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PROFESSOR BARRIE KELLAM

PROFILE

A Professor of Medicinal Chemistry with over 15 years experience heading up a thriving research group dedicated to the design, synthesis and exploitation of new chemical entities in numerous areas of chemical biology including molecular pharmacology, cell-signalling, biospectroscopy and drug discovery.

EDUCATION

University of Nottingham — PhD in Medicinal Chemistry, 1996

University of Nottingham — BPharm (hons) 1st Class, 1991

EMPLOYMENT

Professor of Medicinal Chemistry School of Pharmacy, University of Nottingham
2013-present

Associate Professor in Pharmaceutical Medicinal Chemistry School of Pharmacy, University of Nottingham
2006-2013

Lecturer in Pharmaceutical Medicinal Chemistry, School of Pharmacy, University of Nottingham, 1997-2006

Postdoctoral Research Assistant, School of Pharmacy, University of London 1996-1997

DIRECTORSHIPS

CellAura Technologies Ltd. Director of Medicinal Chemistry, 2006 - 2014

EXTERNAL POSITIONS

Member of the General Pharmaceutical Council Accreditation Panel, 2012 - present

Member of the Royal Pharmaceutical Society Faculty Panel (Curriculum), 2013 - present

UG TEACHING

Chair of MPharm Teaching & Learning Committee, 2007 - 2012

MPharm Teaching Modules: B31ESP (Essential Skills for Pharmacy), B31DYS (Dyspesia), B33E11 (Molecular Therapeutics), B34ADD (Advanced Drug Discovery)

PG TEACHING

Course Director of MSc in Drug Discovery & Pharmaceutical Sciences, 2012 - present

MSc Teaching Modules: B34FDD (Fundamentals of Drug Discovery), B34DTP (Drug Targets and Pharmacodynamics), B34DD1 (Drug Discovery & Development I), B34DD2 (Drug Discovery & Development II), B34RES (Research Project).

