



<http://cbac.wustl.edu>

Newsletter

No. 3, Spring 2007 issue

Yoram Rudy, Director

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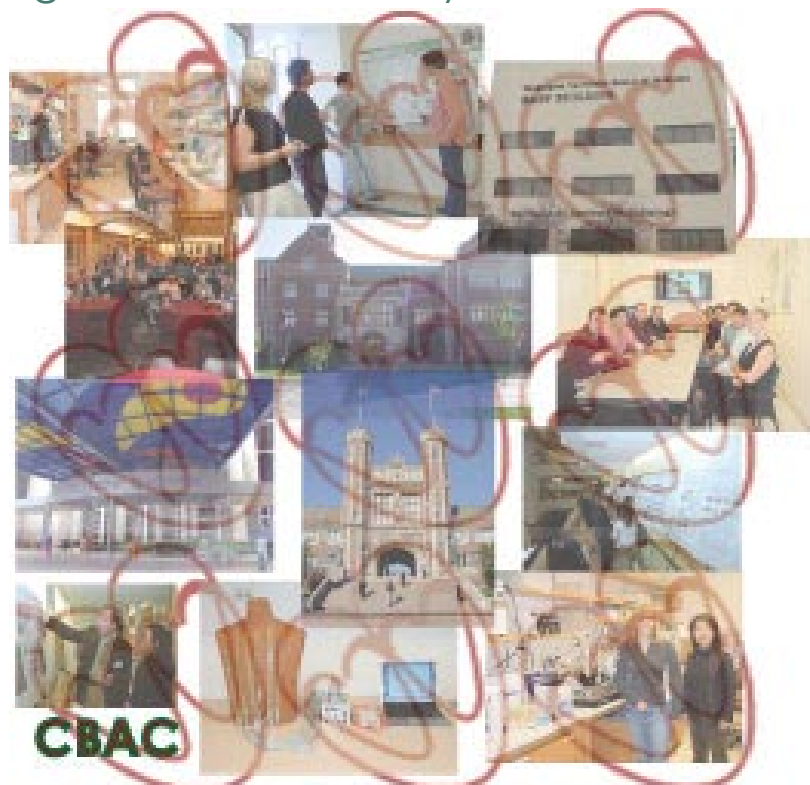
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The **Cardiac Bioelectricity & Arrhythmia Center (CBAC)** is saying farewell to its Coordinator and Webmaster, **Jennifer Godwin-Wyer**. She departs at the end of February after the birth of her first child, Callum Michael, to follow her husband, Dr. Paul Wyer, to Houston, Texas where he has accepted a new position. We wish Jennifer and her family all the best for the future as she will be missed by all at CBAC. Her dedication and devotion to the center and its members was evident and always showed in the excellent work she produced including coordinating the seminars, being the webmaster for the CBAC website, creating and designing the newsletter, and all the other multitude of jobs she performed. See Page 10 for a personal farewell from Jennifer.

The fourth session of the **CBAC Seminar Series** began January 2007 and will run until April. The Spring 2007 seminar schedule includes several outside speakers including David Wilber, Craig January, David Van Wagoner, Elliot McVeigh, Paul Volders, and Bruno Taccardi, as well as CBAC faculty members [the Spring schedule can be found on Pages 9-10 as well on the CBAC website at <http://cbac.wustl.edu/pageBulletinBoardClubs.asp>]. The seminars are held most Monday afternoons at 5:30 pm in Whitaker Hall, room 218 on the Danforth campus.

The **CBAC Website** is being given a face lift. Due to the popularity of the CBAC seminar series, online seminar video archives and the newsletter, which are all integral parts of the center, the website has been revamped to display these items more prominently and allow users to navigate to them more quickly. See Page 7 for more details.

The **CBAC** center welcomes 4 new faculty members this year. See Page 10 for more details on the new members, and Pages 5-6 for a complete listing of all CBAC faculty members.



