

Summary of basic science activities at the European Society of Cardiology Congress in Barcelona 2014

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Abstract

With >35 000 participants, the European Society of Cardiology (ESC) congress was one of the biggest ESC events ever and basic science activities were well implemented. I here summarize the basic science activities during the congress. This includes a section 'Basic science activities in a nutshell' summarizing the most important sessions as well as 'Emerging science activities in the ESC' section with special focus on novel research fields such as the characterization of long non-coding RNAs in cardiovascular research.

Keywords Basic science; Hot line; microRNA; Long non-coding RNA; Stem cells

Introduction

With >35 000 participants, the ESC congress was one of the biggest ESC events ever and basic science activities were well implemented. As one can imagine, it is impossible to cover all those aspects in a single short review. However, I would like to stress that not only excellent science was presented but also the ESC congress successfully brought together basic scientists with clinicians and translational scientists. In the following, I will highlight selected basic science events in a chronological manner starting from Saturday morning sessions (30 August 2014) to Wednesday (3 September 2014). Topics that are covered result from visits of the sessions, posters and submitted and presented abstracts. I sincerely excuse myself already now for not highlighting every study, which is simply impossible, and thus, this review may be somehow biased by my personal flavours for attractive research topics (although I tried to be as fair and balanced as possible).

As most of the research findings on this congress have not been published yet, I highlight the individual abstract/session number in brackets where appropriate. Using the search field provided in the following link: <http://congress365.escardio.org/Basic-Science#.VGMODE0U-Ul>, the content of these abstracts and in certain cases the complete presentation can be found.

Basic science activities in a nutshell

Saturday, 30 August 2014

On Saturday, in a session chaired by Garcia-Dorado and Iliodromitis, exciting studies were presented in the field of extracellular and intracellular components of protection against ischaemia/reperfusion injury. This covered aspects

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of the endothelial nitric oxide synthase (NOS3) (abstract 40), nanoparticle-mediated targeting of cyclosporine to mitochondria (41), exosome-mediated intercellular communication (42), and many other aspects. This session importantly demonstrated that also extracellular cytokines and vesicles are involved in cardiac pathology and thus might be interesting therapeutic targets.¹ In a parallel session chaired by Garcia and Fauconnier, cardiac tissue engineering was discussed. In this well-attended session, researchers from Germany, France, Netherlands, and Spain presented novel developments in engineered heart valves (46), bioactive implants (47), bioprotheses (48) as well as vascular tissue engineering (49). Later that day, in a moderated poster session, details about the role of inflammation in cardiovascular diseases were actively discussed under supervision of S. Frantz and D. Duncker. Seven posters shed new light on the importance of interleukines (P176), blocking antibodies (P177), secreted phospholipases (P178), and other molecules in the pathogenesis and potential treatment of cardiovascular inflammation. Interesting poster sessions in the afternoon included the session on 'The right ventricle and basic science', discussed by K. Konstantinides, where 10 groups presented compelling data about the uniqueness of the biology of the right ventricle and the differences in molecular mechanisms and treatment options when compared with the left ventricle. Three other poster sessions were focused on development, genetics, and stem cells. A top score poster described the occurrence of BAG family molecular chaperone regulator 3 (BAG3) mutations in Polish patients with dilated cardiomyopathy (P611).

Sunday, 31 August 2014

Sunday started with a firework; the hot line session on novel therapies for cardiovascular diseases chaired by Jessup and Bueno. Although no real basic science was presented, this hot line session will have important influence on many areas of basic science. Examples are that it was made clear that we need more understanding about the molecular mechanisms of the beneficial effects of iron supplementation or use of colchicine in post-operative atrial fibrillation treatment. In a parallel session, H. Shimokawa was awarded with the ESC William Harvey Award on basic science and gave a talk on the importance of coronary vasomotion abnormalities (912). In another parallel session, new insights into the basic mechanisms of cardiac arrhythmias were discussed. One interesting talk presented exciting data about how nuclear factor of activated T-cells 3 (NFAT3) gene transfer could counteract pro-arrhythmic changes accompanying pathological cardiac hypertrophy (1043). A corresponding morning poster session also covered genetic aspects of arrhythmias

