

Meeting Report

**“Signal transduction and beyond:
from targets to new treatments
in cardiac disease”**



Annual Meeting 2011



of the
**Working Group on
Myocardial Function**

and the
**Working Group on
Cell Biology**



Villa Monastero, ITALY

April 14 to 17, 2011

The organisation of this meeting is supported by an unrestricted grant offered by Diemag-C Ltd.

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Meeting Report

We have organized our annual working group meeting for the second time in the Villa Monastero in Varenna Italy.

A total number of 88 participants were present (most of them throughout the meeting).

The nucleus of myocardial function hold their nucleus meeting on April 14 in the Villa Monastero starting at 11.00 till 15.00 pm and in the evening (20.00 to 22.00) of April 16 2011 in the Hotel Villa Cipressi. The minutes of the whole nucleus meeting are provided separately.

Registration was open from 15.00 on April 14 2011 and the program started timely 16.25 with the opening remarks from Denise Hilfiker-Kleiner (Chair of WG on myocardial function).

After the first session we all met for a wonderful welcome dinner in the Hotel Villa Cipressi. During this dinner Prof. Gerd Heusch gave a brief overview on the history of the working group. He also informed us that Prof. Otto Hess, one of the founding members, had died shortly before and that Prof. Helmut Drexler, also a member of the early days had died in 2009. Prof. Gerd Heusch acknowledged the great personalities of Prof. Hess and Prof. Drexler, the impact of their research for cardiovascular science and their contribution to the working group.

On April 15 the meeting started timely with the 2nd session, which was the start to a wonderful interacting day of scientific discussions, a feature that was maintained throughout the meeting. In the afternoon highly interactive poster sessions provided an excellent platform for all scientists to present and discuss their ongoing projects.

In between everybody enjoyed the special atmosphere of the venue including the nice coffee brakes in the botanical garden surrounding the villa and the excellent Italian food served for lunch and dinner in the Hotel Villa Cipressi.

April 16 the meeting continued with the “how to” session. Both, the easy understandable introduction in ECG monitoring in mice and the development and use of AAV were greatly appreciated. It was followed by the 2nd poster session, which was again very interactive. The special Lecture provided by PD Dr. med Heiko von der Leyen (Hannover, G) “Design and Realization of Clinical Trials - from bench to bedside” was very informative and specifically emphasized the importance of reproducibility of results between different labs before entering clinical trial steps.

After lunch the afternoon was free. About 25 participants went on a hiking trip led by Prof. Jean-Luc Balligand leading to the picturesque Castello Di Vezio above Varenna and further up the mountain behind it. It was great and photos of the trip (and the entire meeting) are provided on our webpage.

April 17 was the last day of the meeting with again wonderful speakers (guest speakers from the US and from other ESC working groups, i.e. Cardiac Cellular Electrophysiology) and great discussions.

At the end of the meeting we felt that we all had learned a lot, made new friends and found interesting collaborations. Apart from the excellent science and the great location, the format of the meeting being a bit less packed and leaving time for interactions proved to be a success.

For information the program of the meeting is attached. In addition, contact information of all participants is also attached to this document.

We would also thank ESC and the Basic Science Council for the financial and organizational support, especially to Corine Gomez and Céline Serio, which enabled us again to offer housing, meals and registration to all participants at a very low fee of only 100€.

In addition, we like to thank Meike Jungesblut und Olga Sorokin for their great work running the meeting on site secretary.

Thanks to everyone and best wishes

Denise Hilfiker-Kleiner (Chair of the Working Group on Myocardial function)

Scientific Program

Villa Monastero, ITALY

April 14 to 17, 2011

*“Signal transduction and beyond:
from targets to new treatments in cardiac disease”*

Thursday 14th April

11.00 – 16.00 Nucleus Meetings: Part 1

16.25
remarks Denise Hilfiker-Kleiner (Hannover, G): Welcome and opening

Session I: News and views on microRNA Chair: Johann Bauersachs (Hannover, G)/ Gianluigi Condorelli (Milan, I)

16.30 – 17.00 Thomas Thum (Hannover, G) mi-RNA-based therapeutics:
where do we go?

