards science that positively and directly affects the lives of as many people as possible.

Education and Research Experience

- 2015-2016 **Wellcome Trust Sanger Institute – Postdoctoral Research Fellow**
Advised by: Dr. Pentao Liu; Department of Cellular Genetics
- Led a translational collaboration between the Wellcome Trust Sanger Institute, Cancer Research Technology and the Department of Pharmacology (University of Cambridge). The industrial nature of this position required meeting tight deadlines and frequently presenting results to members of the funding body.
 - Demonstrated accurate gene editing using CRISPR/Cas9 on cells with limited homology-directed repair (the machinery required for conventional gene-editing).
 - Developed protocols for the efficient knock-in of cancer genomes, which are difficult to target.
- 2011-2015 **University of Cambridge – Ph.D. (St. John’s College)**
Advised by: Professor Colin Taylor; Department of Pharmacology
Thesis title: High-resolution analyses of inositol 1,4,5-trisphosphate receptor behavior.
- Created two large-scale algorithms (written in IDL) for the automated detection and analysis of inositol-1,4,5-trisphosphate (IP₃)-evoked Ca²⁺ release events and sites in mammalian cells.
 - Discovered a new population of ‘low-frequency’ Ca²⁺ release sites in mammalian cells.
 - Provided new evidence to support the argument that globally delivered IP₃ evokes Ca²⁺ release from many of the same sites as agonist delivered IP₃.
 - Dramatically improved the protocols in the lab for prolonged stimulation with agonist in mammalian cells.
 - Characterized IP₃-evoked Ca²⁺ release events/sites in HEK293 cells for the first time.
 - Synthesized N-terminal fragments of the IP₃ receptor (IP₃R) with a high purity/concentration for structural-function analysis by deuterium exchange mass spectrometry.
 - Measured the interaction between IP₃ receptors (IP₃R) and fluorescent-IP₃ at the single-molecule level using total internal reflection fluorescence (TIRF) microscopy.
- 2010-2011 **University of Cambridge – Research Assistant**
Advised by: Professor Colin Taylor; Department of Pharmacology
- Pioneered single-molecule fluorescence microscopy in the lab by creating an assay for measuring the interaction between an individual molecule of the IP₃R and an individual molecule of fluorescent-IP₃.
- 2009-2010 **University of Minnesota – Research Specialist**
Advised by: Professor Jonathan Marchant; Department of Pharmacology
- Characterized the sub-cellular localization and morphology of two-pore channel (TPC) isoforms overexpressed in the oocytes of *Xenopus laevis*.
 - Identified a pigmentation phenotype associated with TPC2 expression, which helped identify the role of the TPC complex in endolysosomal trafficking.
- 2004-2009 **University of Minnesota – B.S.**
Major: Genetics, Cell Biology & Development (GCD), Major: Neuroscience, cum laude;
Advised by: Professor Jonathan Marchant, Professor Peter Santi and Professor Andrew Oxenham.

Technical Skills

Molecular Biology

- CRISPR engineering of mammalian cell-lines (monomeric and dimeric, HDR and NHEJ strategies)
- Conventional cloning, TOPO cloning, Gibson assembly, point mutagenesis, PiggyBac, genotyping
- *In silico* tools: Lasergene, UCSC, Ensembl, NCBI, BioEdit, ExPASy, Clustal, Primer3, Zifit CRISPR (Zhang, MIT), WTSI Genome Editing, E-CRISPR, GPP (Broad)
- qPCR

Cell Culture

- Human iPS cells (SNL/STO feeders, EPSC, CDM or KSR +FGF medium)
- Embryonic stem cells (mouse 129 strain, feeder-free, N2B27 medium)
- Immortalized adherent cell lines (HEK293, HeLa, U2OS, MLO-Y4, S2R+, MDA-MB-231)
- FACS (Sorters: BD Influx, MoFlo Legacy, MoFlo XPD, and BioRad S3; Analyzers: BD LSRFortessa)
- Single-cell expansion (via antibiotic selection/manually picking colonies, sorting or limiting dilution)

- Biochemistry**
 - Large scale production, purification and concentration of soluble protein
 - Column chromatography (affinity, ion-exchange and size-exclusion)
 - Protein assaying (Bradford, Western, silver stain, Luciferase activity)
 - 3D structural analysis (PyMol)
- Imaging**
 - Total internal reflection fluorescence (TIRF)
 - High-speed spinning disk confocal
 - Prolonged live-cell imaging with repeated drug stimulation
 - Image analysis (ImageJ, Amira, R[^]cell, Metamorph)
- Cell Physiology**
 - High-throughput Ca²⁺ measurements (96-well FLEX station, single wave-length indicator)
 - Single-cell Ca²⁺ responses at the population level (mounted slides, single or dual wave-length indicators)
 - High-resolution (TIRF) measurements of elementary Ca²⁺ events (puffs)
- Binding**
 - Competition binding with ³H-IP₃
- Animal Handling**
 - Sprague Dawley rat (survival surgery - neural)
 - *Xenopus laevis* (survival and sacrificial surgery – oocyte harvest)
 - Follicular removal (manual and enzymatic)
 - Transgenic expression in oocytes via microinjection
- Programming & Computational Biology**
 - IDL (3 large-scale algorithms written)
 - R (1 large-scale algorithm written)
 - Matlab, Python, Java, Octave (familiar/proficient)
 - Organization, cleaning and formatting of large data sets.
 - Familiarity with NGS analyses, including Rsamtools and GATK
 - Familiarity with Machine Learning algorithms and theory (Andrew Ng's course, Coursera)

