



In Translation

The Newsletter of the International Society for Cardiovascular Translational Research

Vol 1/No 1

Welcome to *In Translation*

Despite advancements in medical education and technology, innovation and product development are still lagging in attention. The resulting consequence: many extraordinary innovations are never launched.

The International Society for Cardiovascular Translational Research was born from a desire to ensure those sparks continue to ignite the advancement of medicine and health care, bringing the latest from the lab to the bedside as quickly and safely as possible by

helping navigate those translational pathways.

As more individuals have joined the ISCTR, our need to communicate about our society and our field has expanded. And thus we have created this newsletter, *In Translation*, to keep you current with both.

Inside you will find a mix of articles ranging from society news, including the schedule for our annual symposium, to an introduction to our innovative eTextbook to an overview of recent articles in *JCTR*, the journal of the ISCTR. These



ISCTR President Nabil Dib, MD, MSc

are the types of features you can expect each issue as we keep you current on news from the ISCTR.

We hope you enjoy *In Translation*, and we look forward to your feedback!

Honoring Genius: Glen Nelson and Eugene Braunwald

When one thinks of innovation in translational research, it is likely that two names spring quickly to mind. It is fitting, then, that the International Society for Cardiovascular Translational Research has established an award that will be named for one and be bestowed for the first time on the other.

The ISCTR Board of Directors announced that it has established the Glen and Marilyn Nelson Award for Cardiovascular Innovation and Translational Research and the first recipient will be Eugene Braunwald, MD, MACC, MACP. The award will be presented at the 9th Annual ISCTR Symposium on April 4 in Chicago.

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ISCTR

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What is the ISCTR?

At its heart, the International Society for Cardiovascular Translational Research ([ISCTR](#)) is a visionary group of clinicians, researchers, scientists, inventors, regulators, and more who came together with a goal to expedite scientific discovery to clinical application (patients). Originally founded in 2007 by Dr. Nabil Dib, the ISCTR has expanded its reach and its borders to include members from around the globe united in a desire not only to safely and swiftly accelerate bench to bedside breakthroughs to benefit patients, but also advocate for critical health care policy and quality cardiovascular care through education, research promotion, and development and application of standards and guidelines.

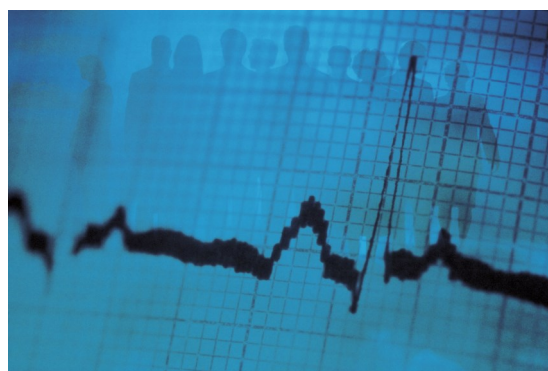
Recently, members of the ISCTR board convened a meeting with industry representatives and guideline writing committee leaders to discuss whether technology that had garnered FDA approval and was in wide use could and would be included with the next focused guideline update. The presentations and lively discussion will help inform research and reporting efforts moving forward.

Education is considered key at all levels of the ISCTR. Our ninth annual scientific symposium, held in conjunction with the annual Scientific Sessions of our collaborator, the American College of Cardiology, is coming up on April 4 in Chicago, Illinois. For more information about our outstanding cadre of speakers, please see the article on page 9.

When it comes to education, the ISCTR has taken a long look at the educational curriculum of medical school's residency and fellowship programs and have found none that teach about the *process* of innovation. This means everything from such topics as product development and testing and trial design to understanding intellectual property issues and laws and regulatory pathways while learning how to write business plans and fundraise. This multidisciplinary structure forms the building block for translational research.

