Present a Conference

on

PHOSPHODIESTERASE IN HEALTH AND DISEASES

Wednesday, 5th - Friday, 7th December 2001
Le Meridien Park Atlantic, Porto, Portugal

Conference Chairmen:
Professor Clive Page and Dr Daniela Bundschuh

Faculty includes:

V Arshavsky  Boston
D Bundschuh  Konstanz
M Conti  Stanford
D Hay  King of Prussia
M Houslay  Glasgow
J Kotera  Saitama
K Loughney  Bothell
V Manganiello  Bethesda
J O’Donnell  Memphis
K Omori  Saitama
A Robichaud  Dorval
C Schudt  Hannover
C Stief  Konstanz
WJ Thompson  London
R Williams
PHOSPHODIESTERASE IN HEALTH AND DISEASES
5th - 7th December 2001
Porto, Portugal

INTRODUCTION
It is now recognised that there are at least 11 families of Phosphodiesterase (PDE) enzymes which are intimately involved in the regulation of cell activation. Inhibitors of PDE are already available for the treatment of erectile dysfunction and inhibitors of other PDE families are in late stage development for a range of clinical conditions. This conference will provide a “state of the art” overview of the various PDE enzyme families and their regulation and review the current knowledge of the clinical development of inhibitors of PDE enzymes in a range of diseases including asthma, COPD, rheumatic disease and CNS disorders.

WEDNESDAY, 5th DECEMBER

16.00 to 18.30  Registration
19.00 to 20.00 Welcome Reception and Finger Buffet

THURSDAY, 6th DECEMBER

Chairmen: Clive Page & Daniela Bundschuh

09.30  Molecular biology of human PDE enzymes
The human 3', 5'-cyclic nucleotide phosphodiesterase gene family has grown to include 21 genes. These are grouped into 11 families on the basis of substrate specificity, regulation sensitivity to small molecule inhibitors and sequence homology. Alternative splicing at 5' and 3' ends leads to more than 40 proteins.
Speaker: Kate Loughney
IC C S, Washington, U SA

10.15  Intracellular targeting and regulation of PDE4 cAMP specific phosphodiesterases
Four genes encode around 16 PDE4 isoforms that seem poised to influence distinct regulatory processes. Specific isoforms show distinct patterns of intracellular targeting, interaction with scaffold proteins, cleavage by caspase-3 during apoptosis and phosphorylation by ERK, MAP kinase and by cAMP dependent protein kinase.
Speaker: Miles Houslay
U niversity of G lassgow, U K

11.00  Coffee and Posters

11.30  PDE knockouts-what can we learn/what do they tell us?
The use of PDE4-selective inhibitors have indicated an important function for PDE4 in the pathophysiology of asthma and other chronic inflammatory disorders of the lung. This presentation will describe a genetic approach to dissect the role of individual PDE4s in the airway and inflammatory cell functions.
Speaker: Marco Conti
Stanford U niversity Medical Center, California, U SA

12.15  PDEs and visual transduction
The unusually high catalytic efficiency of PDE6 from vertebrate photoreceptors along with the ability of PDE6 to regulate the duration of its own activation by G protein makes this enzyme uniquely suited for its function as the effector in the phototransduction cascade.
Speaker: Vadim Arshavsky
H arvard Medical School, M assachusetts, U SA

13.00  Lunch and Posters

13.45  PDE7-news and views
PDE7 is a cAMP-specific phosphodiesterase with a low Km value. Two isoforms, PDE7A and PDE7B, and their splice variants exhibit different tissue distribution. Specific expression of these genes suggest that PDE7 plays specific roles via cAMP signalling in various tissues. In this presentation, data will be presented on the fundamentals of PDE7.
Speaker: Jun Kotera
Tanabe Selyaku C o Ltd, Saitama, Japan

15.00  The growing PDE families: topics on recently discovered PDEs, PDE10A and PDE11A
PDE10A and PDE11A are a dual substrate PDE and categorised into GAF-PDE family. Expression of transcripts for these PDEs is confined to specific tissues, implying a possibility of these PDE inhibitors as a new type of drug for medication of diseases in these tissues. In this presentation, recent topics of these PDEs will be discussed.
Speaker: Kenji Omori
Tanabe Selyaku C o Ltd, Saitama, Japan

