BCVS Scientific Conference 2012 Meeting Report

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Something new, something old would be the best way to characterize the 2012 Basic Cardiovascular Sciences (BCVS) meeting. The conference entitled “Frontiers in Cardiovascular Science and Novel Therapy” highlighted the top scientific and translational discoveries in cardiovascular research in 15 major scientific sessions. The field’s leading pioneers presented alongside junior investigators, invigorating the investigative conversation that keeps cardiac research moving forward.

Two luminaries of cardiology delivered the conference’s keynote addresses: Drs Eugene Braunwald and Valentin Fuster. Dr Braunwald delivered a retrospective that illustrated the great advances in cardiology in the past 50 years. It was of course thrilling to hear about the discoveries and novel treatment modalities of modern cardiology from the man responsible for so much of it. Dr Fuster described the journey he took from examining pathological specimens of patients after myocardial infarction to the characterization of the vulnerable plaque. Dr Fuster went on to describe his recent emphasis on global health and delivering good cardiovascular health at a universal level. Most inspiring in Dr Fuster’s talk was his recent work with Sesame Street trying to mold healthy eating and exercise habits in young children.

The topic of myocardial aging was a feature of this year’s meeting. Studies in animals and humans have rarely considered aging as an independent process, and, only occasionally, cardiac aging in humans has been studied independently from concomitant pathological states. This concept was illustrated by Piero Anversa, who provided evidence that the human heart is a highly dynamic organ. By using retrospective 14C birth dating, myocyte turnover was found to involve 10% to 20% of cells per year in the first 2 decades of life and 5% of cells per year, from 20 to 40 years of age. Myocyte regeneration increases progressively as a function of age, reaching 24% of cells per year in old individuals, in an attempt to counteract partly the enhanced rate of myocyte apoptosis and necrosis in the aged heart. Thus, physiological aging involves a previously unexpected magnitude of myocyte renewal, and the human heart changes its myocyte compartment ≈10× during the course of life. Other talks challenged the dogma that senescence is an evolutionarily conserved process, and Sirt 1, a member of the sirtuin family of longevity genes, was shown to have important cardiovascular effects.

Protein modification, homeostasis, and turnover represent the central theme in the Molecular Signaling talks at BCVS 2012. Dr Jonathan Stamler presented his recent findings in protein S-nitrosylation in cardiovascular regulation. S-nitrosylation directly modifies proteins involved in cGMP pathways, calcium handling, and adrenergic receptor signaling complex to impact on cardiac contractility and rhythm.
Therefore, S-nitrosylation biology may represent a promising new area of investigation for a broad spectrum of cardiovascular conditions.

In the past year, significant breakthroughs occurred in mitochondrial biology because the mitochondrial calcium uniporter that was reported >50 years ago was finally identified via a combined approach genomics, molecular biology, and mitochondrial physiology. In addition, the molecular identity of another important mitochondrial channel, the ATP-sensitive mitochondrial potassium channel, Mito-K$_{ATP}$, was also revealed.

A major motivation of our effort to advance current molecular understanding in cardiovascular system has been to develop molecular-based therapy to treat the underlying diseases. In 2012 BCVS, we heard several exciting developments in translating these molecular discoveries into clinical utilities. **Dr Francis Spinale** presented his vision of exploiting proteolytic elements in the extracellular matrix (such as matrix metalloproteinases and its regulating microRNAs) as potential biomarkers as well as drug targets for heart diseases. **Drs Howard Rockman and Ruiping Xiao** explored biased or isoform-specific G-protein–coupled receptor signaling to develop novel therapies based on novel agonists. **Dr David Kass** presented current status of heart failure trails targeted to protein kinase G signaling based on his findings of local cGMP signaling in cardiac regulation. **Dr Douglas Sawyer** discussed recent progress in neuregulin-1–based therapy, especially in the context of anticancer drug-induced cardiotoxicity. These encouraging developments share a common path from basic discovery at fundamental mechanistic level to future therapy that exemplifies the promise as well as challenges of translating basic scientific knowledge into clinical practice.

Although molecular characterization can lead to in-depth understanding of each player in cardiovascular system, understanding their interaction and integrating their function at whole-cell, whole-organ, and whole-organism level remain a major challenge to the field. BCVS 2012 featured several pioneering efforts based on systems approaches. A major advancement in the field is the rapid development in novel Omics tools. These include metabololmic profiling during pathological hypertrophy, heavy water labeling technique combined with high throughput, systems analysis on
human failing heart samples to discover novel gene-interaction modules associated with high-throughput chemical genomics to discover small molecules that promote cardiac regeneration, high-resolution proteomic approach to analyze protein turnover at systems level, and the development of hybrid mouse diversity panel to study heart failure and other complex diseases. There is no doubt that these emerging approaches will advance the basic understanding of the cardiovascular system and accelerate translation to disease diagnosis and treatment.

Long-standing topics such as cardiac remodeling and fibrosis were also on the program, and the various talks offered novel perspective in the molecular mechanisms underlying cardiac adverse remodeling. Stress-responsive cytokines, protein kinase C signaling, integrins, and sarcomeres were exposed as important determinants of cardiac remodeling. Fibrosis continues to gain importance in the setting of left ventricular dysfunction, and Stefan Engelhardt discussed a novel intriguing function of the multidrug resistance family of proteins that extrude cyclic nucleotides and affect the behavior of cardiac fibroblasts.