Without actual training in these essential areas, the interaction between regulatory authorities, scientists, and industries often grows unproductive, resulting in frustration that translates to delay of product approval and increased costs, a scenario that benefits no one and ultimately hurts patients. The ISCTR is paving the way to provide this critical path through education by establishing a new curriculum and scholarship for cardiovascular translational research and specialized educational centers equipped with the infrastructure that has the ability to deliver such education. A major first step: authoring *Cardiovascular Translational Research*, a new text that delves into the critical pathways for product development of devices, biologics, and drugs. More on this groundbreaking eTextbook is on page 6.

Innovation in education and advocacy is the hallmark of the ISCTR and its members. This newsletter will help you stay updated on both via the ISCTR.



Member News and Notes

Jacques, Bax Join ISCTR Board

At a recent meeting, the ISCTR Board of Directors expanded its numbers and reach by electing two new directors: Louis Jacques, MD, and Jeroen Bax, MD, PhD.

“We are extremely pleased that two such distinguished professionals are joining the ISCTR board. Both Dr. Jacques and Dr. Bax are world renowned experts in the field and understand the rapid and dynamic changes cardiovascular medicine faces today,” noted **Nabil Dib, MD**, ISCTR President. “We welcome Louis and Jeroen and look forward to an effective collaboration with them for years to come.”

Louis Jacques, MD, is Chief Clinical Officer and a Senior Vice President at ADVI, a health care advisory services firm with offices in Washington DC, Austin, and San Francisco. Before joining ADVI in 2014, Dr. Jacques was the Director of the Coverage and Analysis Group (CAG) in the Centers for Medicare & Medicaid Services (CMS), where he managed Medicare fee for service coverage policy development on technologies as diverse as molecular diagnostic

testing, advanced imaging, chemotherapeutics, wound care, and screening and preventive services.

Before joining CMS in 2003, he served as the Associate Dean for Curriculum at Georgetown University School of Medicine, where he also saw patients at the Lombardi Cancer Center in his practice of hospice and palliative medicine. While in active clinical practice he was a diplomate of both the American Board of Hospice and Palliative Medicine and the American Board of Family Medicine.

Dr. Jacques earned his undergraduate degree in 1978 from



Louis Jacques, MD

Georgetown University and his MD in 1982 from the University of Maryland. After completing his residency in family practice, he served in a National Health Service Corps assignment in a Waterloo, Iowa, community health clinic. Before returning to

Washington DC, he worked in Detroit with the Henry Ford Medical Group and joined the faculty of the Wayne State University School of Medicine.

Jeroen J. Bax, MD, PhD, is Professor of Cardiology and Director of Noninvasive Imaging at Leiden University Medical Center in Lei-

den, The Netherlands, where he received his medical degree and cardiology training. Dr. Bax received his PhD from the Free University in Amsterdam, where he



Jeroen J. Bax, MD, PhD

supervised the thesis of 26 PhD fellows.

President-Elect of the European Society of Cardiology, Dr. Bax has long served the ESC in numerous capacities, including chair of the Cardiology Practice Guidelines Committee, Chair of the Scientific Pro-

gram, Co-Chair of two International Conferences on Nuclear Cardiology, Chair of the Press Committee, and Co-Editor of two books on cardiac imaging. Dr. Bax continues to serve as Co-Director of the ETP course on Nuclear Cardiology, a position he has held since 2003. He is a Fellow of the ESC as well as the American College of Cardiology and the American Society of Nuclear Cardiology. In 2008, Dr. Bax was honored with a Silver Medal from ESC and the Douglas P. Zipes Award from ACC.

Currently an Associate Editor of the *European Heart Journal* and a Section Editor for UptoDate, Dr. Bax sits on the editorial boards of five additional professional journals and previously was an Associate Editor for the *Journal of the American College of Cardiology*. Widely published, Dr. Bax's major research interest is in applying various noninvasive imaging techniques in clinical cardiology, including coronary artery disease, arrhythmias, and heart failure.



