#### Steven M. Foord

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#### Summary

- 10 year academic career starting with BSc in Physiology, a PhD in Pharmacology, a period of post doctoral work on neuropeptides then a MRC Training Fellowship in Molecular Biology. Published over 30 papers during this period.
- 21year career in the pharmaceutical industry with Glaxo, GlaxoWellcome and GlaxoSmithKline at Greenford, Ware, Stevenage and Harlow. Won company awards for the introduction of molecular pharmacology and leading a drug discovery project from conception to development respectively. Published two of the most cited papers on G protein coupled receptors (GPCRs) of the past 10 years (both in Nature) and more than 30 other papers plus patents and book chapters.
- Engaged in the application of computer biology to drug discovery. Project initiated included GPCR structural biology, 'The Secretome' and the 'Druggable Genome'. The latter was directed at GSKs Association Genetics program and its collaboration with the Structural Genomics Consortium
- Retired 2008 subsequent consultancy for Bristows, Heptares and MVM Investment.

#### Recently

- Consultant for Bristows, LLP, London July-December 2018.
- Consultant for Heptares Therapeutics (2008-2017)
  - Responsible for their collaboration with Bioexcel.
  - o Established the Heptares 'sequence to crystal' database
  - Heptares 'STAR' mutations patent support
  - Consultant for Seventure Venture Capital regarding Syngenta Therapeutics 2009
- Consultant for Eisai regarding several small GPCR companies 2007

#### Previously (Department, Division and Site closed 2007-8)

- Director and Site Head, Computational Biology, GlaxoSmithKline (GSK), Harlow
- Reported to David Searls, Senior Vice President and Head of Computational Biology which supported drug discovery functions in Stevenage, Harlow, Philadelphia and North Carolina
- Accountable for the computational biology support for the neurosciences therapeutic division.

#### **External Profile**

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- Core member of the committee for the International Union of Pharmacology (IUPHAR).
- Referee for Nature, Nature Genetics, BMC & Biochemistry
- Referee for the European Commission and the BBSRC.
- Regularly invited to present at academic and industry oriented conferences. Specialises in the application of bioinformatics, genetics and molecular pharmacology to drug discovery.
- External PhD examiner for The University of London and The Rockefeller University, NYC.

#### GlaxoSmithKline 2000-2007

- Accountable for the bioinformatics support of neuroscience, respiratory and inflammation therapeutic areas. This involved significant staff management and the large scale analysis of microarray expression, proteomics, orthology and genetic association data.
- Responsible for the progressive placement of these resources in the public domain through initiatives associated with the European Bioinformatics Institute (Druggability Portal) and the European Union (Innovative Medicines Initiative).
- Coordinated the mining of the human genome for pharmaceutically relevant targets and the consolidation and organisation of that data into the GSK 'gene index'. Managed the content of this

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index such that it remained GSKs most used BioInformatics database (in terms of diversity and intensity) for eight years.

• Core member of the GSK GPCR targets committee. Successfully wrote grant applications enabling six different post doctoral students to work at GSK on aspects of GPCR pharmacology, structural biology and informatics.

#### GlaxoWellcome, Stevenage, 1997-2000

- Gold Award resulting from the initiation and leadership of the Prostaglandin Receptor Research Program. Programs are now in the portfolio of Convergence Therapeutics after progression to Phase II within GSK
- International responsibility for the identification, mining, data management and progression of new GPCR targets. Enabled the identification, cloning & characterisation of the GPCRs for GABA, Nicotinic and Carboxylic Acids. I am a named inventor on several patents deriving from this work.
- Core member of the GlaxoWellcome BioInfomatics Management committee
- Chair of the Incyte/GW Research Committee, leader of the negotiating and evaluation team and responsible for audit and compliance. This was GWs largest collaborative venture within the Bioinformatics area.

