**Robert K. Campbell, Ph.D.**
bcampbell@mbl.edu

## Current Positions

**Adjunct Associate Scientist**
Josephine Bay Paul Center for Comparative Molecular Biology and Evolution
**Marine Biological Laboratory**
7 MBL Street
Woods Hole, MA 02543

**Visiting Scientist**
Department of Molecular Pharmacology, Physiology, and Biotechnology
**Brown University**
171 Meeting Street
Providence, RI, 02912

**Instructor**
Bioinformatics Program, Rabb School of Continuing Education
**Brandeis University**
480 Old South Street
Waltham, MA 02454

## Awarded Research Projects (*as faculty member at MBL*)

**Validation and development of trypanosomal phosphodiesterase inhibitors for treatment of sleeping sickness (PI)**
Funded by NIH NIAID, 2009-04-01 to 2015-03-31 (7 R01 AI082577-01)
Collaborative project with Michael Pollastri, Northeastern University

**Modulation of trypanosomal cAMP signaling for sleeping sickness therapeutic discovery (PI)**
Funded by Tres Cantos Open Lab Foundation (UK), 2014-02-1 to 2015-08-1 (TC-050)
Collaborative project with Harry De Koning, University of Glasgow, Michael Pollastri, Northeastern University and GlaxoSmithKline Open Lab, Tres Cantos, Spain

## Education and Postdoctoral Training

| | | | |
|---|---|---|---|
| 1980 | B.A. | History | Swarthmore College, Swarthmore, PA<br>Advisor: James A. Field, Jr.<br>Thesis: American Naval Policy in the Far East: 1850-1900 |
| 1982 | M.S. | Physiology | University of Wisconsin, Madison, WI<br>(chose option to exit with M.S. after passing preliminary exams to advance to doctoral dissertation research) |
| 1996 | Ph.D. | Cell & Developmental Biology | University of Medicine and Dentistry of New Jersey and Rutgers, The State University of New Jersey, Piscataway, NJ<br>PhD Advisor: William R. Moyle, Ph.D.<br>Dissertation Project: Structure-activity relationships and protein engineering of glycoprotein hormones. |

## Industry Positions

**1991-2014**
**EMD Serono Research Institute, Billerica, MA (subsidiary of Merck KGaA, Darmstadt Germany - formerly Ares Advanced Technology and Serono**)
Contributed to successful development and worldwide launch of four recombinant protein medicines including interferon beta for relapsing remitting multiple sclerosis and follicle stimulating hormone for infertility and IVF.

*Director External Innovation* (2013-2014)
Company delegate to EFPIA Research Directors Group that manages with the European Commission the strategic focus and implementation of collaborative projects under the Innovative Medicines Initiative (IMI). The IMI program is directed at transforming drug discovery and development to improve health in Europe. The set of first IMI initiatives are underway with €2 billion funding for 40 projects from the European Commission and pharmaceutical industry. The second round of initiatives will be launched in 2014 with an additional €3 billion funding from the EC and EFPIA member companies.

*Global Head of Research, Endocrinology* (2010-2012) – Member of Therapeutic Area Leadership Team with Heads of Clinical Research, Product Development, and Business Unit. Responsible for overall global research strategy in Endocrinology therapeutic areas, alignment of strategy with future clinic and patient needs, and advancement of global Endocrinology product pipeline including seven Global Product Teams advancing drugs through development for phenylketonuria, metabolic disorders, and growth hormone deficiencies.

*Global Executive Director for Strategic Implementation of Protein Therapeutics Pipeline* (2008-2009) - Responsible for strategic alignment of projects directed at the invention and development of new protein therapeutics in oncology, reproductive health, autoimmune and inflammatory diseases, and neurodegenerative diseases.

*Global Head of Protein Engineering and Enabling Technologies* (2007-2008) - Led research department (10 Ph.D.-level staff, 20 total staff in U.S. and Germany) and global project teams (20+ additional staff) in protein engineering and the discovery and development of biotherapeutic candidates for cancer, autoimmune diseases, neurodegenerative diseases, and infertility.

