University of Birmingham

Dr Paul Alexander Foster Ph.D., B.Sc.

Lecturer in Molecular Endocrinology

Endocrinology, Diabetes and Metabolism

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About

Paul's external research webpage can be found at **www.drpaulfoster.co.uk (http://www.drpaulfoster.co.uk)** .

Paul leads the Steroid Metabolism in Cancer Research group at the University of Birmingham. He is an established figure in the endocrinology and cancer fields. With over a decade of experience in both academic and industrial environments, he has extensive research knowledge on a wide-range of areas. He is an author on over 30 scientific peer-reviewed papers, covering endocrinology, oncology, inflammation, cardiology, and drug development, and has various reviews and book chapters to his name.

Paul is an enthusiastic scientist who communicates his academic research on endocrine-related cancers at national and international conferences. He is extremely interested in the identification and targeting of pathways within steroidogenesis in order to develop new treatments for hormone-dependent disease. He is also a strong advocate for the improvement of animal welfare in medical research.

Qualifications

- Ph.D. Pharmacology
- B.Sc. Physiology & Pharmacology

Biography

Paul qualified with a B.Sc. (Hons) in Physiology and Pharmacology. He subsequently went on to do a Ph.D. in Pharmacology at King's College London, where his research focused on the role of nerve growth factor (NGF) as an inflammatory and pain mediator.

Paul remained in the inflammatory field when he took a research associate position at Queen Mary University London in 2001. His primary research areas at that time concentrated on how the kinins, particularly bradykinin, protected against cardiac ischemia/reperfusion injury (I/R). At this time Paul also gained teaching experience as a lecturer on various BMedSci courses.

In 2004, Paul moved into investigating endocrine-related cancer at Imperial College London and Sterix Ltd. (a spin-out company own by Ipsen Pharmacueticals Ltd.) Direction of research focused on two main areas, 1) the development of novel enzyme inhibitors for the treatment of hormone-driven cancers and, 2) the development of novel cytotoxic/anti-angiogenic agents for hormone-refractory cancers. Both research themes resulted in significant successes with various compounds in or about to enter clinical trials. Paul directed all in vivo research at Sterix Ltd. This primarily involved the design and development of novel animal models of hormone-driven cancer to allow drug proof of concept studies. These models have become integral to the pre-clinical development of a number of anti-cancer agents and have informed future clinical drug trials.

Paul has recently joined the University of Birmingham (2011) as a non-clinical Lecturer in Molecular Endocrinology and his future work will focus on three primary areas: 1) Oestrogen action in the development and proliferation of colorectal cancer, 2) Combining taxane therapy with metabolic inhibitors to maximise anti-cancer activity whilst limiting toxicity, and 3) Protein disulfide isomerise inhibitors for the treatment of cancer.

Teaching

Programme and Module Roles:
Deputy Programme Lead – MSc Pharmaceutical Enterprise
Module Lead – MSc Early Drug Discovery
Module Lead – MSc Drug Development to IND and then to Market
Module Lead – MSc Drug IP and Commercialisation
Module Lead – BDS Endocrine
Deputy Module Lead – BDS1 Digestion, Reproduction, and Endocrine
Deputy Module Lead - MBChB 1st year - Cellular Communication Endocrine Pharmacology (CEP)

Other teaching commitments:
BMedSci 3rd year – Endocrinology of Common Metabolic Disorders
MRes – Endocrine-related Cancer
MSc. Translational Medicine – Drug Development
MPharm HDT 1-2 – Pathophysiology of bone, Parathyroid and calcium regulation
BClin Sci (Intercalating) – New Drugs for Breast Cancer

Postgraduate supervision

Paul is always interested in recruiting talented new PhD students and postdoctoral associates. Please feel free to contact him for further information on current opportunities. If you are interesting in furthering your studying any endocrine-related cancers please contact Paul on the contact details above, or for any general doctoral research enquiries, please email: dr@contacts.bham.ac.uk or call +44 (0)121 414 5005.

For a full list of available Doctoral Research opportunities, please visit our Doctoral Research programme listings.

Current and past Group Members:

PhD Students:
Lorna Gilligan
Vasilis Chortis

MRes Researchers:
Lorna Gilligan (2012)
Joanne Longman (2013)

Undergraduate Researchers:
Vivien Tang (2014)
Maryam Hussain (2014)
William Evans (2013)
Alice Ross (2013)
Kamalpreet Aulakh (2013)
Rachel Arnold (2012)
Roseanna Petrova (2012)
Maha Adam (2012)

Research

Research Themes

Endocrinology, Oncology, Oestrogen Metabolism, Colorectal Cancer, Breast Cancer, Metabolic inhibitors, Novel in vivo Cancer Modelling.