RESEARCH

PUBLICATIONS

1. Solid Phase Applications of Dde and the Analogue Nde: Synthesis of Trypanothione Disulfide. Kellam, B.; Bycroft, BW.; Chhabra, SR. *Tetrahedron Lett.*, 1997, 38, 4849-4852.
2. Transient Affinity Tags Based on the Dde Protection/Deprotection Strategy: Synthesis and Applications of 2-Biotinyl- and 2-Hexanoyldimedone. Kellam, B.; Chan, WC.; Chhabra, SR.; Bycroft, BW. *Tetrahedron Lett.*, 1997, 38, 5391-5394.
3. Solid Phase Synthesis of C-Terminal Carbohydrate Modified Enkephalins. Drouillat, B.; Kellam, B.; Dekany, G.; Starr, MS.; Toth, I. *Bioorg. Med. Chem. Lett.*, 1997, 7, 2247-2250.
4. Solid Phase Strategies: Applications of 2-Acetyl-4-nitroindane-1,3-dione as a selective protecting group for primary amines.Kellam, B.; Bycroft, BW.; Chan, WC. and Chhabra, SR. *Tetrahedron*, 1998, 54, 6817-6832.
5. Dekany, G.; Drouillat, B.; Kellam, B.; Toth, I., Novel Dde-Protected Glycoamino Acids and Glycoazido Acids in Saccharopeptide Synthesis. *Peptides, Frontiers of Peptide Science*, Proceedings of the Fifteenth American Peptide Symposium, (Tam, J.P.; Kaumaya, P.T.P. Eds.), Kluwer/Escom, 1998, 719-720.
6. Kellam, B.; Starr, MS.; Lamidi, TG.; Toth, I. A Novel Lipoamino Acid Based System for the Delivery of Leu-Enkephalinamide Derivatives Through the Blood-Brain Barrier. *Peptides, Frontiers of Peptide Science,* Proceedings of the Fifteenth American Peptide Symposium, (Tam, J.P.; Kaumaya, P.T.P. Eds.), Kluwer/ Escom, 1998, 837-838.
7. Synthesis and Evaluation of Lipoamino Acid and Carbohydrate Modified Enkephalins as Potential Antinociceptive Agents. Kellam, B.; Drouillat, B; Dekany, G.; Starr, MS.; Toth, I. *Int. J. Pharm.*, 1998, 161, 55-64.
8. Solid Phase Synthesis of Lipoamino Acid and Carbohydrate Modified Peptide Entities. Kellam, B.; Drouillat, B.; Dekany, G.; Flinn, N.; Starr, MS.; Toth, I., *Innovations and Perspectives in Solid Phase Synthesis and Combinatorial Libraries*, (Epton, R., Ed.) Mayflower Scientific, 1998, 151-154.
9. Non-Destructive Real-Time Monitoring in Solid Phase Synthesis by Near-Infrared Reflectance Spectroscopy – Esterification of a Resin-Bound Alcohol. Hammond, J.; Kellam, B.; Moffat, AC.; Jee, RD. *Anal. Commun.*, 1999, 36, 127-129.
10. A novel method for solid-phase synthesis of oligosaccharides using the N-1-(4,4-dimethyl-2,6-dioxocyclohexylidene)ethyl (Dde) linker. Drinnan, N.; West, ML.; Broadhurst, M.; Kellam, B.; Toth, I. *Tetrahedron Lett.*, 2001, 42, 1159-1162.
11. A Dde-based carboxy linker for solid-phase synthesis. Chhabra, SR.; Parekh, H.; Khan, AZ.; Bycroft, BW.; Kellam, B. *Tetrahedron Lett.*, 2001, 42, 2189-2192.
12. Cell Type-specific adhesion onto polymer surfaces from mixed cell populations. Quirk, RA.; Kellam, B.; Bhandari, RM.; Davies, MC.; Tendler, SJB.; Shakesheff, KM. *Biotech. Bioeng.*, 2003, 81, 625-628.Recent Progress in the Design of Selectin Inhibitors. Chhabra, SR.; Abdul Rahim, AS.; Kellam, B. *Mini Rev. Med. Chem*. 2003, 3, 679-687.
13. Surface Engineering of Living Myoblasts Via Selective Periodate Oxidation. De Bank, PA.; Kellam, B.; Kendall, DA.; Shakesheff, KM. *Biotech. Bioeng.*, 2003, 81, 800-808.
14. Chemical modification of mammalian cell surfaces. Kellam, B.; De Bank, PA.; Shakesheff, KM. *Chem. Soc. Rev*. 2003, 327-337.
15. Convenient syntheses of (3S, 5S)-carbapenam-3-carboxylates and their biosynthetic relevance. Bycroft, BW.; Chhabra, SR.; Kellam, B.; Smith, P. *Tetrahedron Lett*. 2003, 44, 973-976.
16. Biosynthesis of Carbapenem Antibiotics: New carbapenam substrates for carbapenem synthase (CarC). Sleeman, MC.; Smith, P.; Kellam, B.; Chhabra, SR.; Bycroft, BW.; Schofield, CJ. *ChemBioChem*, 2004, 5, 879-882. RJ.; Yates, AS.; George, MW.; Kellam, B.; Hill, SJ. *Faraday Discuss.*, 2004, 126, 197-207.
17. Quantitative analysis of the formation and diffusion of A1-adenosine receptor-antagonist complexes in single living cells. Briddon, SJ.; Middleton, RJ.; Cordeaux, Y.; Flavin, FM.; Weinstein, JA.; George, MW.; Kellam, B.; Hill, SJ. *Proc. Nat. Acad. Sci USA.* 2004, 101, 4673-4678.