*US Head of Molecular Biology, Bioinformatics, and Systems Biology Departments* (1998-2007) – Led functions responsible for protein engineering and initial characterization of drug candidates, and for target discovery and validation. Also worked as Discovery Project Leader for projects with responsibility from compound discovery to preclinical development.

*Executive Director – Research Quality Assurance* (1995-1998) – Took global responsibility for collaborative research with academic groups in multiple myeloma and cytokine research. Member of regulatory registration team member for interferon beta (Rebif®) and leader of molecular biology assessment and presentation EMA rapporteur (Sweden) to reverse initial non-approval decision. Presented molecular biology components of the project to FDA and other agencies for approval.

*Executive Director (Head of Research US)* (1992-1995) - Head of Institute overseeing molecular biology, cell biology, protein chemistry and recombinant protein production (35 lab staff) for U.S. discovery research programs.

*Principal Investigator* (1991-1992): Led research projects on protein and peptide engineering of glycoprotein hormones.

**1983-1986**
**Squibb Corporation, Princeton, NJ**
Contributed to successful clinical development of five small molecules launched as medicines for cardiovascular, metabolic and infectious disease indications - captopril, zofenopril, fosinopril, aztreonam, and pravastatin.

*Clinical Data Auditor*
Partner in the development of Squibb's Clinical Quality Assurance program supporting all clinical trials. Conducted internal and field audits, assessing over 100 clinical study sites. Trained clinical research teams in GCPs and QA practices. Participant in final review team for clinical sections of two NDAs (captropril as first line treatment for hypertension, and aztreonam for gram negative bacterial infections).

## Academic Positions

**2006-present**
***Adjunct Associate Scientist***
**Josephine Bay Paul Center for Comparative Molecular Biology and Evolution, Marine Biological Laboratory, Woods Hole, MA**
Research Activities: NIH-funded research program to discover candidate treatments for Sleeping Sickness (RO1). Identification and functional characterization of the druggable targets from human parasite genomes, repositioning of drug discovery programs to address neglected diseases, evolution of complex systems. This project was built on bioinformatics driven assessments of parasite targets – work that was part of the creation of the TDR Targets online database of neglected disease drug targets. Current work include crystallographic studies of target-inhibitor complexes for structure-based drug discovery, and a multi-institution collaboration on trypanosome screening and hit advancement with GlaxoSmithKline.
*Current funded projects:*
1) Validation and development of trypanosome phosphodiesterase inhibitors for treatment of sleeping sickness (PI)
Funded by NIH, 2009-04-01 to 2015-03-31 (7 R01 AI082577-01)
2) Modulation of trypanosomal cAMP signaling for sleeping sickness therapeutic discovery (PI)
Funded by Tres Cantos Open Lab Foundation 2014-02-01 to 2015-08-01 (TC-050)

**2013-present:**
***Visiting Scientist***
**Department of Molecular Pharmacology, Physiology, and Biotechnology, Brown University, Providence, RI**
Research activities: Collaboration on crystallography of *Trypansoma* cyclic nucleotide phosphodiesterases.

**2003-present:**
***Instructor***
**Bioinformatics Program, Rabb School of Continuing Education, Brandeis University, Waltham, MA**
Teaching Activities: Created graduate course on Drug Discovery and Development (focus of course is on malaria, tuberculosis, and neglected tropical diseases). Note: last taught in 2010

**1997-2009:**
***Adjunct Assistant Professor***
**Obstetrics, Gynecology and Reproductive Sciences, UMDNJ-Robert Wood Johnson Medical School, Piscataway, NJ**
Research Activities: Functional properties and evolution of glycoprotein hormones.