(P1454). Later that day at 10 a.m., there was a moderated poster session on vascular remodelling. One interesting poster showed an unexpected role for B cells in abdominal aneurysm formation (P1095). 'Cardiovascular pathophysiology' was discussed in another poster session by M. Dweck, and a Spanish group presented interesting data about a microRNA (miRNA) to serve as a biomarker for calcified aortic stenosis (P1499). Next door, 'Cardiac biology' was discussed by E. van Rooij, and one interesting poster showed also here interesting results of miRNA patterns distinguishing between patent vs occluded target vessels in acute myocardial infarction (P1527). Again, in parallel, 'Heart Failure Pathophysiology' was discussed with F. Parthenakis, and the top score poster showed that myeloperoxidase (MPO)-deficiency attenuated dilated cardiomyopathy in mice (P1724). 'Understanding Remodeling' was another topic in the morning poster session as discussed by J.L. Balligand (P1736). During the lunch time, the Young Investigator Award session in basic science took place, and young researchers presented data about miR-126 containing microvesicles (1800), beta3-adrenoceptors (1801), pluripotent stem cells (1802), and prollyl-isomerase 1 (1803). In a symposium at 2 p.m., transcriptional regulation of the genome by miRNAs, long non-coding RNAs, and splicing and transcription factors were discussed (1957–1960). The afternoon was busy with sessions about 'Vascular Cells and New Vessels', where in a rapid fire, mode 8 interesting papers were presented (2148–2155). In parallel, the 'Frontiers in the treatment of heart failure' session took place as well as the hot line basic and translational science session on cardiac disease chaired by Balligand and Priori, where basically stem cells and transcription factors were discussed (2170–2176). Afternoon poster sessions in basic science included the basic and electrophysiological mechanisms in atrial fibrillation session (P2441), as well as sessions about ischemia and reperfusion (P2496), growth factors, and signalling pathways (P2507) and integrative physiology (P2518).

Monday, 1 September 2014

Monday morning started with two parallel sessions in basic science, one 'Hot Line Session on basic and Translational Science on Vascular Disease', covering inflammation of the vascular wall (2851) and validation of novel human genes in atherosclerosis (2854) amongst other topics; the other session was on 'Novel Therapeutic Strategies for Cardioprotection', covering mitochondria (2857), exosomes (2858), miRNAs (2859), and stem cells (2860). 'Pathophysiology of Hypertension' and 'Biology of Stem Cells' was discussed at 10 a.m. at moderated poster sessions. 'Hot' topics presented included transplantation of mesenchymal adipose tissue mesenchymal stem cells

to improve post-MI cardiac remodelling (P2999) and inhibition of a microRNA, miR-195, to improve stem cell function by telomere re-lengthening (P3001). Novel gene therapy approaches were presented by four speakers in a session on 'Antiarrhythmic Gene Therapy' (3177–3180). Exiting basic science regular morning poster session titles were the following: 'Atherosclerosis: Basic Aspects' (P3418), 'Inflammation and the vessel wall' (P3429), and 'Update on Cardiotoxicity' (P3633) with many encouraging results. An important monday afternoon session covered 'Genome Editing' chaired by Hulot and Schulze-Bahr, and eight short talks covered many aspects including genome-wide homozygosity analysis, methyltransferases, and long non-coding RNAs. A highlight of the monday afternoon science day at the ESC was the 'State of the Art lecture on Functional Importance of Regulatory RNA species'. There were five talks that were summarized by a final speaker at the end; topics included more emerging data about long non-coding RNAs (4082, 4083, 4086, 4087) and miRNAs (4084). In the afternoon basic science poster sessions, Hoffmann discussed 'Basics in Valve Disease' (P4289) with information about different gene expression in various forms of aortic stenosis or novel innovative treatment approaches. Other topics covered in the afternoon poster session included 'Vascular Cell Dysfunction' (P4411, P4422) and 'Endothelial Function: Basic' (P4433).

Tuesday, 2 September 2014

In a moderated poster session on tuesday, 'Remodelling and Death of cardiac Myocytes' was discussed by Samuel and Eschenhagen at 10 a.m. (P4925–P4931). In parallel, Symposia Balligand and Hulot discussed 'Novel insights into myocardial responses to adrenergic stress' with four talks on subcellular microdomains (5005), beta adrenoceptor kinetics (5006), novel protective mechanisms (5007), and takotsubo cardiomyopathy (5008). Next door, at the same time, Mach and Schunkert chaired a session on 'New molecular players in atherosclerosis' with six interesting talks covering things from T-cells (5009) to kinases (5012). Tuesday's basic science poster sessions were about 'Genetics in Hypertension' (P5182), cardiomyopathies (P5227, P5238, P5249), basic science in atrial fibrillation (P5273), cardiac biology (P5349), cardiac hypertrophy and heart failure (P5362), as well as thrombosis and anticoagulation and treatment (P5506, P5517, P5554), and heart failure basics (P5604).

In the afternoon, one session was dedicated on 'Lipid Signalling and Inflammation' by Waltenberger and Reiner (2 p.m.) and another one by Pinto and Medeira on 'Translational Research and Hot Clinical Topics in Cardiomyopathies' covering important translational approaches.