18. N-alpha-Dmc protected amino acid aglycones: Versatile hydrogenolysis stable acceptors for O-glycosylation. Kellam, B.; Ward, PA; Rahim, ASA.; Chhabra, SR. *Tetrahedron. Lett*. 2005, 46, 1703-1706.
19. Altered cellular response to adsorbed matrix protein by chemoselective ligation of small molecules. De Bank, PA.; Kellam, B.; Kendall, DA.; Shakesheff, KM. *J. Mater. Chem.* 2005, 15, 2047-2055.
20. Chemical modification of the naphthoyl 3-position of JWH-015: In search of a fluorescent probe to the cannabinoid CB2 receptor. Yates, AS.; Doughty, SW.; Kendall, DA.; Kellam, B. *Bioorg. Med. Chem. Lett.* 2005, 15, 3758-3762.
21. Fluorophore-Tagged Ligands for GPCRs. Middleton, RJ.; Kellam, B. *Curr. Opin. Biol. Chem.* 2005, 9, 517-525.
22. Binding of the anticancer prodrug CB1954 to the activating enzyme NQO2 revealed by the crystal structure of their complex. AbuKhader, M; Heap, J; De Matteis, C; Kellam, B; Doughty, SW; Minton, N; Paoli, M. *J. Med. Chem.* 2005, 48, 7714-7719.
23. Functionalizing human amylin (20-29) fibrils. Sedman. VL.; Allen, S.; Chan, WC.; Kellam, B.; Tendler, SJB. *FEBS J.* 2005, 272, Suppl. 1, 517-518.
24. New fluorescent adenosine A(1)-receptor agonists that allow quantification of ligand-receptor interactions in microdomains of single living cells. Middleton, RJ.; Briddon, SJ.; Cordeaux, Y.; Yates, AS.; Dale, CL.; George, MW.; Baker, JG.; Hill, SJ.; Kellam, B. *J. Med. Chem.*, 2007, 50, 782-793.
25. Accelerated Formation of Multicellular 3-D Structures by Cell-to-Cell Cross-Linking. De Bank, PA.; Hou, O.; Warner, RM.; Wood, IV.; Ali, BA.; MacNeil, S.; Kendall, DA.; Kellam, B.; Shakesheff, KM.; Buttery, LDK. *Biotech. Bioeng.* 2007, 96, 1617-1625.
26. Agonist-occcupied A3 adenosine receptors exist within heterogeneous complexes in microdomains of individual living cells. Cordeaux, Y.; Briddon, SJ.; Alexander, SPH.; Kellam, B.; Hill, SJ. *FASEB J.* 2008, 850-860
27. Influence of fluorophore and linker composition on the pharmacology of fluorescent adenosine A1 receptor ligands. Baker, JG; Middleton, R; Adams, L; May, LT; Briddon, SJ; Kellam, B; Hill SJ. *Br. J. Pharmacol.* 2010, 159, 772-786.
28. 'Smart Culture' of Mouse Embryonic Stem Cells. Dey, S.; Alexander, M.; Kellam, B.; Alexander, C.; Rose, F. R. *J. Pharm. Pharmacol.* 2010, 62, 1497-1498.
29. Enzyme-passage free culture of mouse embryonic stem cells on thermo-responsive polymer surfaces. Dey, S.; Kellam, B.; Alexander, M.; Alexander, C.; Rose, F. R. *J. Mat. Chem.* 2011, *21*, 6883-6890.
30. Briddon, S. J.; Kellam, B.; Hill, S. J. Design and use of fluorescent ligands to study ligand-receptor interactions in single living cells. *Methods Mol. Biol.* 2011, *746*, 211–236.
31. Jadhav, G. P.; Chhabra, S. R.; Telford, G.; Hooi, D. S. W.; Righetti, K.; Williams, P.; Kellam, B.; Pritchard, D. I.; Fischer, P. M. Immunosuppressive but Non-LasR-Inducing Analogues of the Pseudomonas aeruginosa Quorum-Sensing Molecule N-(3-Oxododecanoyl)-l-homoserine Lactone. *J. Med. Chem*. 2011, *54*, 3348– 3359.
32. Baker, J.; Adams, L., Salchow, K.; Mistry, S.; Middleton, R.; Hill, S. J.; Kellam, B. Synthesis and characterization of high-affinity 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY)-labeled fluorescent ligands for human beta-adrenoceptors. *J. Med. Chem.* 2011, 6874-6887.
33. Dale, C. L.; Hill, S. J.; Kellam, B. New potent, short-linker BODIPY-630/650 labelled fluorescent adenosine receptor agonists. *Med. Chem. Commun*. 2012, *3*, 333–338.
34. Vernall, A. J.; Stoddart, L. A.; Briddon, S. J.; Hill, S. J.; Kellam, B. Highly Potent and Selective Fluorescent Antagonists of the Human Adenosine A3 Receptor Based on the 1,2,4-Triazolo[4,3-a]quinoxalin-1-one Scaffold. *J. Med. Chem*. 2012, 55, 1771–1782.
35. Stoddart, L. A.; Vernall, A. J.; Denman, J. L.; Briddon, S. J.; Kellam, B.; Hill, S. J. Fragment Screening at Adenosine-A3 Receptors in Living Cells Using a Fluorescence-Based Binding Assay. *Chem. Biol*. 2012, 19, 1105–1115.
36. Mistry, S.N.; Baker, J.G.; Fischer, P.M.; Hill, S.J.; Gardiner,S.M.; Kellam, B. The synthesis, in vitro and in vivo characterisation of highly R1-selective R-adrenoceptor partial agonists. *J. Med. Chem.* 2013, 56: 3852–3865.

