WILLIAM HARVEY
RESEARCH CONFERENCES

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	Konstanz
C Stief	Hannover
WJ Thompson	Horsham
R Williams	London

PHOSPHODIESTERASE IN HEALTH AND DISEASES

5th - 7th December 2001
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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 PDE5 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**
ICOS, Washington, USA

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**
University of Glasgow, UK

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 University Medical Center, California, USA

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**
Harvard Medical School, Massachusetts, USA

13.00 *Lunch and Posters*

Chairmen: **Clive Page & Daniela Bundschuh**

14.15 **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 PDE7B.

Speaker: **Jun Kotera**
Tanabe Seiyaku Co 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 Seiyaku Co Ltd, Saitama, Japan

15.45 *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 Heart, Lung and Blood Institute, NIH, Maryland, USA

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 Gulden, Konstanz, Germany

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**
University of Tennessee Health Science Center, USA

09.45 **PDE4 inhibitors for the treatment of asthma**

The latest update on the development of new generation PDE4 inhibitors will be presented. Pre-clinical 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 Gulden, Konstanz, Germany

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. As in many other myocytes phosophodiesterases 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*

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

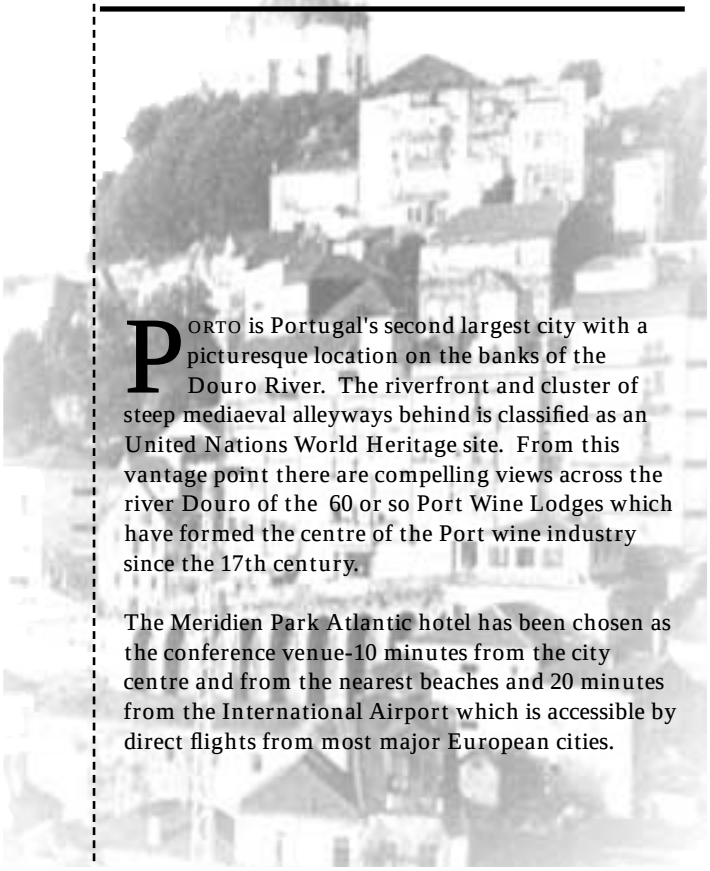
Beyond Heparin: Novel Therapeutic Uses for Heparin and Related Drugs
6th - 8th June 2001
Hotel Plaza,
Nice, France

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



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 an 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.

ADMINISTRATIVE DETAILS

DATE:
Wednesday, 5th -
Friday, 7th December 2001

VENUE:
Le Meridien Park Atlantic
Av da Boavista 1466
Porto, Portugal
Tel: +351 22 607 2500
Fax: +351 22 600 3214

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 Welecome 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 Escudos to: HSBC, International Branch, PO Box 181, 27-32 Poultry, London EC2P 2BX, UK. Account No: 37923824 Sort Code: 40-05-15 Swift Code: MIDLGB22. Please instruct your bank to incude the delegate's 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.

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-formata. Deadline for submission of abstracts, which must be accompanied by registration and payment, is 1st November 2001.

It may be necessary for reasons beyond the control of the organisers to alter the content and/or timing of the programme or the identity of the speakers.

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.

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.

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 reservatons must be made via the Conference office. Please do not contact the hotel directly.

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
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London EC1M 6BQ
Tel: +44 (0)20 7882 6181 Fax: +44 (0)20 7882 6084
E-mail: whconferences@mds.qmw.ac.uk WebSite: ww.whconferences.demon.co.uk

REGISTRATION FORM

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

Title	Initials	Surname	Position
Name of Company/Institution			
Address			County
Town			Post Code
Country		Telephone:	
E-mail:		Facsimile:	

PHOSPHODIESTERASE IN HEALTH AND DISEASES
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Industry Fee(s) @ PTE 296,595
Faculty Member(s) @ PTE 140,400
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*

Please charge my credit card
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Signature

Expiry Date

Please provide card billing address if different from company address