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EDITORIAL

GPCR Theme Editorial

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This themed section of BJP includes 11 reviews on the biology of G-protein coupled receptors (GPCRs) and the drug targets that these present, 21 research papers on the pharmacology of a range of GPCRs and Commentaries on four of the papers. Areas reviewed include molecular interactions, particular in respect of hetero-dimerisation between receptors and other membrane-located proteins and other key signalling molecules including cAMP and G12/13 proteins and recently de-orphanised receptors including the Neuromedins U & S and the Free Fatty Acid receptors FFA2 & FFA3.
The research papers cover the pharmacology of a range of agents acting at GPCRs, including adrenoceptors, purinoceptors, 5HT, opioid, cannabinoid & PAR-2 receptors. A group of papers is concerned with the interesting and rapidly developing pharmacology of drugs acting at β_2-adrenoceptors.
The reach of GPCRs is illustrated by the range of physiological systems and therapeutic applications involved, including pain, cancer, cardiovascular, gastrointestinal, visual and respiratory and central nervous systems.
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G-protein coupled receptors (GPCRs) are the largest set of receptors for pharmacophores (Alexander *et al.*; 2008) and have resulted in the greatest number of drug targets yet investigated. Over a Century ago, J.N. Langley described the concept of the *receptor* as 'receptive substances, which are acted upon by chemical bodies and in certain cases by nervous stimuli. The receptive substance affects or is capable of affecting the metabolism of the . . . chief function of the cell such as contraction and secretion' (Langley, 1905). Knowledge of the chemical nature of the 'receptor' and how it affected cell function had to wait a bit longer.

Almost ninety years later Alfred G. Gilman and Martin Rodbell were awarded the 1994 Nobel Prize for Medicine or Physiology, for their ground-breaking work on G-proteins, a key link between the receptor and cell function, and which lead to the discovery of one of the major classes of receptor, the G-Protein Coupled Receptors (GPCRs) (Gilman, 1995; Rodbell, 1995). Ever since then, work on this important family of receptors has generated new insights to fundamental signalling mechanisms and continues to produce new drug targets through the translation of fundamental biology into therapeutic applications.

This themed issue of BJP focuses on the pharmacology of GPCRs.

This includes new Reviews on molecular interactions, particular in respect of hetero-dimerisation between receptors and other membrane-located proteins (Milligan, 2009; Franco; Sebastiao & Ribiero) and other key signalling molecules including cAMP (Zaccolo, 2009; Borland *et al.*, 2009) and G12/13 proteins (Juneja & Casey, 2009; Siehler, 2009). Also covered is the pharmacology of recently de-orphanised receptors including the Neuromedins U & S and the Free Fatty Acid receptors FFA2 & FFA3 (Milligan *et al.*, 2009), while Jones *et al.* (2009) review the development of strategies and therapeutic applications of prostanoid receptor antagonists.

Original research papers cover the pharmacology of a range of agents acting at GPCRs, including adrenoceptors, purinoceptors, 5HT, opioid, cannabinoid & PAR-2 receptors (for references see Table 1). There is also an interesting group of papers concerned with the currently hot area of the pharmacology of drugs acting at β_2-adrenoceptors (Ufer & Germack, 2009; Szczuka *et al.*, 2009; Salameh *et al.*, 2009; Salim *et al.*, 2009; Düringer *et al.*, 2009; Giembycz, 2009; Sayers *et al.*, 2009; Bexis & Docherty, 2009; Scola *et al.*, 2009).

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Table 1 Papers appearing in the GPCR Virtual themed issue http://www.brjpharmacol.org/VirtualIssues and in the current issue. The Reviews and Papers with Commentaries, all shown in the first two columns of papers, are included in the virtual issue. The other papers can be accessed through Wiley InterScience at http://www3.interscience.wiley.com/journal/121548564/issueyear?year=2009 or from the reference list in the html version of this Editorial. Papers in the current issue are shown in blue

