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Dr Sam Butterworth

Lecturer in Medicinal Chemistry

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About

As a Lecturer in Medicinal Chemistry Sam is involved in the development and delivery of the Medicinal Chemistry course that forms an integral part of the new Master of Pharmacy (MPharm) undergraduate degree programme within the College of Medical and Dental Sciences.

Sam joined the university from AstraZeneca where he worked for 8 years. During this time he was accountable for chemistry strategy and delivery for all phases of discovery projects through externalised pre-portfolio collaborations, HTS, Lead Generation, Lead Optimisation to Pre-clinical development. His work at AstraZeneca led to the development of a promising targeted anti-cancer agent AZD9291, that is currently undergoing phase 2 clinical trials in late stage lung cancer.

In academia Sam is appling the understanding he gained from industry to educate students about medicinal chemistry and drug discovery while developing innovative, translational research programmes in collaboration with clinicians and biomedical researchers from other disciplines.

Qualifications

- DPhil in Organic Chemistry (Oxford)
- MChem (Manchester)

Biography

Sam studied chemistry at the University of Manchester (M Chem) and Oxford (DPhil, supervisor Prof. Tim Donohoe).

After leaving Oxford Sam moved back to the northwest to take a position as a Medicinal Chemist at AstraZeneca, Alderley Park where he worked for 8 years. While at AZ his design and synthetic contributions led to the discovery of a promising targeted anti-cancer agent AZD9291, that is currently undergoing phase 2 clinical trials in late stage lung cancer.

While working on earlier-stage projects Sam led AstraZeneca's strategic activities for 2 Oncology target classes, and headed the chemistry evaluation of a screening platform leading to a multi-million dollar collaboration to find leads against undruggable targets.

In addition to this he worked to define screening strategies, conducting HTS work up and led hit-to-lead activities for 4 successful HI/LI projects against several target classes, including developing new analytical approaches to identify hit families and understand selectivity/SAR from HTS data.

He also spent a year working with cross-disciplinary 'Campaign 1' delivery teams, responsible for rapid synthesis of kg-scale batches to support late-stage discovery and pre-clinical studies across infection, diabetes and oncology projects, including doing some kg scale synthesis with his own hands.

Over 8 years Sam line-managed teams of up to 6 synthetic chemists including Graduates, PhDs and Post-Docs and led teams of up to 16 chemists in a matrix environment.

In his final role at AstraZeneca Sam was able to apply the broad understanding of drug discovery and biological processes he had developed a role by developing and evaluating both internal and external clinical opportunities in diverse disease areas. In particular this involved leading chemistry input on repositioning projects delivered through strategic collaborations, open innovation platforms and outsourcing.

Teaching

Pharmacy (MPharm) - Module coordinator for Chemistry for Pharmacists 1: This module covers the application of orbital theory, basic synthesis and an introduction to the molecular basis of drug action.

MSc - Delivering material on drug dicovery and medicinal chemistry for several taught MSc courses.

Postgraduate supervision

Sam's research group currently comprises 3 PhD students, 2-3 Masters students and a PDRA.

Research

The motivation for Sam's research is to work at the interface of organic/medicinal chemistry and biomedical reaserach.

By working closely with researchers from other disciplines he hopes to utilise his knowledge, creativity and experience to develop projects that can translate fundamental research within universities into benefit to patients.

Initial interest lies in the areas of:

- Design and synthesis of novel nucleoside mimetics with potential utility in treatment of glioblastoma.
- Design, synthesis and development of kinase inhibitors as potential treatments for glioblastoma, neuronal injury or breast cancer (2 projects).
- Design, synthesis and development of modulators of 5-HT receptors with novel mode of action and/or modified distribution characteristics.
- Evaluating the potential for utilising receptor-mediated internalisation to deliver RNA or small molecule therapies to defined cell populations, for example towards treatment of fibrotic disease.

Publications

Ward, R. A., Anderton, M. J., Ashton, S., Bethel, P. A., Matthew Box, Butterworth, S., *et al.*: Structure- and Reactivity-Based Development of Covalent Inhibitors of the Activating and Gatekeeper Mutant Forms of the Epidermal Growth Factor Receptor (EGFR). *Journal of Medicinal Chemistry* 2013 56, 7025-7048.

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