Fraser J. Moss Ph. D.

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Research Interests

I employ fluorescence and electrophysiological methods to investigate:

- Sodium-coupled bicarbonate transporter structure-function
- Acid-base homeostasis and sensing
- Oligomerization and trafficking of solute transporters

Research Experience

2014-present	Instructor. Case Western Reserve University, Dept. Physiology & Biophysics
2009-2014	Postdoctoral Fellow. Case Western Reserve University, Dept. Physiology & Biophysics (*Mentor: Walter F. Boron*)
2008-2009	Staff Research Scientist, California Institute of Technology, Div. Biology (*Mentor: Henry A. Lester*)
2004-2009	Academic Collaborator, Neurion Pharmaceuticals, Pasadena CA, (*Liaison: Mark W. Nowak*)
2002-2008	Postdoctoral Scholar, California Institute of Technology, Div. Biology (*Mentor: Henry A. Lester*)
1998-2002	Graduate Student (Ph.D.), University College London, Dept. Pharmacology (*Mentor: Annette C. Dolphin*)
1998-1999	Ph.D. Graduate student industry placement, GlaxoSmithKline Medicines Research Centre, Stevenage, UK. (*Mentor: Jeffrey J. Clare*)
1998	B.Sc. Honors. Thesis. Center for Biological Sciences, Univ. Southampton, UK (*Mentor: John E. Chad*)
1996-1997	Undergraduate Research Student, Eli Lilly Research Centre Ltd. Windlesham, UK (*Mentor: John R. Boot*)

Education

2002	Ph.D. Pharmacology, University College London, UK (*Advisors: Annette C. Dolphin and Jeffrey J. Clare*)
1998	B.Sc. Hons. 1st Class, Physiology & Pharmacology, Univ. of Southampton, UK

Patents

02/04/2014	Patent Number: US-8,642,352 Serial Number: 12/701,482 Methods and Systems for Detection of Stoichiometry by Förster Resonance Energy Transfer. Serial Number: 12/701,482 Filed: 2/5/2010

Honors & Awards

2013	American Physiological Society Postdoctoral Travel Award IUPS 2013
2005-2007	American Heart Association (Western States Affiliate) Postdoctoral Fellowship.
2005-2009	Co-authored NIH R01 HL079350
2005-2007	Most Valuable Scientist – www.scientistsolutions.com
1998-2001	GlaxoSmithKline/Medical Research Council CASE Ph. D. Scholarship

Teaching/Mentorship/Supervisory

Case Western	Dept. Physiology & Biophysics, PHOL 481, Block 4 Renal lectures. Medical School Teaching - Cardiovascular Cell Physiology Summer Medical & Dental Education Program – Project reviewer and judge Mentored Graduate Students Austin Coley and Ahlam Salmeh Supervisor to Boron lab technicians
CalTech	Mentor to Graduate Students Princess Imoukhuede and Shawna Frazier Mentor to undergraduate research fellow Kimberly Scott I also trained numerous other graduate students in fluorescence imaging, electrophysiology, molecular biology and cell culture techniques in Henry Lester and Dennis Dougherty's labs at Caltech.
UCL	Mentor to undergraduate biochemistry student Alex Graham

Service and Professional Memberships

Journal reviews
Journal of Neuroscience
Nature Neuroscience
Journal of Physiology
Proceedings of the National Academy of Sciences USA

Society membership

2001-2011, 2013-	Society for Neuroscience
2004-Present	Biophysical Society
2010-Present	American Physiological Society
1998-2002	Physiological Society (London)

Lifescience community
Scientistsolutions.com
2009-Present President
2009 Senior moderator of all forums
2008 Neuroscience moderator

Citizenship

Naturalized citizen of the USA and citizen of the United Kingdom by birth.

Experimental Techniques

Microscopy Wide field and confocal, including spectral acquisition.
Förster resonance energy transfer (sensitized emission, donor recovery after acceptor photobleach) in live and fixed cell cultures.
Pixel-by-pixel analysis of protein stoichiometry and interactions by FRET.
Total internal reflectance microscopy.

