

ET-15 Conference Program

Thursday, October 5, 2017

8:30-10:00 **Symposium I**

ENDOTHELIN SIGNALING AND MECHANISMS OF ENDOTHELIN ACTION

Chairs: Pedro d'Orléans-Juste, Josef Zicha

8:30-9:00 Key Note Lecture

Pharmacology of Endothelin Receptors: Prospects for the Next Decade

Anthony P. Davenport

University of Cambridge, UK

9:00-9:15 **Structural Basis for Ligand Recognition by Endothelin ET_B Receptor**

Wataru Shihoya¹, Izume Tamaki¹, Nagiri Chisae¹, Akiko Okuta², Kazutoshi Tani², Tomohiro Nishizawa¹, Yoshinori Fujiyoshi², Osamu Nureki¹, Tomoko Doi³

¹Department of Biophysics and Biochemistry, Graduate School of Science, University of Tokyo, Japan, ²Cellular and Structural Physiology Institute, Nagoya University, Japan, ³Department of Biophysics, Graduate School of Science, Kyoto University, Japan

9:15-9:30 **ET-1 and NO Production Are Distinct in the Endothelium and Renal Epithelium**

Kelly A. Hyndman, Jennifer S. Pollock

University of Alabama at Birmingham, Department of Medicine, Division of Nephrology, Section of Cardio-Renal Physiology and Medicine, Birmingham, USA

9:30-9:45 **Evidence of an Interaction Between the Collecting Duct Prorenin Receptor and the Endothelin System**

Nirupama Ramkumar, Deborah Stuart, Nikita Abraham, Donald E. Kohan

Division of Nephrology, University of Utah Health Sciences Center, Salt Lake City, USA

9:45-10:00 **Necroptosis of Brain Microvascular Endothelial Cells (BMVECs) Can Be Modulated by Endothelin-1**

Yasir Abdul¹, Rebecca Ward², Adviye Ergul¹

¹Department of Physiology Augusta University, Augusta, USA, Charlie Norwood Veterans Administration Medical Center, Augusta, USA, ²Department of Neuroscience and Regenerative Medicine, Augusta University, Augusta, USA

10:30-12:00 **Symposium II**

PHARMACOLOGY, NEW DRUGS AND DRUG INTERACTIONS

Chairs: Janet Maguire, Anil Gulati

10:30-11:00 Key Note Lecture

Pharmacological Interventions Targeting the Endothelin Pathway: the Status Quo and Future Perspective

Noriaki Emoto

Kobe University, Japan

11:00-11:15 **ET_A Receptors Blockade, by Activating ET_B Receptors, Increases Vascular Permeability and Induces Exaggerated Fluid Retention**

Magali Vercauteren, Frederic Trenz, Anne Pasquali, Christophe Cattaneo, Daniel S. Strasser, Patrick Hess, Marc Iglarz, Martine Clozel

Idorsia Pharmaceuticals Ltd., Drug Discovery Department, Allschwil, Switzerland

11:15-11:30 **Alterations in Endothelin Receptors Following Hemorrhage and Resuscitation by Centhaquin**

Anil Gulati¹, Seema Briyal¹, Ravina Gandhakwala¹, Mahnoor Khan¹, Manish S. Lavhale²

¹Department of Pharmaceutical Sciences, Midwestern University Chicago College of Pharmacy, Downers Grove, IL, USA, ²Pharmazz Research Center, Pharmazz India Private Limited, Greater Noida, UP, India

11:30-11:45 **Unmasking the Functionality of Super-Sensitive ET_B Receptors in Non-Anesthetized Mice**

Louisane Desbiens, Hanène Touil, Julie Reghem, Pedro D'Orléans-Juste

Department of Pharmacology and Physiology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, PQ, Canada

11:45-12:00 **Pharmacology of ACT-132577, a Dual Endothelin Receptor Antagonist for the Treatment of Resistant Hypertension**

Frédéric Trensz, Céline Bortolamiol, Daniel Wanner, Hakim Hadana, Hervé Farine, Daniel S. Strasser, Patrick Hess, Marc Iglarz, Martine Clozel