Published by the Cardiac Bioelectricity and Arrhythmia Center (CBAC)

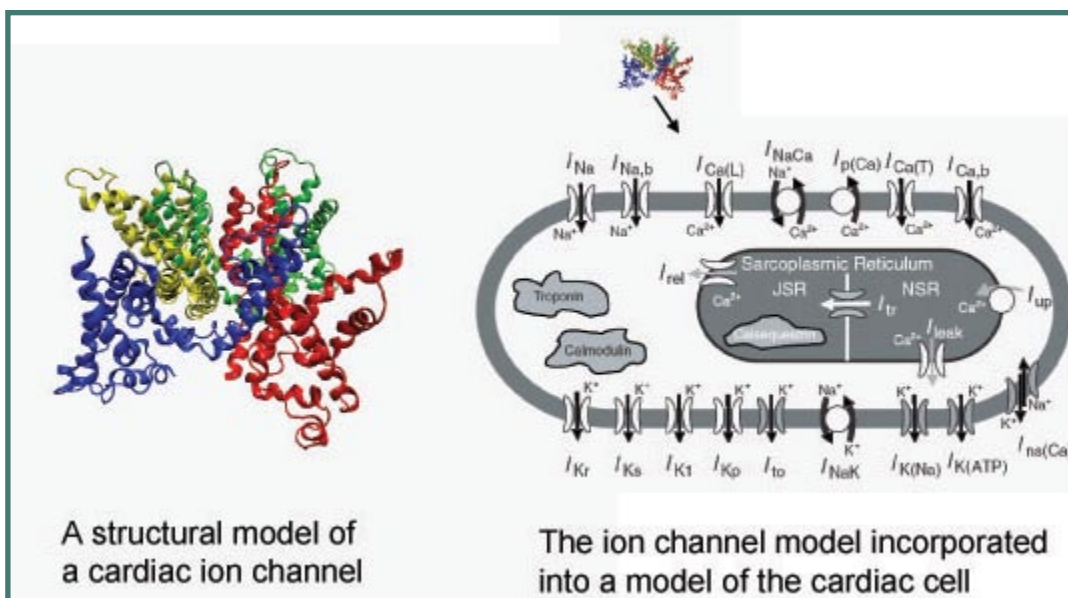
Washington University in St. Louis
Whitaker Hall, Room 290
1 Brookings Dr., CB 1097
St. Louis, MO 63130-4899



This newsletter No. 3 marks one year since the first **CBAC** newsletter was published. During the past year, the interdisciplinary nature of the center has been established and strengthened. We have had many distinguished scientists and clinicians visiting the CBAC and presenting state-of-the-art work in the field of cardiac bioelectricity in our Monday evenings seminar series. Many of them commented on the unique molecule-to-bedside environment that CBAC provides and the unique research opportunities that arise from such environment. We also hosted a scientific delegation from the National Cheng Kung University of Taiwan, headed by the Vice President of the University and Dean of the College of Medicine, and started planning research collaborations between **CBAC** and Cheng Kung U.



Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S.



A structural model of a cardiac ion channel

The ion channel model incorporated into a model of the cardiac cell

The seminars have proven to be a wonderful forum for learning about the latest developments in cardiac arrhythmia research and clinical care. It has been very rewarding to see the large attendance and listen to discussions that usually continued long after the formal presentation had ended. My thanks to all of you for actively participating in this **CBAC** activity.

I would like to take this opportunity to remember a dear colleague and friend, **Dr. Denis Escande** who passed away last November at the age of 53 after battling with illness. Professor Escande was the Director of the Institut du Thorax of the Inserm ("Institut National de la Santé et de la Recherche Médicale") Unit U533 in Nantes, France. He was also the Director of the Department of Clinical Physiology of Nantes University Hospital. Denis was a pioneer and a leader in the field of cardiac ion channels and arrhythmia research. In particular, he studied the genetic basis of cardiac arrhythmias and sudden death. We will miss his contagious enthusiasm for science, his inquisitive questions in scientific meetings and his happy laughter when a new concept was defined and understood. I will personally miss his joie de vivre and the many discussions we have had on issues other than science, from politics to literature. I know that his wife, Dr. Sophie Demolombe, will continue his great work with equal enthusiasm.

Finally, we regretfully have to say goodbye to **Jennifer Godwin-Wyer**, the CBAC Coordinator since its first day. Jennifer and husband, Paul, recently had a baby boy named Callum. The family is relocating to Houston, where Paul is embarking on a new career. Jennifer has been instrumental to the success of CBAC. Her loyalty to its mission and pride in its vision were commented on by many of you and the visitors to the center; she even edited and produced this issue of our newsletter during her last days with us. We will miss Jennifer greatly (see Page 10 for her personal farewell).

ABOUT CBAC

CBAC is an interdisciplinary center set up to foster intellectual interactions and collaborations between researchers and clinicians from the Washington University Danforth and Medical School campuses in an effort to understand the heart's irregular rhythms and to prevent their fatal consequences. The **CBAC** center includes 33 faculty members from various departments in the Danforth and Medical School campuses. [CBAC Faculty member directory can be found on Pages 5-6].