Electrophysiology Two electrode voltage-clamp of *Xenopus* oocytes.
Ion-sensitive microelectrode electrophysiology.
Whole-cell patch clamp electrophysiology on mammalian cell lines.
Out-of-equilibrium solution perfusion that varies the $[CO_2]_o$ while maintaining constant $[HCO_3^-]_o$ and pH_o, or varies $[HCO_3^-]_o$ while maintaining constant $[CO_2]_o$ and pH_o
Cellectricon Dynaflow chip-based laminar flow perfusion system.
Single-cell electroporation of mammalian cells (using Axoporator 800A).

Molecular Biology Cloning, subcloning, mutagenesis,
AAV and adenovirus vector design and production
Rapid and site-specific integration of large cDNA fragments for fusion-protein construction by PCR
RT-PCR, 5' & 3' RACE, Splice-overlap PCR, site directed mutagenesis.
Northern blot.
mRNA and tRNA *in vitro* transcription.
Standard cDNA, total RNA, mRNA isolation techniques.

Cell & tissue culture N2a, HEK293, CHO, COS, PC12, renal proximal tubule cell lines and rat cerebellar granule cells.
Cationic lipid /commercial transfection techniques of cell lines.

Viral transduction Stereotaxic microinjection of AAV vectors into mouse brain.
Microinjection of Adenovirus vectors in to mouse kidney.
Viral transduction of cell lines and neuronal cultures.

[^{3}H] uptake assays I developed a non-saturated, linear neurotransmitter uptake protocol for studying neurotransmitter transporter function *in vitro*.

Flow-cytometry	Size and shape analysis of red blood cells using BD LSRII for forward- and side-scatter analyses, and the Amnis ImageStream for flow-cytometry integrated with image analysis.
Cytochemistry	DAB and fluorescence immunohistochemistry in fixed wax-embedded or frozen brain slices. Fluorescence immunocytochemistry in cultured cells and acutely isolated neurons.
Biochemistry	Rabbit reticulocyte *in vitro* translation. SDS–PAGE electrophoresis and western blot. Affinity purification of antibodies from sera. Expression and purification of recombinant proteins. ELISA.
Microfluorimetry	Medium-throughput Fluo-3 calcium imaging for lead compound discovery.

Presentations

Invited talks

hERG K^+ channel block underlying acquired Long-QT syndrome probed with natural and unnatural amino acid mutagenesis in mammalian cells. 6th Annual Aurora Biomed Ion Channel Retreat. Vancouver BC, Canada June 23 - 25, 2008.

Presentations at other professional meetings

1. **Moss F.J**., Lee S.K., Parker M.D., Boron W.F. (2014) Distinguishing HCO_3^- from $CO_3^=$ transport by the electrogenic Na/HCO_3 cotransporter NBCe1 (SLC4A4). FASEB Journal 28, 1098.7

2. **Moss F.J**., Boron W.F. (2014) Distinguishing between the possible carbon substrates for transport by the electrogenic Na/HCO_3 cotransporter NBCe1 (SLC4A4). *Biophysical J* 106: Issue 2, Pos-L4462

3. Gonzalez-Reyes L. E., **Moss F.J.**, Boron W.F and Durand D.M. Selective hippocampal viral gene delivery restores normal seizure susceptibility in electroneutral Na/HCO_3 co-transporter NBCn1 (slc4a7) null mice. Presentation Number: 314.2. (2014) Neuroscience Meeting Planner. Washington, DC: Society for Neuroscience, 2014. Online.