17.00 – 17.30 Kai C. Wollert (Hannover, G) GDF-15 - acting through a novel
anti-inflammatory mechanism - promotes survival after
myocardial infarction

17.30 – 18.10 2 Oral Presentations:
Leonardo Elia (San Diego, USA): Role of microRNA-143 and -
145 in cardiovascular diseases
Paula da Costa Martins (Maastricht, NL): Regulation of
pathologic cardiac remodeling by miR-199 family members

19.30 Dinner (Villa Cipressi)

Friday 15th April

Session II: Genetic/Epigenetic effects in cardiac pathophysiology

Chair: Angela Clerk (Reading, GB)/ Stephane Heymans (Maastricht, NL)

- 09.00 – 09.30 Johannes Backs (Heidelberg, G): Epigenetic effects in cardiac pathophysiology
- 09.30 – 10.00 Stuart Cook (London, GB): Genetic background in experimental cardiovascular models
- 10:00 – 10:40 2 Oral Presentations
- Melanie Hoch (Hannover, G): Interactions of endogenous EPO/EPOR and CCR2 signaling systems in the cardiac niche regulate the endothelial differentiation of cardiac progenitor cells
- Claudia Noack (Hamburg, G): Krueppel-like factor 15 controls cardiac progenitor cell fate during aging and stress induced remodeling in the adult heart via inhibition of β -catenin
- 10.40 – 11.00 Coffee break (Villa Monastero)

Session III: Mitochondrial biogenesis and dynamics

Chair: Rainer Schulz (Essen, G)/ Fabio Di Lisa (Padua, I)

- 11.00 – 11.30 Stephane Heymans (Maastricht, NL): Role of inflammation-microRNAs in heart failure
- 11.30 – 12.00 Luca Scorrano (Padua, I): Mitochondria-SR interaction
- 12.00 – 12.40 2 Oral Abstract presentations
- Mélanie Paillard (Lyon, F): Sphingosine-1-Phosphate Produced by Sphingosine Kinase 2 in the Mitochondria Interacts with Prohibitin 2 to Regulate Complex IV Assembly and Respiration
- Marisol Ruiz-Meana (Barcelona, E): Preconditioning of isolated mitochondria
- 12.40 – 13.40 Lunch (Villa Cipressi)

Session IV: Moderated Poster session (I)
guided by Charles Steenbergen (Baltimore, USA) and Ralph Knoell (London, GB)

13.40 – 17.20 Poster session (see page 20-21)

17.20 – 17.40 Coffee break (Villa Monastero)

Session V: Mitochondria and cardioprotection
Chair: Michel Ovize (Lyon, F)/ Gerd Heusch (Essen, G)

17.40 – 18.10 Derek Hausenloy (London, UK): Modulation of mitochondrial morphology and cardioprotection

18.10 – 18.40 Sandrine Lecour (Cape Town, SA): The novel pro-survival SAFE pathway – importance of mitochondria?

18.40 – 19.20 2 Oral Abstract Presentations
Michael Kohlhaas (Homburg, G): STAT3 preserves dynamic control of mitochondrial NAD(P)H redox state to prevent ROS-production after chronic β -adrenergic stimulation in vivo
Anna Fusco (Neapel, I): MITOCHONDRIAL LOCALIZATION A NOVEL ROLE FOR GRK2 IN THE REGULATION OF OXIDATIVE METABOLISM

19.30 Dinner (Villa Cipressi)

Saturday 16th April

Session VI: “How to” sessions

Chair: Leon J. de Windt (Maastricht, NL)/ Guido Tarone (Turin, I)

08:45 – 09.20 Thorben König (Hannover, G): ECG Telemetry

09.20 – 09.55 Oliver Müller (Heidelberg, G): AAV-vectors for
cardiac gene transfer

09.55 – 10.10 Coffee break (Villa Monastero)

Session VII: Moderated Poster session (II)

guided by Barbara Casadei (Oxford, GB)/ Guido Iaccarino (Naples, I)