15.45  C Coffee and Posters

16.15  Potential therapeutic uses for PDE3 inhibitors
PDE3A isoforms are relatively highly expressed in platelets, cardiovascular tissues, airway smooth muscle and oocytes; PDE3Bs, in tissues important in energy homeostasis, namely fat, liver and pancreas, where they are regulated by insulin, IGF-1 and leptin. Selective inhibitors or delivery systems might thus provide novel therapies for diabetes/obesity.
Speaker: Vincent Manganiello
National H art, Lung and Blood Institute, N IH, Maryland, U SA

17.00  Is there a future for a combined PDE3/PDE4 inhibitor?
In vitro, activation of T-cells, macrophages or dendritic cells or contraction and proliferation of smooth muscle cells are more efficaciously reduced by combined inhibition of PDE4 and PDE3 as compared to inhibition of either PDE3 or PDE4. The therapeutic potential in asthma and pulmonary hypertension will be discussed.
Speaker: Christian Schudt
Byk G ulden, Konstanz, G ermany

FRIDAY, 7th DECEMBER

Chairmen: Miles Houslay & Clive Page

09.00  PDE4 inhibitors for the treatment of depression and other CNS disorders
PDE4 is involved in neuronal signal transduction mediated by beta adrenergic and NMDA receptors. The action of PDE4 inhibitors on these processes produces effects that suggest utility in the treatment of depression and cognitive dysfunction.
Speaker: James M. O’Donnell
U niversity of Tennessee Health Science C enter, U SA

09.45  PDE4 inhibitors for the treatment of asthma
The latest update on the development of new generation PDE4 inhibitors will be presented. Preclinical data on in vitro and in vivo efficacy, exemplified by roflumilast, will be summarised, and an overview on the phase II/III clinical studies will be provided.
Speaker: Daniela Bundschuh
Byk G ulden, Konstanz, G ermany
10.30 Coffee and Posters

11.00 **PDE4 inhibitors for the treatment of COPD**
Inhibition of PDE4 has become a recognised strategy for the development of potential novel therapies for pulmonary diseases. A review will be presented of the scientific rationale and the preclinical and clinical data in support of the utility of this class of compounds in COPD.

**Speaker:** Douglas WP Hay

GlaxoSmithKline, Pennsylvania, USA

11.45 **PDE4 inhibitors for the treatment of rheumatoid arthritis**
This presentation will focus mainly on pre-clinical studies designed to evaluate the efficacy of PDE4 inhibitors and other cyclic AMP-elevating agents to down-regulate both immune and inflammatory responses to protect against joint damage in arthritis.

**Speaker:** Richard Williams

Kennedy Institute of Rheumatology Division, London, UK

12.30 Lunch and Posters

Chairmen: Clive Page & Daniela Bundschuh

13.45 **Toxicology/safety of PDE4 inhibitors-new insights**
The therapeutic potential of PDE4 inhibitors has been greatly impaired by the side effects of nausea and vomiting. The results of recent studies addressing the characterisation and mechanism of PDE4 inhibitor-induced emesis will be discussed.

**Speaker:** Annette Robichaud

Merck Frosst Canada & Co, Quebec, Canada

14.30 **PDE inhibitors for the treatment of impotence**
Cavernous smooth muscle relaxation is the local key event for penile erection. A sin many other myocytes phosphodiesterases play a major role in smooth muscle tone regulation. Our studies showed the presence of 8 PDE-isoenzymes, three isoforms of PDE1 and four isoforms of PDE4 in human cavernous tissue. Of these, PDE3 and 5 had the most prominent functional role.

**Speaker:** Christian Stief

Hannover Medical School, Germany

15.15 Coffee and Posters

15.45 **PDEs and apoptosis-implications for novel tumour therapy?**
Exisulind (Aptosyn™) and analogues induce apoptosis in colon and other epithelial tumour cells, but not normal cells, via cyclic GMP mediated pathways. Inhibition of cyclic GMP phosphodiesterases (PDE5, 2 and 1) by exisulind and other selective apoptotic antineoplastic drugs (SAANDs) plays a critical role in PKG activation and induction by these new chemotherapeutic agents. PKG regulation of β-catenin and JUN kinase results in tumour cell death.

**Speaker:** W. Joseph Thompson

Cell Pathways Inc, Pennsylvania, USA

16.30 Close of Meeting

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**WILLIAM HARVEY RESEARCH CONFERENCES**

This meeting is organised by the conference arm of the William Harvey Research Foundation, an independent research centre with charitable status: a not-for-profit organisation.