Idorsia Pharmaceuticals Ltd., Drug Discovery Department, Allschwil, Switzerland

13:00-14:00 **Moderated Poster Session I**

(Moderators: *Matthias Barton, Antony P. Davenport, Pedro D'Orléans-Juste, Pavel Jansa*)

14:00-15:15 **Symposium III**

PHYSIOLOGY AND PATHOPHYSIOLOGY OF CARDIOVASCULAR FUNCTION

Chairs: Noriaki Emoto, Pavel Jansa

14:00-14:30 Key Note Lecture

Mas and ET_BR – a New Partnership in Vascular Pathobiology

Katie Y. Hood, Augusto C. Montezano

BHF Glasgow Cardiovascular Research Centre, University of Glasgow, UK

14:30-14:45 **Molecular Imaging of Endothelin A Receptor Expression in Atherosclerosis**

Miriam Stöltzing¹, Moritz Wildgruber¹, Christiane Geyer¹, Walter Heindel¹, Giovanni Panucci², Guiseppe Torsello², Carsten Höltke¹

¹Translational Research Imaging Center, Department of Clinical Radiology, University Hospital Muenster, Germany,

²Department of Vascular and Endovascular Surgery, University Hospital Muenster, Germany

14:45-15:00 **Cardiac Metabolic Deregulation Induced by The Tyrosine Kinase Receptor Inhibitor Sunitinib Is Rescued by Endothelin Receptor Antagonism**

Joëvin Sourdon¹, Franck Lager², Thomas Viel¹, Daniel Balvay¹, Gilles Renault², Pierre-Louis Tharaux¹, Dhaun Neeraj³, Bertrand Tavitian^{1,4}

¹Paris Centre de Recherche Cardiovasculaire (PARCC), INSERM U970, Paris, France; Université Paris Descartes - Sorbonne Paris Cité, Paris, France, ²Institut Cochin, Université Paris Descartes, INSERM U1016, Paris, France,

³University/British Heart Foundation Centre of Research Excellence, University of Edinburgh; and The Queen's Medical Research Institute, Edinburgh; and Department of Renal Medicine, Royal Infirmary of Edinburgh, UK,

⁴Service de Radiologie, Hôpital Européen Georges Pompidou, Assistance Publique-Hôpitaux de Paris (AP-HP), Paris, France

15:00-15:15 **Attenuated Endothelin Type B Receptor-Mediated Dilation Contributes to Endothelial Dysfunction in the Microvasculature of Women Who Have Had Preeclampsia**

Anna E. Stanhewicz, Lacy M. Alexander

Department of Kinesiology, The Pennsylvania State University, University Park, PA, USA

16:00-17:30 **Symposium IV**

PULMONARY FUNCTION AND PULMONARY HYPERTENSION

Chairs: Martine Clozel, Rita Tostes

16:00-16:30 Key Note Lecture

Advances in Pathophysiology and Treatment of Chronic Pulmonary Hypertension

Pavel Jansa

Charles University, Prague, Czech Republic

16:30-16:45 **Ac-PGP Induces Endothelin-1 Release Both *In Vitro* and *In Vivo***

Xin Xu, Jin-dong Li, James Wells, Liliana Viera, Carmel M. McNicholas-Bevensee, Swati Gulati, Greg Payne, J. Edwin Blalock, Amit Gaggar

Division of Pulmonary, Allergy and Critical Care Medicine, Program in Protease and Matrix Biology, Department of Medicine, Department of Pediatrics, University of Alabama at Birmingham, Birmingham, AL, USA

16:45-17:00 **Endothelin-1 from Pulmonary Circulation Correlates With Pulmonary Vascular Resistance in Adult Patients With Secundum Type Atrial Septal Defect**

Dyah W. Anggrahini, Lucia K. Dinarti, Anggoro B. Hartopo, Abdus S. Wahab, Budi Y. Setianto

Department of Cardiology and Vascular Medicine, School of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia

17:00-17:15 **Ece1 Ablation Downregulates Pathways Important for Lung Tissue Repair**