10.10 – 12.10 Poster session (see page 22-23)

Session VIII:

Chair: Peter Ferdinandy (Szeged, H) / Adelino Leite-Moreira (Porto, P)

12.10 – 12.50 Special Lecture: Heiko von der Leyen (Hannover, G): Design
and Realization of Clinical Trials - from bench to bedside

12.50 –13.05 Experimetria Ltd. - company presentation

13.00 –14.00 Lunch (Villa Cipressi)

Free afternoon (hiking with Jean-Luc and Denise)

Sunday 17th April

Session IX: Novel aspects of basic and applied NO/cyclic GMP biology in cardiovascular disease

Chair: Denise Hilfiker-Kleiner (Hannover, G)/ Jean-Luc Balligand (Brussels, B)

- 09.00 – 09.30 Barbara Casadei (Oxford, GB): Altered EC coupling from uncoupled cardiomyocyte NOS
- 09.30 – 10.00 Ulrich Martin (Hannover, G): iPS cells: just another stem cell or groundbreaking development for future cellular therapies?
- 10.00 – 10.30 Elizabeth Murphy (Baltimore, USA): Identification of new nitrosylated proteins in the cardiac proteome: potential role in pathology
- 10.30 – 10.50 Coffee Break (Villa Monastero)

Session X: Special Lecture

Chair: Adelino Leite-Moreira (Porto, P)/ Ralph Knoell (London, GB)

- 10.50 – 11.40 David Eisner (Manchester, GB): A fresh look at EC coupling mechanisms affecting inotropism and relaxation in HF
- 11.40 Michel Ovize (Lyon, F): Closing remarks and farewell
- 13.00 – 17.00 Nucleus Meetings: Part 2
- (14.30 – 14.50 Incl. Coffee break, Villa Monastero)

Poster Presentations:

Friday 15th April - 13.40 – 17.20

**Session IV: Moderated Poster session (I)
guided by Charles Steenbergen (Baltimore, USA) and Ralph Knoell (London, GB)**

1. Anna Pia Plazzo: *Functional role of the specific neuro-cardiac interaction on cardiomyocyte β -AR activation*
2. Tania Zaglia: *Resting cardiac sympathetic activity regulates cardiomyocyte size by suppressing MuRF-1 expression*
3. Tamas Csont: *Biglycan: a potential cardioprotective therapy?*
4. Nerea Hermida-Blanco: *Statins prevent LV remodeling through anti-fibrotic effects rather than direct effects on cardiomyocytes in a mouse model of metabolic syndrome*
5. Oktay Tutarel: *ADMA IS A MORE SENSITIVE BIOMARKER FOR HEART FAILURE IN ADULTS WITH CONGENITAL HEART DISEASE THAN NT-proBNP*
6. Péter Bencsik: *The role of nitrosative stress and matrix metalloproteinases in ischemic heart disease patients*
7. Michela Nosedà: *Clonal analysis of adult mouse cardiac progenitor cells*
8. Martinus Oerlemans: *Inhibition of RIP1-mediated necrosis ameliorates myocardial ischemia-reperfusion injury and attenuates adverse remodeling*
9. Jean-Luc Balligand: *Inhibition of the endogenous Wnt/beta-catenin signalling pathway mediates differentiation of cardiac resident progenitor cells into cardiomyocytes*
10. Alexander Nickel: *Mitochondrial transhydrogenase is a key regulator of antioxidative capacity in cardiac myocytes*
11. Roberto Gaetani: *Cardiac tissue engineering by using tissue printing technology and human Cardiac progenitor Cells*
12. Noppe Gauthier-Thibaut: *A-769662 demonstrates anti-fibrotic properties: a new potential role for AMP-activated protein kinase*
13. Ann Friart: *Paracrine NO potentiates the differentiation of adult cardiac resident stem cells in co-culture with cardiac myocytes*
14. Julien Auquier: *The AMP-activated protein kinase improves insulin-sensitivity in the heart by multiple molecular mechanisms*
15. Mechthild Westhoff-Bleck: *Gender related differences of the systemic right ventricle after atrial switch operation*