37. Vernall, A.; Stoddart, L.; Briddon, S. J.; Ng, H-W.; Laughton, C. A.; Doughty, S.; Hill, S.J.; Kellam, B. Conversion of a Non-Selective Adenosine Receptor Antagonist into A3-Selective High Affinity Fluorescent Probes Using Peptide-Based Linker. *Org. Biomol. Chem.*, 2013, 11 (34), 5673 – 5682.
38. Corriden, R.; Self, T.; Akong-Moore, K.; Nizet, V.; Kellam, B.; Briddon, S. J.; Hill, S. J. Adenosine-A3 receptors in neutrophil microdomains promote the formation of bacteria-tethering cytonemes. *EMBO Rep.*, 2013, 14: 726–732.
39. Dickens, M.P.; Roxburgh, P.; Hock, A.; Mezna, M.; Kellam, B; Vousden, K.H.; Fischer, P.M. 5-Deazaflavin derivatives as inhibitors of p53 ubiquitination by HDM2. *Bioorg. Med. Chem.* 2013, 21: 6868–6877.
40. Vernall, A. J.; Hill, S. J.; Kellam, B. The Evolving Small-Molecule Fluorescent-Conjugate Toolbox for Class a GPCRs. *Br. J. Pharmacol*. 2014, 171, 1073–1084.
41. Hill, S. J.; May, L. T.; Kellam, B.; Woolard, J. Allosteric Interactions at Adenosine A1 and A3 Receptors: New Insights Into the Role of Small Molecules and Receptor Dimerization. *Br. J. Pharmacol*. 2014, 171, 1102–1113.
42. Skilling, K. J.; Citossi, F.; Bradshaw, T. D.; Ashford, M.; Kellam, B.; Marlow, M. Insights Into Low Molecular Mass Organic Gelators: a Focus on Drug Delivery and Tissue Engineering Applications. *Soft Matter* 2014, 10, 237–256.
43. Stoddart, L. A.; Kellam, B.; Briddon, S. J.; Hill, S. J. Effect of a Toggle Switch Mutation in TM6 of the Human Adenosine A3 Receptor on Gi Protein-Dependent Signalling and Gi-Independent Receptor Internalization. *Br. J. Pharmacol*. 2014, 171, 3827–3844.
44. Corriden, R.; Kilpatrick, L. E.; Kellam, B.; Briddon, S. J.; Hill, S. J. Kinetic Analysis of Antagonist-Occupied Adenosine-A3 Receptors Within Membrane Microdomains of Individual Cells Provides Evidence of Receptor Dimerization and Allosterism. *FASEB J*. 2014. DOI: 10.1096/fj.13-247270

BOOK CHAPTERS

1. "Combinatorial Chemistry" *in Principles of Drug Design and Action 4th Edition.* Smith, HJ. Ed; CRC Press. 2005**.**

