ESF EMRC Workshop:

CARDIOVASCULAR GENOMICS: NEW PATHOPHYSIOLOGICAL CONCEPT

Maastricht, Netherlands, 30 November - 2 December 2001

Executive summary

Four years ago - in December 1997 - the first European Science Foundation Workshop on Cardiovascular Specific Gene Expression was held in Maastricht. The progress in the field in the four years until December 2001 has been spectacular. In 1997, gene expression was still an art focused on individual genes; in 2001, many labs have access to microarray facilities to determine the expression of thousands of genes simultaneously. In 1997, gene expression was an area of fundamental research in basic molecular biology laboratories; in 2001, clinical cardiovascular research has incorporated gene expression approaches. In 1997, the interpretation of a gene expression experiment was usually straightforward; in 2001, advanced bioinformatics tools are used to interpret the extreme complexities of genetic control of cell and tissue function.

The second symposium of this series was focused on cardiovascular genomics: new patho-physiological concepts. The organizing committee chose to invite a group of renown scientists and young investigators around four topics of eminent importance in cardiovascular research. The topics reflect the major present-day clinical cardiovascular problems: atherosclerosis, hypertension, arrhythmias and heart failure. In addition to these four disease-driven topics, the workshop had sessions on gene expression methodologies and cellular transplant approaches to cardiovascular disease.

In the opening session, dr. E. Olson from Dallas gave a brilliant review on transcriptional regulation of cardiac development and hypertrophy. The atherosclerosis session contained in-depth presentations on gene expression analysis in the vessel wall and the plaque. Several groups of genes related to phenomena like cell growth and apoptosis, matrix structure and cell-cell connection now emerge as vital in the process of atherosclerosis. The hypertension session also had a focus on the vessel wall. Developmental aspects, endothelial function and cell signaling pathways were reviewed by the speakers in this session.

The two sessions devoted to cardiac aspects covered gene expression pathways involved in arrhythmias, hypertrophy and failure. A particular focus was given to the role of contractile proteins. The arrhythmia session reviewed the gene expression of various ion channels.

The session of gene expression analysis provided a didactic overview of the major methodological approaches used in gene expression analysis. Finally, a series of lectures was devoted to the use of cellular therapies to improve cardiac function. This novel area of research offers exciting perspectives for therapeutic applications.

The whole meeting offered science at the highest possible level. The formula of the workshop - limited participation, mix of established and young investigators, international, predominantly European speakers, extensive discussion periods - was ideally suited for its highly ambitious purposes.

Future direction

The expected impact of the meeting will depend on new european collaborative initiatives. Some collaborations have already been setup after three months. This is especially true for for exchange of animal models and genomic analysis in the places where the systems are up and running. This will save time and money and lead to interpretable results faster. It was obvious that the general feeling at the meeting was that genomics and proteomics are crucial tools for understanding the genome. However, the rate limiting step for fast genetic and genomic analysis is the physiomic approach. Several institutes have some techniques for functional analysis, but few have them all, which leads to incomplete phenotypic analysis. Investments and improvements in the infrastructure to perform physiomic analysis more efficient would be the way to go.

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Switserland	1
Italy	2
Spain	1
USA	7
France	2
Belgium	4
UK	1
Japan	1
Sweden	2

FINAL PROGRAMME

NOVEMBER 29

Introsession
Chairman **P. Doevendans**

18.30 Welcome: **Prof. H. Struijker Boudier**

18.40 *Cardiovascular disease: the clinical problems*: **Prof. H.J. Wellens**

19.00 *Transcriptional regulation*: **E. Olson**

20.15 **DINNER (castle Vaeshartelt)**

NOVEMBER 30

Please note that all speakers have 25 minutes for the presentation and 5 minutes discussion

SESSION 1 08.00-09.55
Gene expression analysis
Chairman **M. Hofker**

08.00 *Microarray*: **G. Porter**

08.30 *SAGE*: **B. Rossier**

09.00 *Proteomics*: **C. Michiels**

09.30 *Bioinformatics*: **M. Huynen**

10.00 Coffee break

SESSION 2 10.30-12.25
Genomics and pathophysiology of atherosclerosis
Chairman **M. Daemen**

10.30 *Micro-arrays to unravel atherosclerosis*: **S. Schwartz**

11.00 *In vitro-in vivo gene analysis*: **A. Horrevoets**

11.30 *Gene expression and plaque complexity*: **M. Daemen**

12.00 *The role of apoptosis in atherosclerosis progression*: **M. Kockx**

12.30 **LUNCH**

SESSION 3 14.00-16.25
Genomics and hypertension
Chairman **P. de Leeuw**

14.00 *Disease complexity*: **P. Corvol**

14.30 *Predisposition for hypertension*: analysis of candidate genes **G. Bianchi**

15.0 *Vascular gene transfer/therapy: from animals to humans*:
A. Dominiczak

15.30 *Hormones and signalling pathways*: **G. Lembo**

16.00 *Endothelial changes in hypertension*: **S. Lamas**

19.00 Bustransport Castle Vaeshartelt to Castle Neercanne for
DINER

DECEMBER 1

SESSION 4 08.00-09.55
Gene expression in cardiac hypertrophy and failure
Chairman **P. Doevendans**

08.00 *Microarrays and cardiac tissue*: **H. Smeets**

08.30 *Ca handling proteins*: **H. Rockman**

09.00 *Adaptation of contractile proteins*: **M. Sussman**

09.30 *Cardiac Signalling Pathways*: **L. de Windt**

10.00 Coffee break

SESSION 5 10.30-12.55
Molecular remodelling in arrhythmias
Chairman **M. Nabauer**

10.30 *Ion channel regulation: from genes to channels to arrhythmias*:
K. Donahue

11.00 *Differential expression and regulation of delayed rectifier channels*: **M. Vos**

11.30 *Ion channel polymorphisms and their role in ventricular arrhythmogenesis*: **S. Kaab**

12.00 *Altered gene expression in atrial fibrillation*: **B. Brundel**

12.30 *G-protein 3 subunit polymorphism and atrial fibrillation*: **U. Ravens**

13.00 **LUNCH**

SESSION 6 14.30-16.25
Cellular transplant
Chairman: **L. Field**

14.30 *Genetic modification of stemcells*: **T. de Vries**

15.00 *Human Embryonic stemcells*: **C. Mummery**

15.30 *Bone marrow derived cardiomyocytes*: **K. Fukuda**

16.00 *Cellular Cardiac reinforcement*: **P. Smits**