16. Henning Kempf: *Analysis and control of MAPK pathway activity to improve cardiomyogenic differentiation of pluripotent human stem cells with small molecules*
17. Aurélie Timmermans: *The new AMPK activator A-769662 does not stimulate glucose uptake alone but potentiates effects of others AMPK activators in adult cardiomyocytes*
18. Krijn Vrijzen: *Cardiomyocyte Progenitor Cell Derived Exosomes Stimulate Migration Of Endothelial Cells*
19. Elisabetta Borchi: *Monoamine oxidase activity and oxidative stress markers in left and right ventricles from non failing and failing human hearts*
20. Mathias Hohl: *Nuclear export of HDAC4 mediates histone demethylation at H3K9 in the promoter region of ANF in response to elevated cardiac preload*
21. Magali Balteau: *Caveolar compartmentalisation of signaling elements required for hyperglycemia-induced ROS production through NADPH oxidase in cardiomyocytes*
22. Magali Balteau: *NADPH oxidase activation by hyperglycemia in cardiomyocytes is independent of glucose metabolism but requires the sodium/glucose cotransporter, SGLT-1*
23. Mauro Sbroglio: *Melusin triggers cardiomyocyte hypertrophy and survival activating MEK-ERK1/2 pathway through Focal Adhesion Kinase and the MAPK scaffold protein IQGAP1*
24. Ines Falcão-Pires: *Diabetes mellitus exacerbates diastolic dysfunction in aortic stenosis patients: importance of myocardial fibrosis, advanced glycation endproducts and resting tension*
25. Byambajav Buyandelger Buyandelger: *MLP, MLP-interacting proteins and heart failure*
26. Evasion Pasini: *mTOR EVALUATION AS MARKER OF IMPAIRED INTRACELLULAR SIGNALING TO QUANTIFY CARDIOVASCULAR RISK FACTORS IN THE METABOLIC SYNDROME*

Saturday 16th April - 10.10 – 12.10

Session VII: Moderated Poster session (II)

guided by Barbara Casadei (Oxford, GB)/ Guido Iaccharino (Naples, I)

27. Faye Drawnel: *Interaction between the transcription factors NFAT and AP1 allows integration of cellular signalling pathways during cardiac hypertrophy*
28. Carolina Nunes França: *Effect of rosuvastatin and clopidogrel alone and combined in endothelial progenitor cells and endothelial microparticles*
29. Carolina Nunes França: *Influence of different hypolipemiant therapies in endothelial progenitor cells and microparticles levels in patients with subclinical carotid disease*
30. Tomasz Bonda: *Expression and activity of Src is upregulated in atrial tissue of patients with postoperative atrial fibrillation*
31. Karol Kaminski: *Transcriptional and posttranscriptional regulation of CCN genes in experimental model of heart failure*
32. Angela Serena Maione: *THE ROLE OF CaMKII IN THE REGULATION OF CARDIAC HYPERTROPHY PROVIDES A NOVEL THERAPEUTIC TARGET*
33. Ludovic Gomez: *Failure to precondition Sphingosine Kinase 2-KO mice: Mitochondria Not without RISK*
34. Luis Bras Rosario: *Comparative profiling of microRNA expression in embryos and adult bone marrow and cardiac progenitor cells identifies distinctive markers*
35. Roberta De Rosa: *FOXO3a-Atrogin-1 pathway in human heart failure*
36. Michele Ciccarelli: *G-protein-coupled receptor kinase-2 (GRK2) induces insulin resistance in cardiac myocytes*
37. Britta Stapel: *Low cardiac STAT3 expression is a pre-disposition for heart failure in response to β - but not α -adrenergic stimulation*
38. Marie Fertin: *New biomarkers of cardiac remodeling after myocardial infarction by proteomic analysis in comparison with B-type natriuretic peptide*
39. Angela Lombardi: *GLUCOSAMINE-INDUCED ENDOPLASMIC RETICULUM STRESS: NOVEL MOLECULAR APPROACHES*
40. Gaetano Santulli: *A BETA 2 ADRENERGIC RECEPTOR MECHANISM IN AGE-RELATED IMPAIRED INSULIN SECRETION*

