Meeting Report for Basic Cardiovascular Sciences 2011
Scientific Sessions: From Concept to Clinic: Leading Cardiovascular Translational Science

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The BCVS 2011 Scientific Sessions were held on July 18 to 21, 2011 in New Orleans, Louisiana. The theme of the conference for this year was “From Concept to Clinic: Leading Cardiovascular Translational Science.” The conference gathered 526 attendants, a record number for the BCVS summer conference, from 26 countries. Among them, 280 were either students or early career investigators. There were 74 oral presentations and 352 poster presentations, which were also record numbers for the past 8 BCVS meetings. The sessions were designed around the common theme of translating the most exciting and advanced basic science to further the understanding of disease pathophysiology with an eye toward novel therapeutic approaches. Here, we will briefly highlight some presentations and new features of the BCVS 2011 Scientific Sessions.

The opening session was kicked off by plenary lectures given by the pioneers of several hot spots in cardiovascular research. Dr Eric Olson (University of Texas Southwestern) discussed recent advances in understanding the mechanisms of heart regeneration in mice. Dr Olson found that the regenerative activity of cardiomyocytes declines after birth when miR-195, a member of the miR-15 family, is highly upregulated. RISC RNA sequencing showed that miR-195 targets a number of cell cycle genes, including checkpoint kinase. Cardiomyocyte proliferation is upregulated when the miR-15 family is downregulated by anti-miRNAs treatment. The meeting featured an additional entire session on miRNA biology and translational science.

Dr Jeffery Molkentin (Cincinnati Children’s Hospital) discussed the property of the mitochondrial permeability transition pore that regulates apoptosis and necrosis. He reported the intriguing observation that mitochondria lacking Bax/Bak do not swell but the inner mitochondrial membrane can reorganize, and permeabilization of the outer mitochondrial membrane, by any means, can restore their ability to swell and induce necrosis. Based on these observations, he proposed revised models of mitochondrial permeability transition pore, whose activity is regulated independently by the inner and outer membrane complexes.

Dr Jonathan Stamler (Case Western Reserve) described his groundbreaking work in nitrosylation (S-NO) based post-translational modification. S-NO modifications are involved in G protein coupled receptor (GPCR) signaling and in cardiac excitation contraction coupling, through dynamic influences on the ryanodine receptor. In the past decade, endogenous denitrosylases have been described by the Stamler laboratory and include S-nitrosogluthathione reductase (GSNOR) and thioredoxin.

Dr Piero Anversa (Brigham and Women’s Hospital) described endogenous c-kit+ stem cells, and their role as adult stem cells in both the heart and the lung. Cardiac c-kit+ stem cells can be amplified ex vivo, have trilineage differentiation potential, and are currently being tested in clinical trials for cardiac repair.

A highlight of the meeting was the keynote lecture delivered by Dr. Robert Lefkowitz (Duke University) where he discussed the role of β-arrestin in mediating the signaling of the GPCR. Aside from the traditional heterotrimeric G protein signaling, GPCR mediates the mitogen-activated signaling pathway through interaction with β-arrestin. Beta-arrestin binds to the carboxyl terminus of the GPCR phosphorylated by G protein coupled receptor kinases. Dr Lefkowitz proposed the “Bar-code hypothesis,” in which distinct G protein coupled receptor kinase phosphorylation sites in the β2 adrenergic receptor differentially regulate β-arrestin signaling, which confers an additional layer to the versatility and specificity to GPCR signaling. He showed that GPCR ligands, biased toward either β-arrestin or G-protein signaling, have distinct therapeutic benefits. Beta-arrestin 2 plays an important role in mediating stabilization of β-catenin in the Wnt-frizzled receptor signaling pathway in cancer stem cells. Suppression of β-arrestin 2 inhibits Wnt-mediated stem cell expansion in myeloid leukemia, indicating that β-arrestin 2 is a promising target in cancer therapies.

In the regular sessions, 61 investigators were invited from 9 countries. The unique themes in this year’s conference included longevity and caloric restriction, microRNA and cardiovascular therapies, and myocyte proliferation and tissue engineering. Dr Michael Sack (NIH) presented his recent finding on the mechanism that mediates acetylation of mitochondrial proteins and its functional significance. Sirt3, a member of the sirtuin family, is activated by caloric restriction and endurance exercise and promotes protein deacetylation of mitochondrial proteins, thus enabling adaptation to aging, redox, and mechanical overload. Using bioinformatics and biochemical strategies, he has recently discovered an acetyltransferase enriched in mitochondria. He proposed that Sirt3 and the newly discovered acetyltransferase regulate the level of acetylation, thereby playing an adaptive and a

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maladaptive role, respectively, in regulating mitochondrial function.