Glen and Marilyn Nelson

Nelson Award

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“In discussing the creation of this award, we knew immediately that it should be named for Glen Nelson, who more than anyone in our field today has not just led the field of translational research but bridged its many facets, literally embodying the ISCTR mission, and his wife, Marilyn, a world leader in business and renowned author on leadership. And there is no one in medicine today who represents innovation more, the man credited with transforming the science and practice of cardiology, than Gene Braunwald,” said ISCTR President **Nabil Dib, MD**.

Glen D. Nelson, MD, is chairman of GDN Holdings, LLC, (Medical Products and Services), where he focuses assisting health care startup ventures, utilizing the network and experience amassed over his 50-year career in health care delivery, insurance, and the medical device industry.

Prior to founding GDN Holdings,

Dr. Nelson was a member of the board of directors of Medtronic Inc. from 1980-2002, during which time he served both as executive vice president and vice chairman. Before joining Medtronic, Dr. Nelson practiced surgery from 1969-86. He was chairman, president and chief executive officer of the Park Nicollet Medical Center, a large multi-specialty group practice in Minneapolis from 1975-86. He also was chairman of the board and chief executive officer of American MedCenters, Inc., from 1984-86.

Dr. Nelson served as Chairman of MinuteClinic from its inception until the acquisition by CVS, and currently serves or served on a number of diverse boards, including CSI, Inspire Medical Systems, LLC, Anhesa, LLC, Carlson Holdings, Inc., EarLens Corporation, InterValve, Inc., MyMeds, Inc. NxThera, RedBrick

Health, Travelers, DexCom, Inc., Angiotech Pharmaceuticals and American MedCenters. Dr. Nelson received a BA from Harvard College and an MD from the University of Minnesota. He is an Emeritus Clinical Professor of Surgery at the University of Minnesota.

The former chairman and chief executive officer of Carlson, a global travel and hospitality company, **Marilyn Carlson Nelson** is the co-CEO of Carlson Holdings. She has appeared on Forbes magazine’s list as one of “The World’s 100 Most Powerful Women” and named one of “America’s Best Leaders” by *U.S. News and World Report*. Former chair of the U.S. Travel and Tourism Advisory Board, Nelson also led the National Women’s Business Council, a bipartisan advisory council to the President and Congress. She is the best-selling author of “How We Lead Matters: Reflections on a Life of Leadership.”

Under her leadership, Carlson was the first major North American travel and hospitality company to sign the industry’s international code of conduct against the sexual exploitation of children

in the industry. Carlson also joined with the Queen of Sweden to co-found the World Childhood Foundation to protect street children around the world. In 2014, Nelson was chosen by a committee of Nobel Prize recipients to receive the “Oslo Business for Peace Award,” which recognizes leader-

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There is no one in medicine today who represents innovation more, the man credited with transforming the science and practice of cardiology, than Gene Braunwald.

ship in promoting responsible business practices.

Nelson serves or has served on the boards of the Mayo Clinic Board of Trustees, United Nations Global Compact, the Committee Encouraging Corporate Philanthropy, the National Endowment for Democracy, ExxonMobil, the Minnesota Orchestra, and the Kennedy Center for the Performing Arts. She graduated from Smith College with

a degree in international economics and studied at the Sorbonne in Paris and the Institut des Hautes Etudes Economiques et Politiques in Geneva.

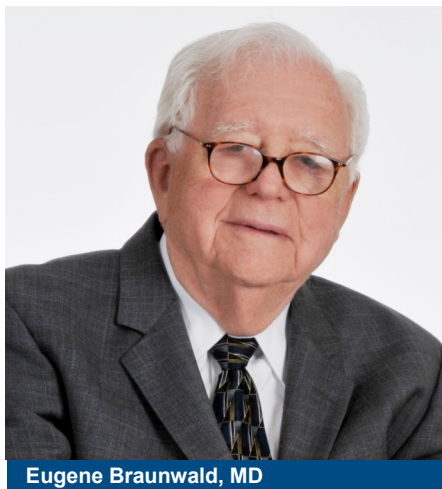
Before the 1950s and 1960s, heart attacks were often considered death sentences by the public and little better by the physicians attempting to treat them. Credit the work of **Eugene Braunwald, MD**, considered the leading name in cardiology, for proving that an MI was not a sudden shot to the heart but a dynamic process that could be treated and in doing so, transformed the field of cardiology from

one of passive observation to active intervention.