PATENTS

1. Methods for solid-phase or combinatorial synthesis of oligosaccharides. Toth, I.; Dekany, G and Kellam, B. 1998, WO 9808799.
2. Solution and solid phase synthesis of oligosaccharides using protected amino sugars. Toth, I.; Dekany, G and Kellam, B. 1998, WO 9838197.Preparation of cyclic compounds as protecting and linking groups for organic synthesis, Toth, I.; Dekany, G and Kellam, B. 1999, WO 9915510.
3. Fluorescently Tagged Ligands. Kellam, B.; Middleton, RJ.; George, MW.; Hill, SJ. 2003, UK - 0307559.5, PCT - GB2004/001418, WO2004088312-A2; EP1623223-A2; AU2004225696-A1; US2006211045-A1; JP2006523203-W; CN1860364-A, Europe - 04724650.9.
4. High Content Screening. Briddon, SJ; Hill, SJ; Kellam, B. 2005, UK - 0421258.8, PCT - GB2005/03709, WO2006032926-A2.
5. Aggregating population of cells. Shakesheff, K; Kellam, B; Kendall, D; De Bank, P. 2008, WO2007060382-A1.
6. A method for generating a recombinant clonal cell line and novel reagents for use in the method. Kellam, B; Hill, SJ; Hunter, A; Middleton, RJ, 2008, GB0718935.0
7. Novel Compounds and Improved Treatments for Cardiac Disease. Kellam, B; Hill, SJ; Baker, JG; Mistry, SN, 2010, P126586WO.
8. New beta blockers for the treatment of glaucoma. Kellam, B; Hill, SJ; Baker, JG; Fischer, PM. 2010
9. Novel Cyclic Compounds and Improved Treatments for Cardiac and Cardiovascular Disease. Kellam, B; Hill, SJ; Baker, JG; Mistry, Fischer, PM, Fromont, C, Jadhav, G, Daras, E. 2011, P128051GB.

10. Novel Cyclic Amine Compounds and Improved Treatments for Cardiac and Cardiovascular Disease. Kellam, B; Hill, SJ; Baker, JG; Mistry, Fischer, PM, Fromont, C, Jadhav, G, Daras, E. 2011, P128052GB.
11. Novel Cyclic Phenoxy Compounds and Improved Treatments for Cardiac and Cardiovascular Disease. 2011, P128054GB.

GRANTS (over £6.5 MILLION IN THE PERIOD 2006-2014)

£50K from the BBSRC for a Committee Studentship entitled "Molecular interrogation of the human 1-adrenoceptor secondary binding site" (2005-2008) (with Prof SJ Hill).

£296K from BBSRC for a project grant entitled 'the study of adenosine A1-receptor binding and signalling in membrane microdomains of single living cells'. (2005-2008) (with Dr Steve Briddon & Prof Steve Hill)

£100K from Novartis/BBSRC for a CASE award entitled 'Click Chemistry as a Route to BODIPY Labelled Fluorescent Ligands' (2008-2011) (with Prof Steve Hill)

£2,880K from the Wellcome Trust for a Seeding Drug Discovery grant entitled 'Development of highly-selective β1 adrenoceptor antagonists for therapeutic application in patients with concomitant cardiovascular and respiratory disorders'. (2008-2012) (with Dr Jill Baker, Prof Steve Hill and Prof Peter Fischer)

£1,313K from the MRC for a Programme Grant entitled 'Use of Fluorescence Correlation Spectroscopy to study the adenosine A3-receptor in microdomains of single living cells (2009-2014) (with Dr Steve Briddon & Prof Steve Hill).

£60K from the RPSGB for an Academic Excellence award entitled ': In Silico Design, Synthesis and Pharmacological Evaluation of Selective β1-Adrenoceptor Antagonists for Improved Treatment of Cardiovascular Disorders'. (2009-2013) (with Prof Peter Fischer and Dr Charlie Laughton).

€16,000K (UoN Component €500,000) from the EU Innovative Medicines Initiative 'Consortium on Kinetics for Drug Discovery (K4DD)'. (2012-2017) (with Dr Steve Briddon & Prof Steve Hill).

£624K from the MRC for a project grant entitles 'The synthesis and evaluation of new fluorescent-labelled P2Y2 receptor chemical probes'. (2014-2017) (With Dr Mike Stocks and Prof Steve Hill).

£918K from the MRC for a project entitled 'Design, synthesis, and pharmacological profiling of agonists of the human orexin receptors' (2014-2017) (With Profs Peter Fischer, Jill Baker, Steve Hill and Dr Jeanette Woolard)