#### Glaxo Group Research, Ware, 1993-1997

- GGR Head of Research Award for Leadership in Molecular Pharmacology.
- Project Leader for CGRP receptor research leading to the successful identification of the Receptor Activity Modifying Proteins (RAMPs) and the successful de novo cloning of the CGRP, adrenomedullin and amylin receptors. Lead author on the resulting article in Nature.

#### Glaxo Group Research, Greenford, 1988-1993

- Built and validated the screens for angiotensin, CCK and beta3 adrenoreceptors, the first recombinant screens to be run for GPCRs at Glaxo.
- Introduced Xenopus oocyte expression and electrophysiology into Glaxo as an experimental tool.
- Purified and characterised the HIV TAT protein demonstrating that its action was via direct binding to specific RNA sequences transcribed from the HIV genome.

## **1985-1988 MRC Training Fellow, Medical Molecular Biology Unit, Middlesex Hospital Medical School.** Supervisor: Professor R.K.Craig

The laboratory pioneered the use of molecular techniques in the U.K. and co-discovered CGRP. In collaboration with Celltech we characterised the CGRP gene, its receptor and pharmacology. Winner of the Ogden prize in 1987, awarded annually for the best publication from University College, London.

#### 1978-1985 PhD and Post Doctoral Research at University of Newcastle upon Tyne and the

**University of Wales College of Medicine. Luccock Research Scholar.** Supervisor: Professor R. Hall. PhD awarded for 'The role of catecholamines in the control of TSH secretion'. I also spent a year on post doctoral studies directed at a characterisation of neuropeptides secreted by cultures of foetal rat brain.

#### **Education:**

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BSc (Hons) 2(i) Physiology, University of Newcastle upon Tyne, 1978 4 'A' levels, 11 'O'levels, South Hunsley Comprehensive School, Near Kingston upon Hull

#### **Selected Publications and Presentations**

Over 60 peer-reviewed publications in significant scientific journals, written three book chapters, edited an issue of a journal and have made many presentations at international meetings as an invited speaker. My work continues to be highly cited.

#### Selected Invited Presentations at Learned Societies:

2008 Biochemical Society / Royal Society of Chemistry, London
2006 7<sup>th</sup> International Congress of Pharmacology, Beijing
2005 Society for Experimental Biology, Barcelona
2004 Wenner Gren Symposium on Receptor Behaviour, Stockholm
2004 Department of Trade and Industry Satellite Symposium to ISMB, Glasgow
2003 Alfred Nobel Symposium at the Karolinska Institute, Stockholm
2002 6<sup>th</sup> International Congress of Pharmacology, San Francisco
2001 Molecular Pharmacology Gordon Conference, Ventura
2000 2<sup>nd</sup> International Conference on Adrenomedullin and PAMP, Miyazaki, Japan
2000 Current Concepts in Asthma and Respiratory Research, London
1999 Advances in Receptor Regulation, New York Academy of Science, NY
1999 Hormone Action, Gordon Research Conference, Meridien, NH

#### Publications

I have over 60 peer-reviewed publications in significant scientific journals, written three book chapters, edited a journal and held several patents. In Biochemistry/Pharmacology a 'citation classic' is generally considered a publication cited more than 400 times. Seven qualify.
2055 Nature 393: 333-339 (1998) *Discovery of RAMPs*1259 Nature 396: 679-682 (1998) *Nature of the GABA B receptor*1255 J Biol Chem. 2003 278:11312-9. *Discovery of carboxylic acid receptors*763 Pharmacol Rev. 2002 54: 233-46. Review of the Calcitonin family of hormones & receptors
533 Pharmacol Rev. 2005 Jun;57(2):279-88. *Definitive list of GPCRs in the human genome*523 J Biol Chem. 2003 Mar 14;278(11):9869-74. *Discovery of nicotinic acid receptors*433 Mol Pharmacol 56:235-42 (1999) *Discovery of amylin receptors*

## **Peer Reviewed**

Definition of the G protein-coupled receptor transmembrane bundle binding pocket and calculation of receptor similarities for drug design.