Jasmin Kristianto, Jia Shuang, Mary Kaldunski, Martin Hessner, Robert D. Blank

Medical College of Wisconsin, Milwaukee, WI, USA

17:15-17:30 **Glucagon-Like Peptide-1 Receptor Agonist Liraglutide Inhibits Hypoxia-Induced Pulmonary Hypertension in Mice Partly via Recovery of ET_B Receptor Expression**

Junya Honda, Taizo Kimura, Satoshi Sakai, Hidekazu Maruyama, Satoshi Homma, Takashi Miyauchi, Kazutaka Aonuma

Department of Cardiology, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

18:30-21:30 **YOUNG INVESTIGATOR EVENT**

Moderators: Neeraj Dhaun, Věra Čertíková Chábová

Cell-free Synthesis, Folding and Ligand Profiling of the Human Endothelin B Receptor in Defined Nanoparticle Membranes

Fang Dong, J.W. Goethe University, Frankfurt/Main, Germany

On-Surface Labeling of Endothelin Receptors by Peptide-Mediated Fluorophore Transfer

Philipp Wolf, Universität Leipzig, Leipzig, Germany

The Effect of ET Antagonists on Angiogenesis Induced by LPS in Chick Embryo

Shiyao Zhang, Jinan University, Guangzhou, China

The Effect of N-Acetylcysteine on LPS-Induced Angiogenesis: Potential Role of the Endothelin System

Shan Zhong, Jinan University, Guangzhou, China

Endothelin-1 Mediated Neuroprotection Does Not Act Through BDNF Signaling Cascade in Diabetic Conditions of HT22 Neurons

Rebecca Ward, Augusta University, Augusta, GA, USA

Polymorphisms of *CHST3* and *CHST13* in Patients With Pulmonary Arterial Hypertension for Predicting Bosentan-Induced Liver Toxicity

Kenosuke Yorifuji, Kobe Pharmaceutical University, Kobe, Japan

Endothelin-1 (ET-1) Induces NLRP3 Activity via ETA-ROS-NF- κ B Activation and Impairs the Function of Mice Corpora Cavernosa

Rafael Sobrano Fais, University of Sao Paulo, Brazil

The Role of Endothelin in the Pathophysiology of Migraine - A Systematic Review

Afrim Iljazi, University of Copenhagen, Denmark

Role of Endothelin Receptors in the Development of Seizures in the Immature Brain

Kateřina Vondřáková, Institute of Physiology, Czech Academy of Sciences, Prague, Czech Republic

Endothelin-1 Plays an Important Role in the Patients With Single-Ventricle Physiology

Masaya Aoki, University of Toyama, Japan

Friday, October 6, 2017

8:30-10:00 **Symposium V**

METABOLISM, DIABETES, METABOLIC SYNDROME, AND OBESITY

Chairs: John Pernow, Carmine Cardillo

8:30-8:55 Invited Lecture

Bitter Taste of Diabetic Complications: Endothelin

Adviye Ergul

Augusta University, USA

8:55-9:20 Invited Lecture

Novel Aspects on Metabolism and Hypertension – The Nitrate-Nitrite-NO Pathway

Eddie Weitzberg

Karolinska Institutet, Stockholm, Sweden

9:20-9:35 The Roles of Endothelin Receptors in Pressure Natriuresis in Early Experimental Type 1 Diabetes Mellitus

Geoff J. Culshaw, Matthew A. Bailey, David Binnie, Neeraj Dhaun, Patrick W.F. Hadoke, David J. Webb

University of Edinburgh/British Heart Foundation Centre for Cardiovascular Science, Queen's Medical Research Institute, Edinburgh, UK

9:35-9:50 Endothelial Cell-Derived Endothelin-1 Contributes to Accumulation of Myocardial Triglyceride and Diastolic Dysfunction in Diabetes Heart

Bambang Widyantoro¹, Nani Hersunarti¹, Anna U. Rahajoe¹, Kazuhiko Nakayama², Noriaki Emoto², Amiliana M. Soesanto¹