## Honors and Awards

1987 Predoctoral Fellowship, Center for Advanced Biotechnology & Medicine, UMDNJ, Piscataway, NJ

## Teaching

**2003-present:**
Bioinformatics Program – Rabb School of Continuing Education, Brandeis University, Waltham, MA Created and teach the graduate-level course "Drug Discovery and Development" covering all stages of drug discovery. Students use bioinformatics and other tools to identify and assess candidate parasite drug targets, and develop drug discovery project proposals for malaria or sleeping sickness. Note: last taught in 2010, after which EMD Serono international assignments precluded local classroom teaching.
**2000-Present:**
Campbell Laboratory, Marine Biological Laboratory, Woods Hole, MA
Guidance of high school and college student interns working on projects in my lab at MBL.

## Patents

U.S. 5,508,261 Analogs of glycoprotein hormones having altered receptor binding specificity and activity and methods for preparing and using same. Issued April 16, 1996.

U.S. 6,193,972 Hybrid heterodimeric protein hormone. Issued February 27, 2001

U.S. 6,194,177 DNA encoding a hybrid heterodimeric protein. Issued February 27, 2001.

WO0185783 Nucleic acids encoding polypeptides related to the alpha subunit of the glycoprotein hormone family and methods of use thereof. Published November 20, 2001.

U.S. 6,663,867 Hybrid heterodimeric protein hormone containing a TNF binding protein and a glycoprotein hormone subunit. Issued December 16, 2003.

U.S. 7,291,339 Homogeneity and secretion of a recombinant follicle stimulating hormone (FSH) in mammalian systems. Issued November 6, 2007.

U.S. 7.317,095 Mutant glycoproteins. Issued January 8, 2008

U.S. 7,820,165 Compositions and methods of producing hybrid antigen binding molecules and uses thereof. Issued October 26, 2010

### Training Record – Post-doctoral trainees

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|---|---|---|---|
| Maris Laan | Ph.D., University of Helsinki | 1999-2000 | Professor & Group Leader, University of Tartu, Tartu, Estonia |
| M. Afaq Shakir | Ph.D., Toyohashi University | 1999-2001 | Research Scientist, Baylor University, Houston, TX |
| Nicholas Bland | Ph.D. Universty of Glasgow | 2010-2014 | Field work in Global Health |

### Publications: (reverse chronological order)

a. Original Research in Peer-Reviewed Journals

Ochiana, S.O., Bland, N.D., Settimo, L., **Campbell, R.K**., Pollastri, M.P. Repurposing Human PDE4 Inhibitors for Neglected Tropical Diseases. Evaluation of Analogs of the Human PDE4 Inhibitor GSK-256066 as Inhibitors of PDEB1 of *Trypanosoma brucei*. *Chem Biol Drug Des*. doi: 10.1111/cbdd.12443. (2014) PMID: 25283372

Amata, E., Bland, N.D., Hoyt, C.T., Settimo, L., **Campbell, R.K.**, Pollastri, M.P. Repurposing human PDE4 inhibitors for neglected tropical diseases: design, synthesis and evaluation of cilomilast analogues as *Trypanosoma brucei* PDEB1 inhibitors. *Bioorg Med Chem Lett.* 24(17):4084-9. 2014 PMID: 25127163

Woodring, J.L., Bland, N.D., Ochiana, S.O., **Campbell, R.K.**, and Pollastri, M.P. Synthesis and assessment of catechol diether compounds as inhibitors of trypanosomal phosphodiesterase B1 (TbrPDEB1). *Bioorg. Med. Chem.* 23:5971-5974. (2013) PMID: 24042005

Cuihua Wang, C., Ashton, T.D., Bland, N.D., Gustafson, A.E., Ochiana, S.O., **Campbell, R.K.**, and Pollastri, M.P. Synthesis and evaluation of human phosphodiesterases (PDE) 5 inhibitor analogs as trypanosomal PDE inhibitors. 1. Sildenafil analogs. *Bioorg. Med. Chem. Lett.* 22(7):2582-2584. (2012) PMID: 22377518