41. Arash Haghikia: *The Ubiquitin-conjugating enzyme Ube2o protects against enhanced fibrosis and dilated cardiomyopathy after myocardial infarction: Regulation by gp130-JAK/STAT signaling*
42. Uma Mukherjee: *The Novel Role of DJ-1 in Cardioprotection*
43. Emilie Dubois: *Role of PKC epsilon-dependent phosphorylation of troponin T in cardiac contractility during heart failure*
44. Vikram Sharma: *BNIP3 - A potential target of ischaemic preconditioning*
45. Carlo Tocchetti: *Subtle reductions of left ventricular function are detected by speckle tracking echocardiography in antineoplastic therapy-induced cardiotoxicity*
46. Hannah Whittington: *Susceptibility to infarction in an aging, diabetic rat model*
47. Vivek Krishna (Giuseppe D Norata): *MicroRNA 143-145 deficiency is associated with impaired vascular function*
48. Adelino Leite-Moreira: *Diastolic tolerance to afterload is decreased in coronary patients with systolic dysfunction*

Participants

(in alphabetical order)

A

Julien Auquier (Brussels, Belgium)
Université Catholique de Louvain, Unit of Pharmacology and Therapeutics

B

Johannes Backs (Heidelberg, Germany)
University Hospital Heidelberg, Department of Internal Medicine III, Heidelberg, Germany

Jean-Luc Balligand (Brussels, Belgium)
Université Catholique de Louvain, Unit of Pharmacology and Therapeutics

Magali Balteau (Brussels, Belgium)
Université Catholique de Louvain, Unit of Pharmacology and Therapeutics

Johann Bauersachs (Hannover, Germany)
Hannover Medical School, Department of Cardiology and Angiology

Christophe Beauloye (Brussels, Belgium)
Université Catholique de Louvain, Unit of Pharmacology and Therapeutics

Peter Bencsik (Szeged, Hungary)
University of Szeged

Tomasz Bonda (Bialystok, Poland)
Medical University of Bialystok, Department of General and Experimental Pathology

Elisabetta Borchi (Florence, Italy)
University of Florence, Department of Biochemical Sciences

Byambajav Buyandelger (London, United Kingdom)
Imperial College of London, National Heart & Lung Institute

C

Barbara Casadei (Oxford, United Kingdom)
University of Oxford, John Radcliffe Hospital, Department of Cardiovascular Medicine

Michele Ciccarelli (Naples, Italy)
University of Naples Federico II

Angela Clerk (Reading, United Kingdom)
University of Reading, School of Biological Sciences

Gianluigi Condorelli (Milan, Italy)
National Research Council, Department of Medicine, Institute of Biomedical Technologies

Stuart Alexander Cook (London, United Kingdom)
Imperial College London, MRC Clinical Sciences Centre

Tamas Csont (Szeged, Hungary)
University of Szeged

Paula da Costa Martins (Maastricht, Netherlands)
Maastricht University, Cardiovascular Research Institute Maastricht

D

Roberta De Rosa (Naples, Italy)
University of Naples Federico II

Leon De Windt (Maastricht, Netherlands)
Maastricht University, Cardiovascular Research Institute Maastricht

Fabio Di Lisa (Padua, Italy)
University of Padua, Institute of Neuroscience

Faye Drawnel (Cambridge, United Kingdom)
Babraham Institute, Laboratory of Molecular Signalling

Emilie Dubois (Lille, France)
Institut Pasteur de Lille

E

David Eisner (Manchester, United Kingdom)
University of Manchester, Manchester Academic Health Science Centre

Leonardo Elia (California, San Diego)
University of California San Diego Medical Center

F

Ines Falcão-Pires (Porto, Italy)
University of Porto, Physiology Department, Faculty of Medicine

Peter Ferdinandy (Szeged, Hungary)
University of Szeged, Department of Biochemistry