Dr. Braunwald's first major paper was published in *Circulation Research* in July 1954, and he has

authored more than 1,400 articles since as well as *Braunwald's Heart Disease*, recognized as the best book on the subject worldwide. For the past 30 years, as Chairman of the TIMI Study Group, he and his colleagues

demonstrated im-



Eugene Braunwald, MD

proved patient survival with a patent coronary artery which led to the widely accepted "open artery hypotheses." They were the first to show the benefit of preventing adverse remodeling of the infarcted ventricle with ACE inhibition. In the PROVE-IT Trial, they demonstrated the benefit of more intensive reduction of LDL in high-risk CAD patients, favorably affecting the lives of millions.

The Distinguished Hersey Professor of Medicine at Harvard Medical School, Dr. Braunwald received his medical training at New York University and completed his resi-

dency at the Johns Hopkins Hospital. He served as the first Chief of the Cardiology Branch and as Clinical Director of the National Heart, Lung and Blood Institute, founding Chairman of the Department of Medicine at the University of California, San Diego. From 1972 to 1996 he was Chairman of the Department of Medicine at the Brigham and Women's Hospital. He was a founding trustee and Chief Academic Officer of Partners HealthCare System.

Dr. Braunwald has received numerous honors and awards including the Distinguished Scientist Award of the American College of Cardiology, Research Achievement, and Herick Awards of the American Heart Association, and the Gold Medal of the European Society of Cardiology, and is the recipient of 19 honorary degrees from distinguished universities throughout the world. Dr. Braunwald was the first cardiologist elected to the U.S. National Academy of Sciences. The living Nobel Prize winners in medicine voted Dr. Braunwald as "the person who has contributed the most to cardiology in recent years."

Mark your calendar:

ISCTR 2016 Symposium April 4, 2016

Keynote Address presented by Eugene Braunwald, MD, MACC, MACP

The Path to an Angiotensin Receptor Antagonist-Neprilysin Inhibitor in the Treatment of Heart Failure: A Triumph of Academic-Industry Collaboration

Highlight:

Chapter 1

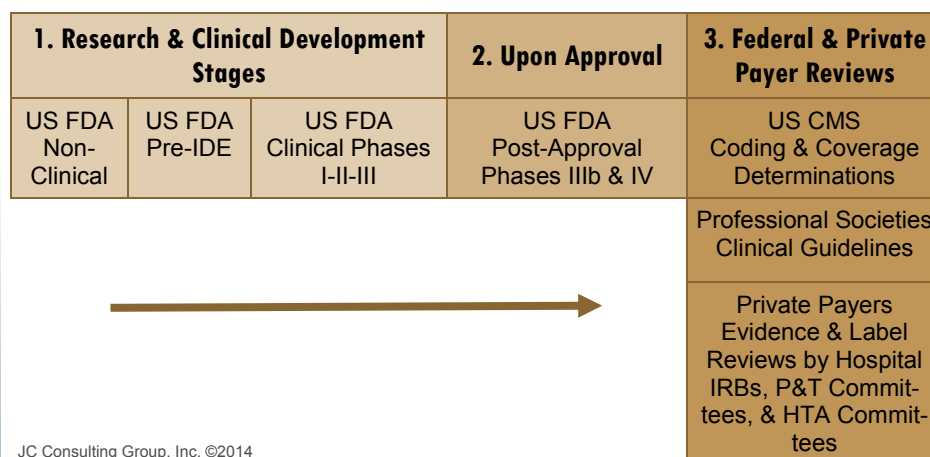
Intellectual Property & Strategy Development

This chapter pulls no punches from its first sentence: Intellectual Property is a business asset.

As such, intellectual property must be protected properly to maximize its benefits as a business asset. The chapter author, attorney Neil K. Nydegger, further details the four different types of intellectual property assets, which protect different interests in the marketplace: patents; trademarks and service marks; copyright; and trade secrets.