Ochiana, S.O., Bland, N.D., Cuihua Wang, C., Russo, M., Gustafson, A.E., **Campbell, R.K.**, and Pollastri, M.P. Synthesis and evaluation of human phosphodiesterases (PDE) 5 inhibitor analogs as trypanosomal PDE inhibitors. 2. Tadalafil analogs. *Bioorg. Med. Chem. Lett.* 22(7):2579-2581. (2012) PMID: 22370268

Bland, N.D., Cuihua Wang, C., Tallman, C., Gustafson, A.E., Wang, Z., Ashton, T.D., Ochiana, S.O., McAllister, G., Cotter, K., Fang, A.P., Gechijian, L., Garceau, N., Gangurde, R., Ortenberg, R., Ondrechen, M.J., **Campbell,**

**R.K.** and Pollastri, M.P. Pharmacological Validation of *Trypanosoma brucei* Phosphodiesterases B1 and B2 as Druggable Targets for African Sleeping Sickness. *J Med Chem*. 54(23):8188-94 (2011) PMID: 22023548

Agüero, F., Al-Lazikani, B., Berriman, M., Buckner, F.S., **Campbell, R.K**., Carmona, S., Chen, F., Crowther, G.J., Hertz-Fowler, C., Hopkins, A.L., McAllister, G., Nwaka, S., Overington, J., Pain, A., Paolini, G.V., Pieper, U., Ralph, S.A., Riechers, A., Roos, D.S., Sali, A., Shanmugam, D., Suzuki, T., van Voorhis, W.C., and Verlinde, C. Genome-scale prioritization of drug targets: TDRtargets.org. *Nature Rev. Drug Discovery*. 7:900-907. (2008) PMID: 18927591

Martini, P.G., Taylor, D.M., Bienkowska, J., Jackson, J., McAllister, G., Keilhack, H. and **Campbell, R.K**. Comparative expression analysis of four breast cancer subtypes versus matched normal tissue from the same patients. *J. Steroid Biochem. Mol.* Biol. 109:207-211. (2008) PMID: 18424034

Rull, K., Hallast, P., Uuskula, L., Jackson, J., Punab, M., Salumets, A., **Campbell, R.K**., and Laan, M. Fine scale quantification of hCG beta gene transcription in human trophoblastic and non-malignant non-trophoblastic tissues. *Mol. Human Reprod*. 14:23-31. (2008) PMID: 18048458

McKenna, S.D., Feger, G., Kelton, C., Yang, M., Ardissone, V., Cirillo, R., Vitte, P.A., Jiang, X., and **Campbell, R.K**. Tumor necrosis factor (TNF)-soluble high-affinity receptor complex as a TNF antagonist. *J. Pharmacol Exp. Ther*. 322:822-828. (2007) PMID: 17495128

Clelland, E., Kohli, G., **Campbell, R.K**., Sharma, S., Shimasaki, S., and Peng, C. Bone morphogenetic protein 15 in the zebrafish ovary: cDNA cloning, genomic organization, tissue distribution and role in oocyte maturation. *Endocrinology* 147:201-209. (2006) PMID: 16210364

Gould, R.M., Morrison, H.G., Gilland, E., and **Campbell, R.K**. Evolution of myelin proteins: homologs of DM20 and PMP22 identified in the ascidian (*Ciona intestinalis*) genome. *Biological Bulletin* 209:49-66. (2005) PMID: 16110093

Anderson, R.J., Weng, Z., **Campbell, R.K**., and Jiang, X. Main-chain conformational tendencies of amino acids. *Proteins* 60:679-689. (2005) PMID: 16021632

**Campbell, R.K.**, Satoh, N., and Degnan, B.M. Piecing together evolution of the vertebrate endocrine system. *Trends Genet*. 20:359-366. (2004) PMID: 15262408