Modeling cardiovascular diseases, in vitro has become possible as a result of induced pluripotent stem cell technology. Several talks showed that such human-induced pluripotent stem cell lines provide a powerful, unlimited source of cells to generate differentiated cardiac cells that can be used to elucidate disease pathogenesis for drug discovery and development, toxicology screening, personalized medicine, and eventually cell replacement therapies. Human 3-dimensional engineered cardiac tissues have been created from these induced pluripotent stem cell–derived cardiomyocytes and characterized in terms of contractile function, structural organization, gene expression, and response to pharmacological intervention, replicating key aspects of natural human myocardium. However, it was clear from the tissue engineering session that more work needs to be done to produce adult-like cardiac tissues from induced pluripotent stem cells.

The cell therapy session was quite animated as cardiac progenitor cells dominated. Dr Roberto Bolli presented follow-up data from the SCIPIO trial showing continued improvements in ejection fraction in the 16 patients who received right atrial appendage–derived cardiac progenitor cells (ckit+). The CADUCEUS study which demonstrated a reduction in infarct size and an increase in viable myocardium was also discussed, whereas the C-CURE study showed improved ventricular function in patients with moderate left ventricular dysfunction. The BAMI trial will enroll in the second quarter of this year to explore further arenas of stem cell therapy. Combination of mesenchymal and ckit+ cell delivery was presented by Dr Joshua Hare as a new promising strategy for further enhancing the effectiveness of cardiac progenitor cells.

Nanoparticles are playing a large role in molecular imaging and delivery systems. Nano-based strategies were showcased for delivering genes to the heart, lungs, and stem cells, whereas multi-imaging modalities are being used to track various stem cells in the cardiovascular system.

Chinese Basic Cardiovascular Research Conference

For the first time at BCVS, a contingent of Chinese investigators joined the meeting with their own 1-day session before the main conference. Organized by Dr Rui-ping Xiao, they came from leading research institutes and universities in China represented by Institute of Molecular Medicine at Peking University, Peking Union Medical College, Shanghai Fudan University School of Medicine, and Chinese Academy of Sciences and Medical Sciences. The topics of the conference ranged from genetics and population studies in cardiovascular diseases to targeted molecular characterization and nonhuman primate models of cardiovascular and metabolic diseases.
They showcased the rapid advancement and many unique opportunities of basic and translational cardiovascular research in China. The highlight of the Chinese Basic Cardiovascular Research Conference included a keynote lecture from Dr Depei Liu on sirtuin-1 in Aging and Caloric Impact on Cardiovascular Systems and a lecture from Dr Wally Koch on the promises and challenges in translational medicine. As predicted by Dr Mark Sussman in his closing remarks, future collaboration between BCVS and China will help us to accomplish our common goal of conquering cardiovascular diseases across the globe.

Career Development Sessions

It is a long-honored tradition at BCVS to promote the scientific careers of next-generation researchers in the field. The 2012 BCVS conference featured 2 career-focused sessions for trainees and for the first time highlighted 11 junior investigators in Oral Abstract presentations as part of the program. Dr Asa Gustafsson organized the first career development session by featuring 3 speakers from 3 diverse career paths. Dr Aarif Khakoo from Amgen, Dr Kathryn Claiborn from Journal of Clinical Investigation, and Dr Brandon Biesiadecki from Ohio State University presented their perspectives on their career development in industry, publishing, and academic routes. The second career development session was organized for an international audience where Dr Wally Koch, Dr Wolfram Zimmerman, and Dr Rui-ping Xiao highlighted the training and research opportunities in the United States, European Union, and China. The main highlight of promoting young investigators at BCVS would be the Outstanding Early Career Investigator Award competition. Selected from 25 initial applicants, 3 finalists (Dr Reza Ardehali, Dr Jin O-Uchi, and Dr Toshitaka Yajima) were judged based on their submitted manuscripts and their performance during their oral presentation to a judge panel consisting of well-established senior investigators led by Dr Jeffery Robbins.

At BCVS dinner on July 25th, 7 Outreach Fellowships and 20 Travel Awards were presented to young trainees for their participation.

Judging from the quality of the abstracts and the winning abstract presentations, it is reassuring to note the outstanding quality and enthusiasm from the young investigators in basic cardiovascular research. They bring a sense of optimism and courage to all of us.

“There is no better way than to spur the imagination than to ignite a dialog between established findings and new modes of inquiry, between what we have come to know and what we seek. Somewhere in between lie the seeds of discovery, and it is meetings such as BCVS that move us closer to them. Looking forward, BCVS 2013 will be hosted by Drs Elizabeth McNally (University of Chicago) and Eric Olson (University of Texas Southwestern) and will be held in Las Vegas, Nevada.

For a selection of presentation slides and video visit americanheart.org. Additionally, all abstracts presented at the BCVS 2012 meeting can be found online at Circulation Research.

Disclosures

None.