4. **Moss F.J**., Boron W.F. (2013) Carbonic anhydrase II enhances activity of endogenous Na-H exchangers and not the Na/HCO_3 cotransporter, NBCe1, when expressed in *Xenopus* oocytes – 37th Congress of IUPS (Birmingham, UK) (2013) Proc 37th IUPS, PCB176

5. **Moss F.J**., Boron W.F. (2012) The role of carbonic anhydrase II on HCO_3^- -initiated transport through the SLC4A4 transporter NBCe1A. FASEB Journal 26,882.4

6. **Moss F.J.**, Boron W.F. (2011). The role of carbonic anhydrase II on HCO_3^--initiated transport through the SLC4A4 transporter NBCe1. FASEB Journal 25, 656.7.

7. **Moss F.J.**, Imoukhuede P.I., Hu J., Jankowsky J.L., Quick M.W., Lester H.A. (2009). Quantification of sensitized FRET from fluorescent GAT1 γ-aminobutyric acid transporters distinguishes between subsurface and plasma membrane resident oligomers and predicts function. *Biophysical Journal*, Supplement, Abstract, 1384-Pos.

8. Pantoja R., Srinivasan R., **Moss F.J.**, Kadambi S., Imoukhuede P.I., Lester H.A. (2009). Characterizing nicotine-induced α4* nAChR receptor upregulation with fluorescence microscopy. *Biophysical Journal*, Supplement, Abstract, 541-Pos.

9. **Moss F.J.**, Frazier S., Nowak M.W., Mackey E., Shiva N., Dougherty D.A., Lester H.A. (2008) hERG K^+ channel block underlying acquired Long-QT syndrome probed with natural and unnatural amino acid mutagenesis in mammalian cells. *Biophysical Journal*, Supplement, Abstract, 1329-Pos.

Publications

Journal Articles - Lead author

1. **Moss F.J.**, Imoukhuede P.I., Scott K., Hu J., Jankowsky J.L., Quick M.W., Lester H.A. (2009). GABA transporter function, oligomerization state and anchoring: correlates with subcellularly resolved FRET. Journal of General Physiology, 134(6), 489-521. PMCID: PMC2806419. **Cover article for the journal issue**.

2. **Moss F.J.**, Dolphin A.C., Clare J.J. (2003). Human neuronal stargazin like proteins, γ2, γ3 and γ4; an investigation of their specific localization in human brain and their influence on $Ca_V2.1$ voltage-dependent calcium channels expressed in *Xenopus* oocytes. BMC Neuroscience, 4, 23. PMCID: PMC270087

3. **Moss F.J.**, Viard P., Davies A., Bertaso F., Page K.M., Graham A., Canti C., Plumpton M., Plumpton C., Clare J.J., Dolphin A.C. (2002). The novel product of a five-exon stargazin-related gene abolishes $Ca_V2.2$ calcium channel expression. EMBO Journal, 21(7), 1514-23. PMCID: PMC125363

Journal Articles – co-authorship

1. Coley A.A., Ruffin V. A., **Moss F. J.**, Hopfer U., Boron W.F., (2013) Immunocytochemical identification of electroneutral Na^+-coupled HCO_3^- transporters in freshly dissociated mouse medullary raphé neurons. Neuroscience, 246, 451-467. PMID:23500099

2. Chen L.M., Qin X., **Moss F.J.**, Liu Y., Boron W.F. (2012) Effect of simultaneously replacing putative TM6 and TM12 of human NBCe1-A with those from NBCn1 on surface abundance in Xenopus oocytes. Journal of Membrane Biology, 245(3), 131-140. PMID: 22383045

3. Srinivasan R., Richards C. I., Dilworth C., **Moss F.J.**, Dougherty D.A., Lester H.A. (2012)

Förster Resonance Energy Transfer (FRET) Correlates of Altered Subunit Stoichiometry in Cys-Loop Receptors, Exemplified by Nicotinic α4β2. International Journal of Molecular Sciences, 13(8): 10022-10040. PMCID: PMC3431844.