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Oestrogens in colorectal cancer
Uncertainty surrounds the actions of oestrogens in colorectal cancers (CRC). Although epidemiological evidence suggests that oestrogens are protective against this malignancy, there is now significant research demonstrating that oestrogen action may increase the incidence and proliferation of colorectal cancer. What is clear is that the regulation of oestrogen synthesis and metabolism is important in CRC. Numerous studies indicate that oestrogen receptor □ (ER□□, which when activated induces apoptosis, □is lost during colonic tumourigenesis. We have shown that steroid sulphatase (STS), which desulphated conjugated oestrogens to their active forms, is elevated in CRC, and therefore active oestrogens may be involved in colorectal cancer development. □Down-regulation of 17□-HSD-2, which oxidises oestradiol (E2) to E1, has also been shown to be a negative prognostic factor for CRC mortality, and the ratio between STS and sulphotransferase (SULT1E1), enzymes that de-sulphate and sulphate E1 respectively, is a potent prognostic factor for CRC clinical outcomes.However, much remains unclear due to a lack of basic molecular research. For example, although the STS/EST ratio in CRC patient tissue has implications on mortality, it is unknown how this effects CRC cell growth, E1S/E1/E2 concentrations, and ER□/ER□ expression in vitro and in vivo. Furthermore, complete profiling of oestrogenic enzyme expression and activity, which would allow a greater understanding of local oestrogen concentrations, is lacking in available CRC cell lines and patient samples. This information, once ascertained, would clarify how oestrogens influence CRC, potentially leading to new therapeutic avenues for this disease.

Metabolic inhibitors combined with cytotoxics as anti-cancer treatment Traditional and novel cytotoxic agents have their efficacy compromised against many cancers due to toxicological complications. Strategies that limit these difficulties without decreasing cytotoxic activity are now important areas of research. One such approach, the combination of glycolytic inhibitors with a lower dose of cytotoxic, has gained significant interest over the past few years. Preliminary research, in breast cancer xenografts, of combining 2-deoxyglucose (2-DG), a glucose analogue that competitively inhibits glycolysis, with an experimental cytotoxic (STX140, Ipsen Pharma. Ltd.), has been positive. A clinical trial investigating 2-DG combination with Taxotere (docetaxel) has also shown some success, and prodrugs of 2-DG are now in development (by Intertech Bio, Houston). Other combinations utilising glycolysis inhibitors (e.g. 2-fluoro-2-deoxy-D-glucose (2-FG), dichloroacetic acid (DCA)), gluconeogenesis inhibitors (e.g. metformin), and cytotoxics (e.g. paclitaxel) remain to be examined. Indeed, DCA, an inhibitor of pyruvate dehydrogenase kinase, has recently moved onto Phase III clinical trials and combinational studies, in order to ascertain this compounds synergistic effects with cytotoxics, are of potential therapeutic interest.

Other activities

Society for Endocrinology Public Relations Committee Member
Society for Endocrinology Working Website Committee Member

Centre for Endocrinology, Diabetes, and Metabolism Post-graduate committee member

Founder of The Ark Hive (**www.the-ark-hive.org (http://www.the-ark-hive.org)**), a website dedicated to promoting the debate about the uses of animals in medical research.

Editorial Board member
- Open Enzyme Inhibition Journal
- Endocrinologist
- Endocrine Connections

Publications

Meyer-Losic F, Newman SP, Day JM, Reed MJ, Kasprzyk PG, Purohit A and Foster PA (2013) **STX140, but not paclitaxel, inhibits mammary tumour initiation and progression in C3(1)/SV40 T/t antigen transgenic mice (http://www.ncbi.nlm.nih.gov/pubmed/?term=10.1371%2Fjournal.pone.0080305)** . *PLoS One* 8(12):e80305

Foster PA (2013) **Oestrogen and Colorectal Cancer: Mechanisms and Controversies (http://www.ncbi.nlm.nih.gov/pubmed/?term=Oestrogen+and+Colorectal+Cancer%3A+Mechanisms+and+Controversies)** . *Int J Colorectal Dis* 28(6):737-49