**FUTURE EVENTS**

- **Beyond Heparin: Novel Therapeutic Uses for Heparin and Related Drugs**
  - 6th - 8th June 2001
  - Hotel Plaza, Nice, France

- **COX-2 Inhibitors**
  - 30th September - 2nd October 2001
  - Hotel Plaza, Nice, France

- **Angiotensin**
  - 4th-6th November 2001
  - Le Meridien Park Atlantic, Porto, Portugal

**FUTURE EVENTS**

I do not wish to attend this conference but would like to receive details of the conference ticked above.

Enter name and address overleaf

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**PORTO** is Portugal’s second largest city with a picturesque location on the banks of the Douro River. The riverfront and cluster of steep mediaeval alleyways behind is classified as a United Nations World Heritage site. From this vantage point there are compelling views across the river Douro of the 60 or so Port Wine Lodges which have formed the centre of the Port wine industry since the 17th century.

The Meridien Park Atlantic hotel has been chosen as the conference venue-10 minutes from the city centre and from the nearest beaches and 20 minutes from the International Airport which is accessible by direct flights from most major European cities.
**REGISTRATION FORM**

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**PHOSPHODIESTERASE IN HEALTH AND DISEASES**

5th-7th December 2001

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<th>Industry Fee(s) @ PTE 296,595</th>
<th>Faculty Member(s) @ PTE 140,400</th>
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**All above prices include tax**

- Bank draft enclosed (made payable to William Harvey Research Conferences)
- Please charge my credit card
- By bank transfer (please send copy of transfer request)
- Please send me an invoice

**INDUSTRY FEES:**

- PTE 296,595 including tax

**FACULTY MEMBERS:**

- PTE 140,400 including tax

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**CANCELLATIONS:**

Cancellations must be received in writing before 1st November 2001 and will be subject to an administration charge of PTE 20,000 plus tax (17%). It is regretted that no refunds can be made for cancellations received after 1st November 2001. However, if you cannot attend, a substitute may attend in your place but please let us know.

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**ACCOMMODATION:**

Rooms have been reserved at a special reduced rate at Le Meridien Park Atlantic. A booking form will be sent to you immediately upon receipt of the registration form and payment of the conference registration fee. In order to obtain the special rate reservations must be made via the Conference office. Please do not contact the hotel directly.

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**ENQUIRIES:**

All enquiries, telephone bookings and alterations to delegate information to: Dr Jenny Maclagan, William Harvey Research Conferences, St Bartholomew's & the Royal London School of Medicine & Dentistry, Charterhouse Square, London EC1M 6BQ, UK.

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**POSTER COMMUNICATIONS:**

There will be provision for posters describing the results of recent research, subject to selection by the organisers. Apply for details and pro-forma. Deadline for submission of abstracts, which must be accompanied by registration and payment, is 1st November 2001.

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**HOW TO REGISTER:**

**Facsimile bookings:**

Firm bookings may be made by faxing a completed registration form to Dr Jenny Maclagan on +44 (0) 20 7882 6084. These must be confirmed in writing within one week, accompanied by payment.

**Postal bookings:**

Please complete the registration form and send it to: Dr Jenny Maclagan, William Harvey Research Conferences, St Bartholomew's & the Royal London School of Medicine & Dentistry, Charterhouse Square, London EC1M 6BQ, UK.

**FEE:**

Portuguese Escudos 253,500 plus tax at 17% (PTE 43,095) which is payable in advance. The fee includes all scientific sessions, an abstract book, refreshments, lunches and a ticket for the Welcome Reception in the hotel on Wednesday, 5th December. A special fee of PTE 120,000 plus tax at 17% (PTE 20,400) is available on request for faculty members, physicians and researchers currently working in University Departments and Hospitals.

Payment can be made by Portuguese Escudo cheque/bank draft drawn on a Portuguese bank (all bank charges to be paid by delegate). Alternatively credit card payment can be made in pounds sterling (we will use the exchange rate in operation on the date of processing your payment). Bank transfers should be made in Portuguese Escudo tax HSBC, International Branch, PO Box 181, 27-32 Poultry, London EC2P 2BX, UK.

Account No: 37023824 Sort Code: 40-05-15 Swift Code: MIDLGB22. Please instruct your bank to include the delegates surname as the reference. A copy of your bank transfer request should be sent with a completed registration form. All bank charges to be paid by delegate. Please note that under Portuguese Custom and Excise regulations all delegates are required to pay tax on events held in Portugal.

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**DATE:**

Wednesday, 5th - Friday, 7th December 2001

**VENUE:**

Le Meridien Park Atlantic
Av da Bowsita 1466
Porto, Portugal
Tel: +351.22 607 2500
Fax: +351.22 600 3214

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