Marie Fertin (Lille, France)
INSERM U744, Institut Pasteur de Lille

Carolina Nunes França (Sao Paulo, Brazil)
Federal University of Sao Paulo

Ann Friart (Brussels, Belgium)
Université Catholique de Louvain, Unit of Pharmacology and Therapeutics

Anna Fusco (Naples, Italy)
University of Naples Federico II, Department of Clinical Medicine
Cardiovascular and Immunological Science

G

Roberto Gaetani (Utrecht, Netherlands)
University Medical Centre Utrecht, Department of Experimental Cardiology

Ludovic Gomez (Lyon, France)
INSERM U1060, Laboratoire de Physiologie Lyon Nord

H

Arash Haghikia (Hannover, Germany)
Hannover Medical School, Department of Cardiology and Angiology

Derek Hausenloy (London, United Kingdom)
University College London (UCL), The Hatter Cardiovascular Institute

Nerea Hermida-Blanco (Brussels, Belgium)
Université Catholique de Louvain, Unit of Pharmacology and Therapeutics

Gerd Heusch (Essen, Germany)
Universitätsklinikum Essen, Institute of Pathophysiology

Stephane Heymans (Maastricht, Netherlands)
University of Maastricht, Center for Heart Failure Research, Cardiovascular Research Institute Maastricht

Denise Hilfiker-Kleiner (Hannover, Germany)
Hannover Medical School, Department of Cardiology and Angiology

Melanie Hoch (Hannover, Germany)
Hannover Medical School, Department of Cardiology and Angiology

Mathias Hohl (Homburg, Germany)
University of the Saarland, Internal Medicine III, Cardiology

Sandrine Horman (Brussels, Belgium)
UCL Medical School, Institute of Experimental and Clinical Research, Pole of Cardiovascular Research

Philippe Housmans (Minnesota, USA)
Mayo Clinic Rochester, Department of Anesthesiology

I

Guido Iaccarino (Naples, Italy)
University of Naples Federico II, Department of Clinical Medicine, Cardiovascular and Immunological Science

K

Karol Kaminski (Bialystok, Poland)
Medical University of Bialystok, Department of Cardiology

Henning Kempf (Hannover, Germany)
Hannover Medical School, Leibniz Research Laboratories for Biotechnology and Artificial Organs (LEBAO)

Ralph Knoell (London, United Kingdom)
Imperial College London, National Heart & Lung Institute

Thorben König (Hannover, Germany)
Hannover Medical School, Department of Cardiology and Angiology

Michael Kohlhaas (Homburg, Germany)
University of the Saarland, Internal Medicine III, Cardiology

L

Sandrine Lecour (Cape Town, South Africa)
University of Cape Town Medical School, Hatter Institute for Cardiology Research

Adelino Leite-Moreira (Porto, Portugal)
University of Porto, Faculty of Medicine, Department of Physiology

Angela Lombardi (Naples, Italy)
University of Naples Federico II, Department of Clinical Medicine, Cardiovascular and Immunological Science

M

Angela Serena Maione (Naples, Italy)
University of Naples Federico II, Department of Clinical Medicine, Cardiovascular and Immunological Science

Ulrich Martin (Hannover, Germany)
Hannover Medical School, Leibniz Research Laboratories for Biotechnology and Artificial Organs (LEBAO)

Oliver J. Mueller (Heidelberg, Germany)
University Hospital Heidelberg, Department of Internal Medicine III, Cardiology, Angiology and Pneumology

Uma Mukherjee (London, United Kingdom)
University College London (UCL), Hatter Cardiovascular Institute

Elizabeth Murphy (Bethesda, USA)
Systems Biology Center Bethesda, Cardiac Physiology Section

N

Alexander Nickel (Homburg, Germany)
University of the Saarland, Internal Medicine III, Cardiology

Claudia Noack (Berlin, Germany)
ECRC Max Delbrück Center Berlin, Asklepios Clinic St. Georg, Department of Cardiology

Gauthier-Thibaut Noppe (Brussels, Belgium)
Université Catholique de Louvain, Institute of Experimental and Clinical Research (IREC), Pole of Cardiovascular Research