Gloriam DE, Foord SM, Blaney FE, Garland SL. J Med Chem. 2009 Jul 23;52(14):4429-42.

<u>The G protein-coupled receptor subset of the dog genome is</u> <u>more similar to that in humans than rodents.</u> Haitina T, Fredriksson R, Foord SM, Schiöth HB, Gloriam DE. BMC Genomics. 2009 Jan 15:10:24.

The role of positive selection in determining the molecular cause of species differences in disease. Vamathevan JJ, Hasan S, Emes RD, Amrine-Madsen H, Rajagopalan D, Topp SD, Kumar V, Word M, Simmons MD, Foord SM, Sanseau P, Yang Z, Holbrook JD. BMC Evol Biol. 2008 Oct 6;8:273.

Important amino acids for the function of the human MT1 melatonin receptor.

Kokkola T, Foord SM, Watson MA, Vakkuri O, Laitinen JT. Biochem Pharmacol. 2003 May 1;65(9):1463-71.

Molecular identification of high and low affinity receptors for nicotinic acid.

Wise A, Foord SM, Fraser NJ, Barnes AA, Elshourbagy N, Eilert M, Ignar DM, Murdock PR, Steplewski K, Green A, Brown AJ, Dowell SJ, Szekeres PG, Hassall DG, Marshall FH, Wilson S, Pike NB.

J Biol Chem. 2003 Mar 14;278(11):9869-74.

The Orphan G protein-coupled receptors GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids.

Brown AJ, Goldsworthy SM, Barnes AA, Eilert MM, Tcheang L, Daniels D, Muir AI, Wigglesworth MJ, Kinghorn I, Fraser NJ, Pike NB, Strum JC, Steplewski KM, Murdock PR, Holder JC, Marshall FH, Szekeres PG, Wilson S, Ignar DM, Foord SM, Wise A, Dowell SJ.

J Biol Chem. 2003 Mar 28;278(13):11312-9.

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Agonist-promoted internalization of a ternary complex between calcitonin receptor-like receptor, receptor activity-modifying protein 1 (RAMP1), and beta-arrestin.

Hilairet S, Bélanger C, Bertrand J, Laperrière A, Foord SM, Bouvier M.

J Biol Chem. 2001 Nov 9;276(45):42182-90.

Protein-protein interaction and not glycosylation determines the binding selectivity of heterodimers between the calcitonin receptor-like receptor and the receptor activity-modifying proteins.

Hilairet S, Foord SM, Marshall FH, Bouvier M. J Biol Chem. 2001 Aug 3;276(31):29575-81.

Pharmacological characterization of receptor-activity-modifying proteins (RAMPs) and the human calcitonin receptor. Armour SL, Foord S, Kenakin T, Chen WJ. J Pharmacol Toxicol Methods. 1999 Dec;42(4):217-24.

Amylin receptor phenotypes derived from human calcitonin receptor/RAMP coexpression exhibit pharmacological differences dependent on receptor isoform and host cell environment.

Tilakaratne N, Christopoulos G, Zumpe ET, Foord SM, Sexton PM.

J Pharmacol Exp Ther. 2000 Jul;294(1):61-72.

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Multiple ramp domains are required for generation of amylin receptor phenotype from the calcitonin receptor gene product. Zumpe ET, Tilakaratne N, Fraser NJ, Christopoulos G, Foord SM, Sexton PM.

Biochem Biophys Res Commun. 2000 Jan 7;267(1):368-72.

<u>Multiple amylin receptors arise from receptor activity-modifying</u> protein interaction with the calcitonin receptor gene product. Christopoulos G, Perry KJ, Morfis M, Tilakaratne N, Gao Y, Fraser NJ, Main MJ, Foord SM, Sexton PM. Mol Pharmacol. 1999 Jul;56(1):235-42.

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