For instance, while patents generally protect inventions and discoveries that pertain to any new and useful process, they do not protect ideas. Legally, a patent is a deed of property rights.

Alternately, trademarks and service marks identify the source of the particular goods or services and protect the goodwill of a business, while copyrights protect the expression of a work. And finally, trade secrets — everything from a secret formula to a manufacturing schedule — hinge on staying secret to provide protection.



eTextbook infographic: Key stages and considerations in US medical device reviews

eTextbook: Parsing Pathways

While medical school curricula focused on the actual translation of translational research into final approved products and processes remains wanting, the ISCTR has created an in-depth, innovative eTextbook dedicated to assist residents and fellows learn more about this critical area of medicine.

Edited by **Nabil Dib, MD, MSc**, **Sir Magdi H. Yacoub, MD**, **Anthony N. DeMaria, MD**, and **Spencer B. King III, MD**, *Cardiovascular Translational Research* has been written by international experts not just in the medical research and patient care but from regulatory agencies and industry as well. The pioneering text is offered in two electronic versions (via the [iOS app for iPad](#) or through the [ISCTR web site](#)), a format that permits continuous updating of material — a key component to support an always-changing field.

The work of 85 authors, eTextbook is divided into 32 chapters in four parts, with the first section dedicated to critical areas in product development of devices, biologics, and drugs, and the subsequent sections focused on the translational pathways for each of those areas. Part 1 leads off with a discussion of intellectual property (see the sidebar to the left) followed by a look at strategies and decision making to obtain reimbursement for investigational and new devices, possible avenues to fund new ventures, the decision-making process regarding incorporating new products into clinical guidelines, and trial design.

The remaining three parts travel very different pathways depending on the topic area. For example, the device pathway offers in-depth reviews of the translation platforms and paths for specific devices, such as cardiac valves and mechanical circulatory support devices while the biologics section offers chapters on various aspects of cell and regenerative therapies including delivery systems. In the section on the drug translational pathway, topics include regulatory considerations and personalized medicine and translational genomics.

The text includes a variety of charts, tables, illustrations, and other graphics (such as the example above) to enhance learning. The eTextbook is available for a subscription fee either for the entire book or as individual sections.

Extra, Extra: *JCTR* Seeking Feedback

The *Journal of Cardiovascular Translational Research* is the official Journal of the International Society for Cardiovascular Translational Research (ISCTR). This may come as a frank surprise to many of you. The ISCTR is a unique and growing society of innovators, scientists, and clinicians. History does not provide many successful models of this type of professional scientific society linked with an academic journal. As the editor of *JCTR*, I am reaching out to all of you to ask for your thoughts and ideas on how we can establish a successful partnership that strengthens both entities.

We publish high-quality novel reviews and original articles focused in areas that bridge basic science, bioengineering, and clinical medicine. Our authors include pioneers in the field including **Eugene Braunwald, MD**, who will be recognized this spring by the ISCTR at the annual symposium in Chicago. Since 2008, the number of submissions to *JCTR* has nearly tripled and the number of Journals that cite *JCTR* articles (a mark of recognition) has grown from 26 to over 200. Our impact factor continues to rise each year, also suggesting that we are publishing papers that are being read and cited in the field.

Some recent articles include:

- *Linking Genes to Cardiovascular Diseases: Gene Action and Gene–Environment Interactions* — This review paper by **Ares Pasipoularides, MD, PhD**, from Duke University, looks at the emerging need to illuminate the physiologic functions of myocardial genes, as well as potential adaptive and



maladaptive modulations induced by environmental/epigenetic factors, and to do so in a cohesive manner to expand clinical utility.