As mentioned above, the meeting devoted a session to miRNAs. Dr Stefanie Dimmeler (Goethe University) presented that cardiovascular cells release and reuptake microRNA, thereby serving as a mediator of cell-to-cell communication. Atheroprotective miR-143/145 is upregulated by shear stress through a Klf2-dependent mechanism in vascular endothelial cells. Interestingly, microvesicles containing miR143/145 are released from endothelial cells and transferred to adjacent smooth muscle cells, which suggests that microRNA not only serve as a biomarker, but also act as a vehicle for cell-to-cell communication.

Dr Anthony Rosenzweig (Beth Israel Deaconess Medical Center) used a qPCR-based screen of all known transcriptional components (Quanytrx) and found that C/EBPβ down-regulates with exercise, thereby mediating physiological hypertrophy. He presented that downregulation of C/EBPβ mediates myocyte proliferation through activation of CITED4, a transcriptional coactivator. He proposed that the signaling mechanism mediating exercise-induced hypertrophy can alleviate pathological hypertrophy and, thus, the pharmacological mimic of exercise may be used for the treatment of heart failure.

Several sessions were dedicated to regenerative medicine and featured speakers including Dr. Roberto Bolli (University of Louisville), who presented early and highly provocative results from the Cardiac Stem Cell Infusion in Patients With Ischemic Cardiomyopathy (SCIPIO) trial, an assessment of the regenerative potential of c-kit+ cardiac stem cells in patients with LV dysfunction due to prior myocardial infarction. Other speakers included Sean Wu (Massachusetts General Hospital) who discussed induced pluripotent stem cell modeling of cardiovascular disease, Dr Joshua Hare (University of Miami) who discussed harnessing endogenous cardiac repair using mesenchymal stem cells, and Dr Rachel Smith (Cedars-Sinai) who discussed the role cardiospheres could play as a novel cell-based therapeutic approach.

This year’s conference also featured a Career Development Workshop organized by Drs Asa Gustafsson and Burns Blaxall. In a career development forum, Dr Ushma Neil, Executive Director of the Journal of Clinical Investigation, illustrated how to write a winning manuscript. Dr Neil succinctly pointed out all-too-common mistakes, but also gave straightforward, experienced advice that is essential for an auspicious start to a manuscript. She covered all aspects, from writing the cover letter to submitting the paper for peer review, necessary for the successful submission of a manuscript.

We also initiated JCS-BCVS joint lectures, given by Drs Yoshinori Ohsumi and Kinya Otsu, and ESC-HFA joint lectures by Drs Ajay Shah and Leon De Windt, in order to strengthen ties between the BCVS and foreign organizations that share interests with the BCVS and to attract more of an audience from all over the world. As you can see, the BCVS is looking forward to actively extending this joint effort to organizations in other countries.

We have initiated several new features this year. We strictly imposed time limits for each presentation, and most speakers completed their presentation within 15 to 18 minutes as requested. This was not an easy task for the speakers, but it was generally well received by the audience, because each presentation was compact so that both the speakers and the audience stayed focused as each session flowed in a smooth and timely manner. This innovation allowed sufficient time for Q&A and, unexpectedly, we were able to listen to instant panel discussion among the speakers after the sessions on metabolism and mitochondria, which was truly precious. We also asked each speaker to submit a 1-sentence summary of their presentation, and this was distributed as a physical handout and also through Twitter updates. We believe that having a take-home message for each presentation beforehand not only helped the audience decide which presentations to follow closely, but also significantly enhanced our ability to understand the content of each presentation. We hope that these implementations will be inherited as reputable traditions for future BCVS meetings.

For those who missed this meeting, some of the presentation slides and provocative video discussions are available online at: http://my.americanheart.org/professional/Sessions/BCVS/ScienceNews/Science-News-BCVS_UCM_316947_SubHomePage.jsp. In addition, interviews were performed of a select group of presenters and these can be found online at the same website.

As the organizers of the BCVS 2011 Scientific Sessions, it is our pleasure to inform you that the authors really appreciated all of the attendance for their excellent presentations as well as the active participation in discussions during the meeting. They are also appreciative of the generous support given by industry. In particular, the BCVS 2011 Scientific Sessions received a record amount of financial support from Japanese pharmaceutical companies, despite the fact that Japan has been experiencing extremely hard times since the Tsunami hit them in March this year. The participants from Japan also increased from 8 last year to 42 this year. Again, the organizers appreciate the Japanese scientists for their fortitude and support for the BCVS. The organizers sincerely hope that this summer meeting will continue to grow internationally and provide members of the field with an excellent opportunity to get to know each other and collaborate to find the cure for cardiovascular disease. The BCVS 2012 will be organized by Drs Yibin Wang (UCLA), Roger Hajjar (Mount Sinai), and Annarosa Leri (Brigham and Women’s Hospital). We hope to see you all again at BCVS 2012 in New Orleans.
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