Michela Nosedà (London, United Kingdom)
Imperial College of London, National Heart & Lung Institute

O

Martinus Oerlemans (Utrecht, Netherlands)
University Medical Centre Utrecht, Laboratory of Experimental Cardiology

Michel Ovize (Lyon, France)
Hopital Cardiologique Louis Pradel, Explorations Fonctionnelles Cardiovasculaires

P

Mélanie Paillard (Lyon, France)
Inserm U1060, Cardioprotection

Evasio Pasini (Lumezzane BS, Italy)
Fondazione S Maugeri

Anna Pia Piazza (Padua, Italy)
Venetian Institute of Molecular Medicine

Vivek Krishna Pulakazhi Venu (Milan, Italy)
University of Milan, Department of Pharmacological Science

R

Anke Renger (Berlin, Germany)
ECRC Max Delbrück Center Berlin, Center for Molecular Medicine

Luis Bras Rosario (Oeiras, Portugal)
Instituto Gulbenkian de Ciência, Cardiac Regeneration Group

Marisol Ruiz-Meana (Barcelona, Spain)
Hospital Vall d'Hebron, Institut de Recerca, Experimental Cardiology

S

Gaetano Santulli (Naples, Italy)
University of Naples Federico II, Department of Clinical Medicine

Mauro Sbroglio (Torino, Italy)
University of Torino, Molecular Biotechnology Center

Rainer Schulz (Essen, Germany)
University of Essen Medical School, Center of Internal Medicine, Institute of Pathophysiology

Luca Scorrano (Geneva, Switzerland)
University of Geneva, School of Medicine

Vikram Sharma (London, United Kingdom)
University College London Division of Medicine, Hatter Cardiovascular Institute

Joost Sluijter (Utrecht, Netherlands)
University Medical Center Utrecht

Britta Stapel (Hannover, Germany)
Hannover Medical School, Department of Cardiology and Angiology

Charles Steenbergen (Baltimore, USA)
Johns Hopkins University School of Medicine

T

Guido Tarone (Torino, Italy)
University of Torino, Medical School and Biotechnology School, Molecular Biotechnology Center (MBC)

Thomas Thum (Hannover, Germany)
Hannover Medical School, IFB, Molecular and Translational Therapeutic Strategies

Aurélie Timmermans (Brussels, Belgium)
Université Catholique de Louvain, Pole of cardiovascular Research

Carlo Tocchetti (Naples, Italy)
Federico II University, Department of Clinical Medicine, Cardiovascular and Immunological Sciences

V

Heiko von der Leyen (Hannover, Germany)
Hannover Clinical Trial Center (HCTC)

Krijn Vrijnsen (Utrecht, Netherlands)
University Medical Center Utrecht

W

Hannah Whittington (London, United Kingdom)
University College London (UCL), Hatter Cardiovascular Institute

Kai C. Wollert (Hannover, Germany)
Hannover Medical School, Department of Cardiology and Angiology

Z

Tania Zaglia (Padua, Italy)
Venetian Institute of Molecular Medicine



Organizers of the Annual meeting

of the

Working Group on Myocardial Function

Prof. Denise Hilfiker-Kleiner, Prof. Johann Bauersachs,

Prof. Jean-Luc Balligand

and the

Working Group on Cell Biology

Prof. Michel Ovize, Prof. Rainer Schulz

Villa Monastero, ITALY

April 14 to 17, 2011



Meeting Organization and Contact:

Prof. Denise Hilfiker-Kleiner
Meike Jungesblut
Olga Sorokin

Hannover Medical School
Department of Cardiology and Angiology

Adresses:

Villa Monastero
Viale Giovanni Palvani
23829 Varenna Lecco, Italy

Hotel Eremo Gaudio
Via Roma, 25
23829 Varenna – LC
Tel. +39 0341 815301
Fax +39 0341 815314
E-mail: eremogaudio@yahoo.it

Villa Cipressi
Via IV Novembre 18
23829 Varenna, Italy
Tel. +39 0341 830113
info@hotelvillacipressi.it

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