4. Srinivasan R., Pantoja R., **Moss F.J.**, Mackey E.D., Son C.D., Miwa J., Lester H.A. (2011) Nicotine up-regulates α4β2 nicotinic receptors and ER exit sites via stoichiometry-dependent chaperoning. Journal of General Physiology, 137(1), 59-79. PMCID: PMC3010053

5. Imoukhuede P.I., **Moss F.J.**, Michael D.J., Chow R.H., Lester H.A. (2009) Ezrin mediates tethering of the γ-aminobutyric acid transporter GAT1 to actin filaments via a C-terminal PDZ-interacting domain. The Biophysical Journal, 96(7), 2949-60. PMCID: PMC2711277

6. Son C.D., **Moss F.J.**, Cohen B.N., Lester H.A. (2009) Nicotine normalizes intracellular subunit stoichiometry of nicotinic receptors carrying mutations linked to autosomal dominant nocturnal frontal lobe epilepsy. Molecular Pharmacology, 75(5), 1137-48. PMCID: PMC2672806

7. Ferron L., Cox D.J., Leroy J., Page K.M., Nieto-Rostro M., Bolsover S., Davies A., Sellaturay P., Pratt W.S., **Moss F.J.**, Dolphin A.C. (2008) Regulation of N-type calcium channel stability and neurite extension by the stargazin related protein γ7. Journal of Neuroscience, 28(42), 10604-17. PMCID: PMC2669593

8. Brodbeck J., Davies A., Courtney J.M., Meir A., Balaguero N., Canti C., **Moss F.J.**, Page K.M., Pratt W.S., Hunt S.P., Barclay J., Rees M., Dolphin A.C. (2002). The ducky mutation in Cacna2d2 results in altered Purkinje cell morphology and is associated with the expression of a truncated α2δ-2 protein with abnormal function. Journal of Biological Chemistry, 277(10), 7684-93. PMID: 11756448

9. Pinto A., **Moss F.**, Lang B., Boot J., Brust P., Williams M., Stauderman K., Harpold M., Newsom-Davis J. (1998). Differential effect of Lambert-Eaton myasthenic syndrome immunoglobulin on cloned neuronal voltage-gated calcium channels. Annals of the New York Academy of Sciences, 841, 687-90. PMID: 9668315

10. Pinto A., Gillard S., **Moss F.**, Whyte K., Brust P., Williams M., Stauderman K., Harpold M., Lang B., Newsom-Davis J., Bleakman D., Lodge D., Boot J. (1998). Human autoantibodies specific for the α1A calcium channel subunit reduce both P-type and Q-type calcium currents in cerebellar neurons. Proceedings of the National Academy of Sciences of the United States of America, 95(14), 8328-33. PMCID: PMC20975

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Book Chapter

1. **Moss F.J.**, Imoukhuede P.I., Just H., Lester H.A. (2009) GABA Transporter Oligomerization, Trafficking and Pharmacology Determine Neuronal Excitability. In: Schwartzkroin PA, Editor Encyclopedia of Basic Epilepsy Research, Vol. 3. Oxford Academic Press; pp1389-1397 [ISBN: 0-12-373688-9].

Manuscripts in preparation

1. **Moss F.J.** and Boron W.F., Carbonic anhydrase II enhances activity of endogenous Na^+/ H^+ exchangers and not the Na^+/ HCO_3^- co-transporter, NBCe1, when expressed in *Xenopus* oocytes-

To submit to the Journal of Biological Chemistry.

2. Lee S.K., **Moss F.J.**, Grichtchenko I.I., Parker M.D., Occhipinti R. and Boron W.F. Distinguishing HCO_3^- from $CO_3^{=}$ transport by SLC4 family members. To submit to Nature.

3. **Moss F.J.**, Parker M.D., Zeise B., Boron W.F. and Morrison A.C. Extreme Blood Pressure mutations in NBCn1 influence bicarbonate independent conductance. To submit to J. Physiology.

4. **Moss F.J.**, Gonzalez-Reyes L. E., Durand D.M. and Boron W.F. Selective hippocampal viral gene delivery restores normal seizure susceptibility in electroneutral Na/HCO_3 co-transporter NBCn1 (slc4a7) null mice. To submit to J. Neuroscience.