Ninety minutes later, at 3.30 p.m., moderated posters started with basic science topics such as 'Genetic Aspects of Arrhythmias' and 'Endothelial Cell function: Bedside to bench'. A related 'rapid fire' abstract session on 'Novel Aspects of endothelial cell function' by Mayr and Yla-Herttula from 4:30–6 p.m. was one of the last exciting basic science actions on that day next to the afternoon poster session mainly covering endothelial biology and inflammation.

Wednesday, 3 September 2014 and conclusions

In an exciting highlight session, Hilfiker-Kleiner summarized several topics of the basic science activities on the last day of the ESC (6687).

Emerging basic sciences of the ESC 2014 congress

Derailed gene expression is the base of pathological cardiac hypertrophy, cardiac remodelling and heart failure (HF). Well-known examples are the up-regulation of certain foetal genes during pathological cardiac hypertrophy, causing the often inevitable deterioration in heart function. A great surprise is the fact, that only although about 80–90% of the mammalian genome is transcribed, less than 2% is ultimately translated into protein,² leaving an unknown biological role of the non-translated RNA species. These non-protein coding transcripts form a vast non-protein coding RNA (ncRNA) world that we have only recently started to study. Many ncRNAs identified act at various steps along the protein biosynthetic process, including transcription, RNA maturation, translation, and protein degradation. Based on size, ncRNAs can be subdivided into two major groups: (1) small ncRNAs (<200 nucleotides short) including microRNAs (miRNA), PIWI-interacting RNAs (piRNA), and endogenous short interfering RNAs (siRNA); and (2) long ncRNAs (lncRNA), which have a length between 0.2 and 2 Kb. Around 1500 to 2000 human miRNAs have been identified, and a few have been tested as therapeutic targets in cardiovascular disease in small and large animal models.^{3–5} During the ESC, there were quite some sessions about new data about non-coding RNA species and their role in cardiovascular development and (patho)biology. Michael Alexanian from Lausanne, presented data about a long non-coding RNA CARMEN that was involved in cardiac development (4082). After describing the different functions of lncRNAs (e.g. RNA decoy or miRNA sponging), he presented expression profiles of

lncRNAs during differentiation of human cardiac precursor cells. The lncRNA CARMEN was expressed and up-regulated during cardiac differentiation. A shRNA approach to decrease CARMEN prevented cardiac differentiation showing a functional role of this lncRNA. Micheletti, also from Lausanne, presented data about cardiac enhancer-associated non-coding RNAs during cardiac development and disease (4083). Two of these ncRNAs MM67 and MM85 showed a similar pattern of expression such as myocardin during cardiac development. These two ncRNAs also had human orthologous. He also showed that foetal cardiac enhancers are reactivated after stress and thus could serve as interesting new therapeutic targets. Nishino from Kyoto presented data about miR-33a to regulate lipogenic pathways *in vivo*. Liver ABCA1 and serum HDL-C levels were increased in miR-33 mice casting doubts about potential ongoing (long-term) therapeutic use of miR-33 inhibitors (4084). Felix Jansen from Bonn showed data about endothelial microparticles (EMPs) and their effects on endothelial cell activation (4085). This group showed that EMPs contain miRNAs such as miR-222 that could be transferred to endothelial cells. EMP transfusion to mice reduced endothelial activation and atherosclerosis development. This might be because of transfer of selected miRNAs such as miR-222 opening a potential new therapeutic approach. Jan Fiedler from Hannover, Germany used

next generation RNA sequencing approaches to identify lncRNAs that are activated by hypoxia in human endothelial cells (4086). He identified several candidates that were highly up-regulated in endothelial cells after hypoxia. A particular transcript entitled HSLNCR-3 was of considerable importance. Silencing of this lncRNA led to decreased proliferation of endothelial cells *in vitro*, as well as impaired vascularization showing potential therapeutic use of modulation of this lncRNA in ischemic diseases that require increased capillary density and blood supply.

Thomas Thum from Hannover gave a lecture presenting novel data on lncRNAs involved in the cardiac hypertrophy process and summarized the session for the audience. During discussions in this session, it became clear that studies with lncRNAs in cardiovascular disease are of great importance as this new group of non-coding RNAs provide new mechanistic understanding and a new avenue of therapeutic options to treat cardiovascular disease.

In conclusion, basic science activities were extremely well represented at this year ESC in Barcelona. Great discussions after the talks and at the posters were well implemented within translational and clinical presentations. For sure, this congress helped to better implement basic science into translational/clinical activities and opened new avenues for future joint collaborations.

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