Dehal, P., Satou, Y., **Campbell, R.K**., Chapman, J., Degnan, B., De Tomaso, A., Davidson, B., Di Gregorio, A., Gelpke, M., Goodstein, D.M., Harafuji, N., Hastings, K.E., Ho, I., Hotta, K., Huang, W., Kawashima T, Lemaire P, Martinez D, Meinertzhagen IA, Necula S, Nonaka M, Putnam N, Rash S, Saiga, H., Satake, M., Terry, A., Yamada, L., Wang, H.G., Awazu, S., Azumi, K., Boore, J., Branno, M., Chin-Bow, S., DeSantis, R., Doyle, S., Francino, P., Keys, D.N., Haga, S., Hayashi, H., Hino, K., Imai, K.S., Inaba, K., Kano, S., Kobayashi, K., Kobayashi, M., Lee, B.I., Makabe, K.W., Manohar, C., Matassi, G., Medina, M., Mochizuki, Y., Mount, S., Morishita, T., Miura, S., Nakayama, A., Nishizaka, S., Nomoto, H., Ohta, F., Oishi, K., Rigoutsos, I., Sano, M., Sasaki, A., Sasakura, Y., Shoguchi, E., Shin-i, T., Spagnuolo, A., Stainier, D., Suzuki, M.M., Tassy, O., Takatori, N., Tokuoka, M., Yagi, K., Yoshizaki, F., Wada, S., Zhang, C., Hyatt, P.D., Larimer, F., Detter, C., Doggett, N., Glavina, T., Hawkins, T., Richardson, P., Lucas, S., Kohara, Y., Levine, M., Satoh, N., and Rokhsar, D.S. The draft genome of *Ciona intestinalis*: insights into chordate and vertebrate origins. *Science* 298:2157-2167 (2002) PMID: 12481130

Morrison, H.G., Zamora, G., **Campbell, R.K**., and Sogin, M.L. Inferring protein function from genomic sequence: *Giardia lamblia* expresses a phosphatidylinositol kinase-related kinase similar to yeast and mammalian TOR. *Comp. Biochem. Physiol. B Biochem. Mol. Biol*. 133:477-491. (2002) PMID: 12470813

Laan, M., Richmond, H., He, C., and **Campbell, R.K**. Zebrafish as a model for vertebrate reproduction: characterization of the first functional zebrafish (*Danio rerio*) gonadotropin receptor. *Gen. Comp. Endocrinol*. 125:349-364. (2002) PMID: 11884080

Xing, Y., Williams, C., **Campbell, R.K**., Cook, S., Knoppers, M., Addona, T., Altarocca, V., and Moyle, W.R. Threading of a glycosylated protein loop through a protein hole: implications for combination of human chorionic gonadotropin subunits. *Protein Science* 10:226-235. (2001). PMID: 11266609

Recombinant Human FSH Product Development Group. Recombinant follicle stimulating hormone: development of the first biotechnology product for the treatment of infertility. *Human Reprod. Update* 4:862-881. (1998)

**Campbell, R.K.**, Bergert, E.R., Wang, Y., Morris, J.C., and Moyle, W.R. Chimeric proteins can be more than the sum of their parts: implications for evolution and protein design. *Nature Biotechnology* 15:439-443. (1997) PMID: 9131622

Cosowsky, L., Lin, W., Han, Y., Bernard, M.P., **Campbell, R.K**., and Moyle, W.R. Influence of subunit interactions on lutropin specificity. *J. Biol. Chem*. 272:3309-3314. (1997) PMID: 9013570

Moyle, W.R., **Campbell, R.K**., Rao, S.N.V., Ayad, N.G., Bernard, M.P., Han, Y., and Wang, Y. Model of human chorionic gonadotropin and lutropin receptor interaction that explains signal transduction of the glycoprotein hormones. *J. Biol. Chem*. 270:20020-20031. (1995) PMID: 7650020

Cosowsky, L., Rao, S.N.V., Macdonald, G.J., Papkoff. H., **Campbell, R.K**., and Moyle, W. R. The groove between the α- and β-subunits of hormones with lutropin (LH) activity appears to contact the LH receptor, and its conformation is changed during hormone binding. *J. Biol. Chem*. 270:2001-20019. (1995) PMID: 7650019