Receptor type or Topic	*Reviews*	*Research Papers with Commentaries*	*Research Papers*
5-HT			Martel *et al.* (2009); Bassil *et al.* (2009)
Adenosine	Sebastião & Ribiero (2009); Zezula & Freissmuth (2008); Wilson (2008)		
α_1-AR		Nelson (2008) comments on Gray *et al.* (2008)	Methven *et al.* (2009); Muramatsu *et al.* (2009); Bexis & Docherty (2009)
α_2-AR			
Amino Acid Sensing Family	Wellendorph *et al.* (2009)		
Annexin-A1	D'Acquisto *et al.* (2008)		
β-AR	Davis *et al.* (2008); Leineweber *et al.* (2009)	Catalucci *et al.* (2008) comment on Brito-Martins *et al.* (2008); Summers (2008) comments on Ngala *et al.* (2008); Charlton (2009) comments on Düringer *et al.* (2009); Coleman (2009) comments on Szczuka *et al.* (2009); Boengler (2009) comments on Salameh *et al.* (2009)	Ufer & Germack (2009); Salim *et al.* (2009); Giembycz (2009); Sayers *et al.* (2009); Bexis & Docherty (2009); Scola *et al.* (2009)
Cannabinoid	Mackie & Ross (2008)		da Fonseca Pacheo *et al.* (2009); Mancini *et al.* (2009); Baldassano *et al.* (2009)
CXCR2 and CXCR3		Mueller (2007) comments on Jopling *et al.* (2007)	Bradley *et al.* (2009)
GPR119	Overton *et al.* (2008)		
Histamine	Leurs *et al.* (2009)		
Melatonin	Jockers *et al.* (2008)		
Neuromedin U & S	Mitchell *et al.* (2009)		
NPY	Parker & Balasubramaniam (2008)		
Opioid	Kelly *et al.* (2008)	Connor (2009) comments on Divin *et al.* (2009); Ingram and Traynor (2009) comment on Bailey *et al.* (2009)	da Fonseca Pacheo *et al.* (2009)
Par2			Kanke *et al.* (2009)
Prostanoid	Jones *et al.* (2009)		Jugus *et al.* (2009)
Purines			Talasila *et al.* (2009)
Agonism	Kelly *et al.* (2008); Hoffmann *et al.* (2008); Strange (2008); Franco (2009); Milligan (2009); Milligan *et al.* (2009)	Summers (2008) comments on Ngala *et al.* (2008); Charlton (2009) comments on Düringer *et al.* (2009); Coleman (2009) comments on Szczuka *et al.* (2009)	Mancini *et al.* (2009); Bradley *et al.* (2009); Sayers *et al.* (2009); Scola *et al.* (2009)
Dimerisation	Milligan (2008; 2009); Milligan *et al.* (2009); Franco *et al.* (2008); Jockers *et al.* (2008); Giraldo (2008); Rovira *et al.* (2009)		Methven *et al.* (2009)
Signalling	DeFea (2008); Tobin (2008); Lohse *et al.* (2008); D'Acquisto *et al.* (2008); Zaccolo (2009); Borland *et al.* (2009); Juneja & Casey (2009); Siehler (2009)	Ingram and Traynor (2009) comment on Bailey *et al.* (2009)	
Pathology or Therapeutic Applications	Parker & Balasubramaniam (2008); Overton *et al.* (2008); Davis *et al.* (2008); D'Acquisto *et al.* (2008); Wilson (2008); Leineweber *et al.* (2009); Juneja & Casey (2009); Jones *et al.* (2009)	Catalucci *et al.* (2008) comment on Brito-Martins *et al.* (2008); Nelson (2008) comments on Gray *et al.* (2008)	Bexis & Docherty (2009)
Cardiovascular	Zaccolo (2009)		Methven *et al.* (2009); Kanke *et al.* (2009); Talasila *et al.* (2009)
Cancer	Juneja & Casey (2009)		
Gastrointestinal			Jugus *et al.* (2009); Baldassano *et al.* (2009); Bassil *et al.* (2009)
Neuro	Franco (2009)		Martel *et al.* (2009); Bailey *et al.* (2009)
Lung		Charlton (2009) comments on Düringer *et al.* (2009); Coleman (2009) comments on Szczuka *et al.* (2009)	Ufer & Germack (2009); Scola *et al.* (2009); Giembycz (2009)
Receptor Theory	Chung *et al.* (2008); Giraldo (2008); Rovira *et al.* (2009); Franco (2009)	Connor (2009) comments on Divin *et al.* (2009)	

The reach of GPCRs is illustrated by the range of physiological systems and therapeutic applications involved, including pain, cancer, cardiovascular, gastrointestinal, visual and respiratory and central nervous systems (see Table 1).

Thus this themed issue, presenting a range of work across the GPCR field, illustrates the emerging depth of understanding of the molecular interactions within GPCR signalling, the range of physiological systems and therapeutic applications that are becoming engaged, and the value of translating knowledge gained at different levels of organisation into an understanding at the organismal level.

These GPCR reviews and 21 others already published (see Table 1), follow up symposia held at the Meeting of the Federation of European Pharmacological Societies (EPHAR) in Manchester, UK, in July 2008, and show the continuing interest in this field. To reflect this and provide access to our extensive portfolio of GPCR papers we have collated the current GPCR Themed Issue with other recent reviews, commentaries and original articles from BJP, in a *GPCR Virtual Issue*, available at: http://brjpharmacol.org/VirtualIssues (see Table 1).

This web resource will be further supplemented in a few months time by a further GPCR Section containing reviews commissioned by guest editor Roger J. Summers.

We hope that this will function as a continuing scientific and educational resource of value to investigators and students alike.

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