¹Department of Cardiology and Vascular Medicine, Universitas Indonesia – National Cardiovascular Center Harapan Kita, Jakarta, Indonesia, ²Division of Cardiovascular Medicine, Kobe University Graduate School of Medicine, Kobe, Japan

9:50-10:05 Transcriptional Regulation of Glucose-Induced Endothelin1 Expression in the Endothelial Cells

Subrata Chakrabarti, Shali Chen, Biao Feng, Anu Thomas, Saumik Biswas

Pathology and Laboratory Medicine, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada

10:30-12:05 **Symposium VI**

PHYSIOLOGY AND PATHOPHYSIOLOGY OF RENAL FUNCTION

Chairs: Neeraj Dhaun, Ivana Vaněčková

10:30-10:55 Invited Lecture

Endothelin Receptor Antagonism and Kidney Disease

Donald E. Kohan

University of Utah, Salt Lake City, USA

10:55-11:20 Invited Lecture

Endothelin and the Kidney Clock

David M. Pollock

University of Alabama, Birmingham, USA

11:20-11:35 **Renin Synthesis and Secretion *In Vivo***

Thomas Neder, Armin Kurtz, Charlotte Wagner

Institute of Physiology, University of Regensburg, Germany

11:35-11:50 **Endothelin Receptor A-Mediated Spontaneous Ca²⁺ Oscillations in Renal Vasculature Are Controlling Renal Vessel Vasomotion**

Andrey Sorokin¹, Oleg Palygin², Bradley Miller¹, Alexander Staruschenko²

¹Department of Medicine, ²Department of Physiology, Medical College of Wisconsin, Milwaukee, USA

11:50-12:05 **Addition of Diuretic to RAS and ET_A Blockade Is Renoprotective in a Model of Chronic Kidney Disease in Ren-2 Transgenic Rats**

Ivana Vaněčková¹, Zdenka Vernerová², Silvie Hojná¹, Lenka Řezáčová¹, Josef Zicha¹

¹Institute of Physiology, Czech Academy of Sciences, Prague, Czech Republic, ²Department of Pathology, Third Medical Faculty, Charles University, Prague, Czech Republic

13:00-14:00 **Moderated Poster Session II**

(Moderators: *Ariela Benigni, Carmine Cardillo, Marilena Loizidou, Bambang Widiantoro*)

14:00-15:30 **Symposium VII**

SEX DIFFERENCES IN PHYSIOLOGY AND DISEASE

Chairs: Jennifer S. Pollock, Hiromi Yanagisawa

14:00-14:30 Key Note Lecture

The Interplay Between Endothelin-1 and Testosterone in the Activation of the Immune System

Rita C. Tostes

University of Sao Paulo, Ribeirao Preto Medical School, Ribeirao Preto, SP Brazil

14:30-14:45 **Exaggerated Placental Ischemia-Induced Hypertension in Endothelin Receptor Type B (ET_B)-Deficient Pregnant Rats Is Independent of Increased sFlt-1 or ROS Levels**

Frank T. Spradley

Department of Surgery, Cardiovascular-Renal Research Center, University of Mississippi Medical Center, Jackson, USA

14:45-15:00 **Endothelin-1 in Vascular Hypertension: a Study in Obese Postmenopause Women**

Kathryn Gradin¹, John Pernow²

¹Department of Neuroscience and Pharmacology, Section for Pharmacology, University of Gothenburg, Sahlgrenska Academy, Gothenburg, Sweden, ²Division of Cardiology, Department of Medicine, Karolinska Institute, Karolinska Hospital, Stockholm, Sweden

15:00-15:15 Endothelin-1 Responsible for Vimentin 3 Production in Sperms: a New Marker for Fertility Proof

Melanie von Brandenstein¹, Ali Tok¹, Tobias Kohl¹, Yasmin Ural¹, Manuel Montesions-Rongen³, Jochen Fries², Axel Heidenreich¹

¹Department of Urology, ²Department of Pathology, ³Department of Neuropathology, University Hospital of Cologne, Germany