- *Peripheral Venous Hemoglobin and Red Blood Cell Mass Mismatch in Volume Overload Systolic Heart Failure: Implications for Patient Management* — In this original paper, **Wayne L. Miller, MD, PhD**, and **Brian P. Mullan, MD**, from the Mayo Clinic, evaluated whether peripheral venous hemoglobin measurements reliably reflect circulating red blood cell mass in patients with volume overload decompensated chronic heart failure — and their findings could hold implications for volume management.
- *Pre-clinical Experience with a Multi-Chordal Patch for Mitral Valve Repair* — Surgical repair of flail mitral valve leaflets with neo-

chordoplasty produces good outcomes, but implementing it in anterior and bi-leaflet leaflet repair is challenging. In an original article now online, Chawla et al. report their pre-clinical experience with a novel multi-chordal patch for mitral valve repair that was designed based on human cadaver hearts, and laser cut from expanded polytetrafluoroethylene.

- *Toward Sex-Specific Guidelines for Cardiac Resynchronization Therapy?* — In this review paper, Zusterzeel et al. review discuss the physiology behind cardiac resynchronization therapy, sex-specific characteristics of heart failure, and cardiac electrophysiology and summarizes the current sex-specific literature to encourage consideration of CRT guidelines for women and men separately.

We are reaching out to ask for engagement from ISCTR members to learn how *JCTR* can better serve the needs of the society and the needs of scientific innovators globally. We welcome your feedback and invite you to read *JCTR* [online](#).

Jennifer L. Hall, PhD

Editor-in-Chief,
Journal of Cardiovascular Translational Research
Lillehei Heart Institute, Department of Medicine, University of Minnesota, Minneapolis

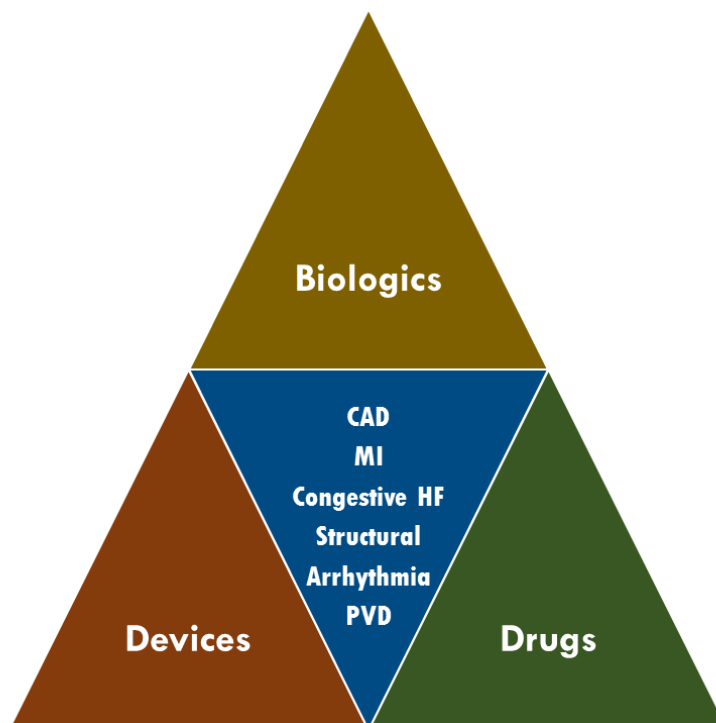
Council Creation Supports ISCTR Curriculum, Certification

In keeping with the ISCTR mission to provide an environment for collaboration and develop guidelines for training and certification in Translational Research, the Board of Directors has created a series of Translational Councils and seeks health care and industry professionals interesting in serving on each.

To change the way new physicians are taught to innovate and develop new therapeutic products, the ISCTR has published the eTextbook *Cardiovascular Translational Research* (see page 6) and, based in large part on this textbook, has established 18 translational pathways in cardiovascular research. Each main subject area — Biologics, Devices, and Drugs — will pursue pathways in arrhythmias, congestive heart failure, coronary artery disease, structural, myocardial infarction, and peripheral vascular disease.

The ISCTR is further collaborating with the Phoenix College of Medicine of the University of Arizona to formalize these pathways into accredited courses providing academic credits, with certification available for each separate pathway; completion of all 18 pathways qualifies for a Master's degree.

