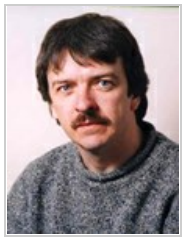
University of Birmingham

Professor Mark Wheatley BSc, PhD, FHEA

Chair of Biochemical Pharmacology



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About

Professor Mark Wheatley has an international reputation for his research into the structure and function of G-protein-coupled receptors (GPCRs). He has national and international collaborations with both academia and the pharmaceutical industry.

Qualifications

BSc (London)

PhD (Nottingham)

Biography

2007-present Chair of Biochemical Pharmacology.University of Birmingham.

2005-2007 Reader in Biochemistry, University of Birmingham.

1995-2005 Senior Lecturer in Biochemistry, University of Birmingham.

1988-1995 Lecturer in Biochemistry, University of Birmingham/

Teaching

I have a full teaching commitment. I lecture on various aspects of biochemistry and cell signalling to undergraduates reading Biochemistry, Biology, Natural Sciences, Medicine, Dentistry and Medical Sciences. I also lecture on MSc courses.

I am a Fellow of the Higher Education Academy.

Postgraduate supervision

For a list of possible PhD projects offered by Prof Wheatley **www.findaphd.com/search/customlink.asp?inst=birm-Biol&supersurname=Wheatley (http://www.findaphd.com/search/customlink.asp?inst=birm-Biol&supersurname=Wheatley)**

Research

Research Theme within School of Biosciences: **Molecular and Cell Biology (/research/activity/cellbiology/index.aspx)**

The structure and function G-protein-coupled receptors

My research addresses the structure and function of G-protein-coupled receptors. In particular, I have maintained a long-standing interest in the receptors for the pituitary hormones vasopressin (AVP) and oxytocin (OT). These peptides have many physiological functions including regulation of blood pressure and urine volume (AVP), lactation and contraction of the uterus at birth (OT). Effects are mediated by a family of four related receptor proteins viz. $V_{1a}R$, $V_{1b}R$, V_2R and OTR.

We use a range of complementary techniques to probe this family of four different receptor proteins including molecular biology and peptide chemistry. As AVP and OT are nonapeptides, they are amenable to modification and derivatisation. Consequently, we have generated a range of biotinylated, fluorescent and chimeric peptides (i.e. incorporating sequence from more than one hormone) to localise receptors and to probe ligand:receptor interaction.

We have also used site-directed mutagenesis and chimeric receptor constructs to identify important residues and domains for ligand recognition, receptor activation, cell-surface expression and intracellular signalling. Mutant receptor constructs are characterised by radioligand binding studies and second messenger assays after expression in cultured cells. The effect of post-translational modification of the receptors is being investigated utilising receptors which have had an antibody epitope engineered into them to allow immuno-precipitation and biochemical analysis.

The peptide hormone ghrelin has an important physiological role in regulating appetite. The receptor for ghrelin is unusual in that it naturally exhibits high constitutive activity (signalling in the absence of agonist stimulation). We have investigated the molecular basis for this high constitutive activity using site-directed mutagenesis.

Overall, we aim to understand how GPCRs for peptide hormones work at the molecular level which will aid rational drug design in the future.

Other activities

I am an active member of the Biochemical Society in the UK and have served on both the Executive and the Council (two terms of office) of the Society. I have also been a member of the Meetings Board and Chair of the Hormone Committee.

I have organised many research conferences and symposia on GPCRs and I am regularly invited to speak at international and national research conferences,

pharmaceutical companies and universities.

Member of the British Pharmacological Society.

Editorial Board Member of Frontiers in Cellular Endocrinology.

Publications

Wheatley, M., Wootten, D., Conner, M.T., Simms, J., Kendrick, R., Logan, R.T., Poyner, D.R. and Barwell, J. (2011) Lifting the lid on G-protein-coupled receptors: The role of the extracellular loops. *Brit. J. Pharmacol.* (in press).

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Jamshad, M., Lin, Y.P., Knowles, T.J., Parslow, R.A., Harris, C., **Wheatley, M**., Poyner, D.R., Bill, R.M., Thomas, O.R., Overduin, M., Dafforn, T.R. (2011) Surfactant-free purification of membrane proteins with intact native membrane environment. *Biochem. Soc. Trans.* **39**: 813-818.

Qi, T., Simms, J., Bailey, R.J., Wheatley, M**.**, Rathbone, D.L., Hay, D.L. and Poyner, D.R. (2010) Structure-function analysis of RAMP1-RAMP3 chimeras. *Biochemistry* 49: 522-531.

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Conner, M., Hawtin, S.R., Simms, J., Wootten, D., Lawson, Z., Conner, A., Parslow, R.A. and Wheatley, M. (2007) Systematic analysis of the entire second extracellular loop of the V1a vasopressin receptor: key residues, conserved throughout a G-protein-coupled receptor family, identified. J. Biol. Chem. 282: 17405-17412.

Wheatley, M., Simms, J., Hawtin, S.R., Wesley, V.J., Wootten, D., Conner, M., Lawson, Z., Conner, A.C., Baker, A., Cashmore, Y., Kendrick, R. and Parslow, R.A. (2007) Extracellular loops and ligand binding to a sub-family of Family A G-protein-coupled receptors. Biochem. Soc. Trans. 35: 717-720.

Hawtin, S.R., Simms, J., Conner, M., Lawson, Z., Parslow, R.A., Trim, J., Sheppard A. and Wheatley, M. (2006) Charged extracellular residues, conserved throughout a G-protein-coupled receptor family, are required for ligand binding, receptor activation and cell-surface expression. J. Biol. Chem. 281: 38478-38488.

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Hawtin, S.R., Wesley, V.J., Simms, J., Argent, C.H., Latif, K. and Wheatley, M. (2005) The N-terminal juxtamembrane segment of the V1a vasopressin receptor provides two independent epitopes required for high affinity agonist binding and signaling. Mol. Endocrinol. 19: 2871-2881.

Hawtin, S.R., Ha, S.N., Pettibone, D.J. and Wheatley, M. (2005) A Gly/Ala switch contributes to high affinity binding of benzoxazinone-based non-peptide oxytocin receptor antagonists. FEBS Letts. 579: 349-356.