15:45-17:05 Symposium VIII**NEUROPHYSIOLOGY, NEUROBIOLOGY, CNS DISORDERS**

Chairs: Adviye Ergul, Radko Komers

15:45-16:15 Key Note Lecture**ET_B Receptors Agonist, IRL-1620, for the Treatment of CNS Disorders**

Anil Gulati

Midwestern University, Downers Grove, USA

16:15-16:35 Reciprocal Pain Sensitization From Low Doses of Endothelin-1 and Nerve Growth Factor

Alla Khodorova, Gary R. Strichartz

Pain Research Center and Women's Pain Group, Brigham & Women's Hospital, Harvard Medical School, Boston, USA

16:35-17:05 The British Pharmacological Society Distinguished Lecture**A Genetic Variant Associated with Five Vascular Diseases is a Distal Regulator of Endothelin-1 Expression**

Rajat M. Gupta

Harvard Medical School, Boston, USA

Saturday, October 7, 2017**8.30-10.00 Symposium IX****IMMUNE SYSTEM AND INFLAMMATION**

Chairs: Ariela Benigni, Josef Zicha

8.30-9:00 Key Note Lecture**Immune Mechanisms in Hypertension**

Ernesto L. Schiffrin

McGill University, Montréal, Canada

9:00-9:15 High Affinity Monoclonal Antibodies Targeting the Human GPCR Endothelin B Receptor

Amaury Herbet¹, Safa Azar², Narciso Costa¹, Aloïse Mabondzo¹, Dina Berrada¹, Jean Philippe Hugnot², Didier Boquet¹

¹Service de Pharmacologie et d'Immunoanalyse (SPI), Institut des Sciences du Vivant Frédéric Joliot, CEA, Université Paris Saclay, Gif-sur-Yvette, France, ²Institut des Neurosciences de Montpellier, INSERM U1051, Université Montpellier, Montpellier, France

9:15-9:35 Induction of Human Endothelin-1 Overexpression for 3 Months Causes Blood Pressure Rise as well as Renal and Vascular Injury

Pierre Paradis¹, Suellen C. Coelho¹, Olga Berillo¹, Sofiane Ouerd¹, Júlio C. Fraulob-Aquino¹, Antoine Caillon¹, Tlili Barhoumi¹, Stefan Offermanns^{3,4}, Ernesto L. Schiffrin^{1,2}

¹Vascular and Hypertension Research Unit, Lady Davis Institute for Medical Research and ²Department of Medicine, Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Montréal, Canada, ³Department of Pharmacology, Max-Planck-Institute for Heart and Lung Research, Bad Nauheim, Germany, ⁴Medical Faculty, J.W. Goethe University Frankfurt, Frankfurt, Germany

10.00-11:30 **Symposium X****CANCER AND METASTASIS**

Chairs: Laura Rosanò, Marilena Loizidou

10.00-10:30 Key Note Lecture

Targeting ET-1 Receptor/ β -Arrestin1 Signaling Circuit in Ovarian Cancer Treatment*Anna Bagnato*

Regina Elena National Cancer Institute, Rome, Italy

10:30-10:45 **The Non-Cell Autonomous Role of Edn3/Ednr β Signaling During Melanoma Lung Metastasis Formation***Juliano Freitas, Martina Cavallini, Jesus Lopez, Joseph Palmer, Lidia Kos*

Department of Biological Sciences, Florida International University, Miami, FL, USA