Non-Technical Skills

Leadership

- 2013-2014 • Head of Academic Affairs - St. John's College Graduate Community
- 2012-2014 • President (re-elected) - Cambridge University Real Ale Society
- 2007-2008 • Head of the Engineering Department - KUOM Radio K
- 2006-2008 • President, Treasurer - University of Minnesota Vo Lam Kung Fu Club

Teamwork

- 2006-present • Participated in 10 scientific collaborations and group projects
- 2015-2016 • Cambridge University Amateur Boxing Club (CUABC): 1st Team (Blues)

Project Management

- 2015-2016 • Independently planned and executed:
 - 2 projects during my Postdoctoral Research Fellowship
- 2011-2015 • 5 projects during my PhD

Initiative

- 2014-2015 • Revolutionized my department by introducing stem cell and CRISPR/Cas9 technologies
- 2012 • Took initiative to learn programming without formal training in order to solve a scientific problem

Communication

- 2009-present • Given 12 talks for a wide range of audiences around the world
- 2007-present • Co-authored 7 peer-reviewed publications and 1 scientific book
- Taught undergraduates in the areas of cell biology and pharmacology:
 - Practical Demonstrator, Department of Pharmacology (University of Cambridge)
 - Teaching Assistant for BIOL4004, Cell Biology (University of Minnesota)
- 2011-2014 • Taught elementary and high-school students, as well as high-school teachers in cell biology:
 - Cambridge Science Festival – Department of Pharmacology (Cambridge, UK)
 - YoungPharmas – Department of Pharmacology (Cambridge, UK)
 - STEMNET Ambassador, Cambridge (Cambridge, UK)
- 2015 • REACH Cambridge (Cambridge, UK)
- 2011-2015 • Wellcome Trust Genetics Course (Villiers Park - Foxton, UK)
- 2014 • Society For Neuroscience's Brain Awareness Week, (Minneapolis, MN - USA)
- 2013-2014 • Wellcome Trust Genetics Course (Villiers Park - Foxton, UK)
- 2012-2014 • Society For Neuroscience's Brain Awareness Week, (Minneapolis, MN - USA)
- 2009 • Society For Neuroscience's Brain Awareness Week, (Minneapolis, MN - USA)

Networking

- 2011-2016 • Initiated 2 inter-lab collaborations by establishing contact and exchanging ideas
- 2011-2013 • Organized a departmental seminar on cell signaling to foster discussion between labs

Problem Solving

- 2010-present • Trouble shot the development and realization of at least 8 new, large-scale techniques and protocols

Publications

- **Keebler, M.V.**, Khaled, W.T., Liu, P. A method for editing the genome of cancer cell-lines with impaired homology directed repair. *In preparation*.
- **Keebler, M.V.**, Taylor, C.W. Sequential stimulation with IP₃-generating agonists reveals a ubiquitous spatial distribution of Ca²⁺ release sites. *In preparation*.
- Lin-Moshier, Y., **Keebler, M.V.**, Hooper, R., Boulware, M.J., Liu, X., Churamani, D., Abood, M.E., Walseth, T.F., Brailoiu, E., Patel, S., Marchant, J.S. (2014). The two-pore channels (TPC) interactome unmasks isoform-specific roles for TPCs in endolysosomal morphology and cell pigmentation. *Proceedings of the National Academy of Science*, 111: 13087-92
- Konieczny, V., **Keebler, M.V.**, Taylor, C.W. (2012). Spatial organization of intracellular Ca²⁺ signals. *Seminars in Cell and Developmental Biology* 23: 172-80.
- Brailoiu, E., Hooper, R., Cai, X., Brailoiu, G.C., **Keebler, M.V.**, Dun, N.J., Marchant, J.S., Patel, S. (2009) An ancestral deuterostome family of two-pore channels mediates nicotinic acid adenine dinucleotide phosphate-dependent calcium release from acidic organelles. *Journal Biological Chemistry*, 285: 2897-2901.
- Oxenham, A.J., Micheyl, C., **Keebler, M.V.**, Loper, A., Santurette, S. (2010). Pitch perception beyond the “existence region” of pitch. *Proceedings of the National Academy of Science*, 108: 7629-34.
- McDermott, J.H., **Keebler, M.V.**, Micheyl, C., Oxenham, A.J. (2010). Musical intervals and relative pitch: Frequency resolution, not interval resolution, is special. *Journal of the Acoustical Society of America*, 128: 1943-1951.
- Micheyl, C., **Keebler, M.V.**, Oxenham, A.J. (2010). Pitch perception for mixtures of spectrally overlapping harmonic complex tones. *Journal of the Acoustical Society of America*, 128: 257-269.
- Oxenham, A.J., Micheyl, C., **Keebler, M.V.** (2009). Can temporal fine structure represent the fundamental frequency of unresolved harmonics? *Journal of the Acoustical Society of America*, 125: 2189-2199.
- Oxenham, A.J., **Keebler, M.V.** (2007) Pitch perception: Frequency selectivity and temporal coding. In: Dau T, Buchholz, J.M., Harte, J.M., Christiansen, T.U. (eds) Auditory Signal Processing in Hearing-impaired Listeners (ISAAR 2007). Helsingor, Denmark, Centertryk A/S, pp. 273-279.