The Councils will mirror the 18 pathways, and council members will be called upon to assist in the development and delivery of the curriculum as well as serve as consultants for investigators and industry. In fulfilling these critical functions, the Councils will further the ISCTR's goal to accelerate and expedite scientific discovery into clinical application while decreasing cost.



Bridging the Chasm

We know that scientific discovery often starts with academia, while developing and producing a therapeutic product along with determining its safety and efficacy belong to industry. Partnerships between researchers and industry to bring life-saving innovations to the public used to be the norm — but now the divide between academic researchers and industry looms large, according to **Jeffrey Drazen, MD**, editor of the *New England Journal of Medicine*.¹

While acknowledging that he and other medical editors have voiced concerns over relationships between researchers and funders, Dr. Drazen added his voice to that of the FDA and other agencies and groups to encourage “greater interaction between academics and industry to provide tangible value for patients.”

The ISCTR Board recognizes the tainted relationship — both real and perceived — and also has identified a knowledge gap common to both disciplines. While the curriculum will help close that gap, the Translational Councils will actively work to improve the relationships with regulators and peer-review publications and the partnerships with industry.

If you are interested in serving on any of the councils or would like more information about what that service entails, please contact info@isctr.org.

¹*N Engl J Med* 2015;372:1853-1854.

2016 ISCTR Symposium Set for April 4

Held in conjunction with the American College of Cardiology's annual Scientific Sessions, the Ninth Annual ISCTR Symposium will run from 10:45 a.m. to 5:15 p.m. on Monday, April 4, in Room S505 at the McCormick Place Convention Center in Chicago, Illinois.

Highlighting the full-day program will be the presentation of the inaugural Glen and Marilyn Nelson Award for Cardiovascular Innovation and Translational Research and the first recipient will be **Eugene Braunwald, MD, MACC, MACP**, who will then deliver the Keynote Address on *The Path to an Angiotensin Receptor Antagonist-Neprilysin Inhibitor in the Treatment of Heart Failure: A Triumph of Academic-Industry Collaboration*.

According to Program Co-Chairs **Robert O. Bonow, MD, MS, MACC**, and **Anthony DeMaria, MD, MACC**, the symposium will cover topics that look at the transition of translational research through the years, weaving together different perspectives from the multitude of partners involved in cardiovascular translational research. Following the Keynote Address, the program is scheduled to include:



Cardiovascular Innovation and Translation I

- Cardiovascular Translational Surgery: Past, Present, and Future *Magdi H. Yacoub*
- Interventional Cardiology, Past, Present and Future *Spencer B. King*
- ISCTR/ACC Mission In CV Translational Research *Nabil Dib*

Cardiovascular Innovation and Translation II

- Perspective from an Innovator *G. Alain Cribier*
- Perspective from Industry (Chief Medical Officer, Abbott) *Charles A. Simonton*
- Perspective from FDA *Bram D. Zuckerman*
- Perspective from CMS (Former Director) *Louis Jacques*

Cardiovascular Innovation and Translation III

- Innovation Challenges *Richard Schatz*
- The Emerging Concept of the Bio-Design Institute for Cardiologists *Todd J. Brinton*
- Novel Adult Cells and Enhancement Strategies for Cardiac Regeneration *Stefanie Dimmeler*
- Update on Cardiovascular Stem Cell Therapy *Andreas M. Zeiher*

Cardiovascular Innovation and Translation IV

- Global Heart Health, Implications for Translational Research: Perspective of the President of the World Federation of Cardiology *Salim Yusuf*
- Consensus of Definition, Clinical Trial Design, and Endpoints *Bram D. Zuckerman*
- Lessons Learned from Randomized Clinical Trials and the National Registry *David R. Holmes*
- What Innovations in Coronary Artery Disease Will Change the Future of Cardiology? *Patrick W. Serruys*
- Emerging Techniques in Cardiac Imaging *Jeroen J. Bax*

For more information about the program, please visit www.isctr.org.