10:45-11:00 **ET-1 Activation of Colon Fibroblasts: Driving Cancer Progression Via Stromal Effects***Michail Chatzikonstantinou¹, Mohamed Elsharif¹, Samer-ul Haque¹, Patricia Redondo¹, Naomi Guppy², Manuel Rodriguez-Justo³, Michael Dashwood¹, Hazel Welch¹, Marilena Loizidou¹*¹UCL Division of Surgery and Interventional Science, ²UCL-Advanced Diagnostics, ³UCL Research Department of Pathology, University College London, London, UK11:00-11:15 **ET-1 Receptor Blockade in Engineered 3D High-Grade Serous Ovarian Cancer Tumouroids***Judith Pape¹, Laura Rosanò², Umber Cheema¹, Mark Emberton³, Marilena Loizidou³, Anna Bagnato²*¹UCL Institute of Orthopaedics and Musculoskeletal Sciences, UCL Division of Surgery and Interventional Science, Stanmore Campus, ²Unit of Preclinical Models and New Therapeutic Agents, Regina Elena National Cancer Institute, Rome, Italy, ³UCL Division of Surgery and Interventional Science, Royal Free Campus, London, UK11:15-11:30 **Knockout of the ET β Receptor Inhibits the Activation of Wnt***Jochen Fries², Monika Schlosser¹, Ali Tok¹, Tobias Kohl¹, Axel Heidenreich¹, Melanie von Brandenstein¹*¹Department of Urology, University Hospital of Cologne, Germany, ²Department of Pathology, University Hospital of Cologne, Germany12.30-14.00 **Symposium XI****ROLE OF ENDOTHELIN IN SELECTED DISEASES**

Chairs: David M. Pollock, Pierre-Louis Tharaux

12.30-13.00 Key Note Lecture

Balloon Angioplasty and Endothelin*Matthias Barton*

University of Zürich, Switzerland

13:00-13:15 **Endothelin-1 Exaggerates Type-1 Diabetes-Accelerated Atherosclerosis Through NADPH Oxidase 1***Pierre Paradis¹, Sofiane Ouerd¹, Nouredine Idris-Khodja¹, Michelle Trindade¹, Suellen C. Coelho¹, Karin A. Jandeleit-Dahm³, Ernesto L. Schiffrin^{1,2}*¹Hypertension and Vascular Research Unit, Lady Davis Institute for Medical Research and ²Department of Medicine, Sir Mortimer B. Davis-Jewish General Hospital, McGill University, Montréal, QC, Canada; ³Baker IDI Heart & Diabetes Research Institute, Melbourne, Victoria, Australia13:15-13:30 **Renal Iron Trafficking – Potential Role for Endothelin System***Malgorzata Kasztan, Kelly A. Hyndman, David M. Pollock*

University of Alabama at Birmingham, Department of Medicine, Division of Nephrology, Cardio-Renal Physiology and Medicine, Birmingham, AL, USA

13:30-13:45 **The Level of Plasma Soluble Endothelin Receptor Type A Was Elevated in Childhood Primary Nephrotic Syndrome**

Fang Yang, Ding Liu, Nian Wei, Zhiqiang Guo, Shuting Peng, Weiyi He, Sui Zhang

Department of Pediatrics, First Affiliated Hospital of Jinan University, Guangzhou, China

13:45-14:00 **ET-1, ADMA and SDMA in Preeclampsia, Systemic Lupus Erythematosus and Antiphospholipid Syndrome**

Karoline Mayer-Pickel, Vassiliki Kolovetsiou-Kreiner, Christina Stern, Uwe Lang, Mila Cervar-Zivkovic

Department of Obstetrics and Gynaecology, Medical University of Graz, Austria

14.30-16.00 **Symposium XII**

ENDOTHELIN RECEPTOR ANTAGONISTS IN CLINICAL TRIALS

Chairs: David J. Webb, Věra Čertíková Chábová

14.30-14.55 Invited Lecture

From Endothelin Research to Drugs

Martine Clozel

Indorsia Pharmaceutical Ltd., Allschwil, Switzerland

14.55-15.20 Invited Lecture

Dual Angiotensin II (Ang II) AT1 and Endothelin (ET) Type A Receptor Inhibition With Sparsentan in Primary Focal Segmental Glomerulosclerosis (FSGS): DUET Trial

Radko Komers

Retrophin, San Diego, USA

15.20-15:45 Invited Lecture

Endothelin Antagonists in the Treatment of Diabetic Nephropathy – An Update

Vladimír Tesář

Charles University, Prague, Czech Republic

16:00-16:30 **Concluding Remarks**

Masashi Yanagisawa

University of Tsukuba, Japan