Moyle, W.R., **Campbell, R.K**., Myers, R.V., Bernard, M.P., Han, Y., and Wang, X. Co-evolution of ligand-receptor pairs. *Nature* 368:251-255. (1994) PMID: 8145825

**Campbell, R.K**., Erfle, H., Barnett, R.W., and Moyle, W.R. Assembly and expression of a synthetic gene encoding the bovine glycoprotein hormone α-subunit. *Mol. Cell. Endocrinol*. 83:195-200. (1992) PMID: 1372275

**Campbell, R.K**., Dean-Emig, D.M., and Moyle, W.R. Conversion of human choriogonadotropin into a follitropin by protein engineering. *Proc. Natl. Acad. Sci. USA* 88:760-764. (1991) PMID: 1899483

Moyle, W.R., Matzuk, M.M., **Campbell, R.K**., Cogliani, E., Dean-Emig, D.M., Krichevsky, A., Barnett, R.W., and Boime, I. Localization of residues that confer antibody specificity using human chorionic gonadotropin/luteinizing hormone β-subunit chimeras and mutants. *J. Biol. Chem*. 265:8511-8518. (1990) PMID: 1692832

Ott. T.J., Herczeg, S.A., and **Campbell, R.K**. Quality assurance of clinical data in a remote data environment. *Drug Info. J*. 21:455-459. (1987)

Ott, T.J., Herczeg, S.A., and **Campbell, R.K**. Clinical quality assurance. *Drug Info J*. 20:195-198. (1986)

b. Review Articles, Books, Book Chapters

Pollasti, M.P. and **Campbell, R.K**. Target repurposing for neglected diseases. *Future Med Chem*. 3(10):1307-15. (2011) PMID: 21859304

**Campbell, R.K.** Molecular pharmacology of gonadotropins. *Endocrine*. 26:291-296. (2005) PMID: 16034184

Arkinstall, S., Wong, G., Hooft, R., Weiser, W., Evans, D., Jiang, X., Lai., J., El Tayar, N., **Campbell, R.K.**, and Fumero, S. Tomorrow's fertility treatment: the path to non-peptide FSH mimetics. In Proceedings, Ovulation Induction, Third World Congress. CIC Edizioni Internationali – Rome pp89-98. (2001)

Loumaye, E., **Campbell, R.K**., and Salat-Baroux, J. Human follicle stimulating hormone produced by recombinant DNA technology: a review for clinicians. *Human Reprod. Update* 1:188-199. (1995)

Moyle, W.R. and **Campbell, R.K**. Gonadotropins. In Reproductive Endocrinology, Surgery and Technology, eds. E.Y. Adashi, J.A. Rock and Z. Rosenwaks. Lippincott-Raven Publishers, Philadelphia pp683-724. (1996)

Moyle, W.R. and **Campbell, R.K**. Gonadotropins, In Endocrinology, ed. L.J. de Groot, W.B. Saunders Co., Philadelphia pp230-241. (1994)

**Campbell, R.K**. Control of gonadotropin binding specificity, In Ovulation Induction, eds. M. Filicori and C. Flamigni, Excerpta Medica, Amsterdam pp185-190. (1994)

**Campbell, R.K**., Matzuk, M.M., Dean-Emig, D.M., Cogliani, E., Myers, R.V., Krichevsky, A., Boime, I., and Moyle, W.R. Use of β-subunit chimeras to study structures of glycoprotein hormones and to develop a model of the β-subunit. In Glycoprotein Hormones, eds. W.W. Chin and I. Boime, Serono Symposia, Norwell, Massachusetts pp37-43. (1990)

**Campbell, R.K.**, Matzuk, M.M., Canfield, R.C., Boime, I., and Moyle, W.R. Use of monoclonal antibodies and mutagenesis to study the structure of human chorionic gonadotropin. In Placental Protein Hormones, eds. M. Mochizuki and R. Hussa, Elsevier Science, New York pp123-132. (1988)