Foster PA*, Day JM*, Tutill HJ, Schmidlin F, Sharland CM, Hargrave JD, Vicker N, Potter BVL, Reed MJ and Purohit A (2013) **STX2171, a 17b-hydroxysteroid dehydrogenase type 3 inhibitor, is efficacious in vivo in a novel hormone-dependent prostate cancer model (http://www.ncbi.nlm.nih.gov/pubmed/?term=STX2171%2C+a+17b-hydroxysteroid+dehydrogenase+type+3+inhibitor%2C+is+efficacious+in+vivo+in+a+novel+hormone-dependent+prostate+cancer+model)** . *Endocr Relat Cancer* 20(1):53-64

Purohit A and Foster PA (2012) **Steroid sulfatase inhibitors for both estrogen- and androgen-dependent cancers (http://www.ncbi.nlm.nih.gov/pubmed/21859802)** . *J Endocrinology* 212(2):99-110

Day JM, Foster PA, Tutill HJ, Parsons MF, Newman SP, Chander SK, Allan GM, Lawrence HR, Vicker N, Potter BV, Reed MJ and Purohit A (2008) **17beta-hydroxysteroid dehydrogenase Type 1, and not Type 12, is a target for endocrine therapy of hormone-dependent breast cancer (http://www.ncbi.nlm.nih.gov/pubmed/18183589)** . *International Journal of Cancer* 122(9):1931-40

Foster PA, Ho YT, Newman SP, Kasprzyk PG, Leese MP, Potter BV, Reed MJ and Purohit A (2008) **2-MeOE2bisMATE and 2-EtE2bisMATE induce cell cycle arrest and apoptosis in breast cancer xenografts as shown by a novel ex vivo technique** (http://www.ncbi.nlm.nih.gov/pubmed/?term=2-MeOE2bisMATE+and+2-EtE2bisMATE+induce+cell+cycle+arrest+and+apoptosis+in+breast+cancer+xenografts+as+shown+by+a+novel+ex+vivo+technique) . *Breast Cancer Research and Treatment* 111(2):251-60

Tagg SL, Foster PA, Leese MP, Potter BV, Reed MJ, Purohit A and Newman SP (2008) **2-Methoxyoestradiol-3,17-O,O-bis-sulphamate and 2-deoxy-D-glucose in combination: a potential treatment for breast and prostate cancer** (http://www.ncbi.nlm.nih.gov/pubmed/?term=2-Methoxyoestradiol-3%2C17-O%2CO-bis-sulphamate+and+2-deoxy-D-glucose+in+combination%3A+a+potential+treatment+for+breast+and+prostate+cancer) . *British Journal of Cancer* 99(11):1842-8

Foster PA, Chander SK, Newman SP, Woo LW, Sutcliffe OB, Bubert C, Zhou D, Chen S, Potter BV, Reed MJ and Purohit A (2008) **A New Therapeutic Strategy against Hormone-Dependent Breast Cancer: The Preclinical Development of a Dual Aromatase and Sulfatase Inhibitor** (http://www.ncbi.nlm.nih.gov/pubmed/?term=A+New+Therapeutic+Strategy+against+Hormone-Dependent+Breast+Cancer%3A+The+Preclinical+Development+of+a+Dual+Aromatase+and+Sulfatase+Inhibitor) . *Clinical Cancer Research* 14(20):6469-77

Foster PA, Chander SK, Parsons MF, Newman SP, Woo LW, Potter BV, Reed MJ and Purohit A (2008) **Efficacy of three potent steroid sulfatase inhibitors: pre-clinical investigations for their use in the treatment of hormone-dependent breast cancer** (http://www.ncbi.nlm.nih.gov/pubmed/?term=Efficacy+of+three+potent+steroid+sulfatase+inhibitors%3A+pre-clinical+investigations+for+their+use+in+the+treatment+of+hormone-dependent+breast+cancer) . *Breast Cancer Research and Treatment* 111(1):129-38

Foster PA, Woo LW, Potter BV, Reed MJ and Purohit A (2008) **The use of steroid sulfatase inhibitors as a novel therapeutic strategy against hormone-dependent endometrial cancer** (http://www.ncbi.nlm.nih.gov/pubmed/?term=The+use+of+steroid+sulfatase+inhibitors+as+a+novel+therapeutic+strategy+against+hormone-dependent+endometrial+cancer) . *Endocrinology* 149(8):4035-42