CBAC publishes information about the center's faculty members and their research through the CBAC website located at <http://cbac.wustl.edu> and the CBAC brochure which is distributed both in print and online in PDF format. The center also publishes educational dissemination materials that currently include the CBAC Video Archives (digital videos in MPEG and DIVX formats of the CBAC seminars that are made available online for public viewing and can be found on the CBAC website at <http://cbac.wustl.edu/pageEducationVideo.asp>), and the CBAC Newsletter which is also distributed both in print and available online in PDF format. To enhance education and outreach goals, **CBAC** sponsors a seminar series held throughout the academic year [the CBAC Spring 2007 seminar schedule is listed on Pages 9-10]. If you would like a printed copy of either the CBAC brochure, or current or past issues of the CBAC Newsletter, please email cbac@biomed.wustl.edu with your name and mailing address.

An Overview of the CBAC center

The CBAC Mission Statement

The **Cardiac Bioelectricity and Arrhythmia Center, CBAC**, is an interdisciplinary center whose goals are to study the mechanisms of rhythm disorders of the heart (cardiac arrhythmias) and to develop new tools for their diagnosis and treatment. Cardiac arrhythmias are a major cause of death (over 300,000 deaths annually in the US alone; estimated 7 million worldwide) and disability, yet mechanisms are poorly understood and treatment is mostly empirical. Through an interdisciplinary effort, CBAC investigators apply molecular biology, ion-channel and cell electrophysiology, optical mapping of membrane potential and cell calcium, multi-electrode cardiac electrophysiological mapping, Electrocardiographic Imaging (ECGI) and other noninvasive imaging modalities, and computational biology (mathematical modeling) to study mechanisms of arrhythmias at all levels of the cardiac system. Our mission is ***"To battle cardiac arrhythmias and sudden cardiac death through scientific discovery and its application in the development of mechanism-based therapy"***.

Research Goals

Research projects at **CBAC** cover the entire spectrum from molecular and cellular processes to mechanisms, diagnosis and treatment of arrhythmias in patients. The cross-disciplinary structure of CBAC promotes collaborations between researchers and clinicians and fosters a multiple-approach strategy to the study, diagnosis and treatment of cardiac arrhythmias. Approaches include molecular, single-cell and whole-animal experiments, mathematical modeling and computer simulations, and patient studies during imaging, catheterization and open-heart surgery. Among the state-of-the-art techniques employed are genetics, biomolecular structural analysis, patch clamp recordings from single ion channels, ion-selective electrode measurements, high resolution electrical mapping, optical mapping of cardiac activation and cell-calcium, Electrocardiographic Imaging, supercomputing and computer graphics, signal processing and image analysis.

Projects include:

- Molecular structure and electrophysiological function of cardiac ion channels
- Development of mathematical models of cardiac ion channels, cells and tissues
- Regulatory pathways in cardiac cells
- Mechanisms of hereditary cardiac arrhythmias
- Arrhythmias in myocardial ischemia and infarction

ABOUT CBAC cont.; FOCUS ON...

- Cell-to-cell communication and action potential propagation in the diseased heart
- Structure and function of the atrio-ventricular node
- Mechanisms of cardiac (ventricular and atrial) fibrillation and new strategies for defibrillation
- Development and application of a novel imaging modality for cardiac arrhythmias
- Mechanisms of cardiac resynchronization therapy for heart failure

Education and Training Goals

An important goal of **CBAC** is to enhance and promote education and training in biomedical engineering, life sciences, and clinical medicine. The cross-disciplinary structure of CBAC facilitates a synergistic relationship between training, research and clinical medicine. The educational component of CBAC builds on graduate programs in the Department of Biomedical Engineering and the Medical School. Through CBAC, graduate students and scientists in engineering and life sciences can participate in clinical lectures, seminars, case presentations and clinical procedures such as diagnosis and treatment of arrhythmias in the catheterization laboratory. Similarly, post-M.D. clinical fellows can participate in lectures and seminars in the basic science departments and in research projects in the basic science laboratories.

Support and Facilities

Research is supported through grants to affiliated faculty. Funding agencies include: NIH, AHA, VA, Whitaker Foundation and NSF. A number of projects are funded through industrial support (pharmaceutical- and device-related studies). Facilities include state-of-the-art laboratories for genetics, molecular biology, cellular and subcellular electrophysiology, optical mapping of action potentials and cell-calcium, multi-electrode mapping of cardiac electrical activity, and theoretical and computer simulations using supercomputing. Studies can also be conducted in clinical facilities for MRI, CT and Ultrasound imaging, and for electrophysiology studies and arrhythmic treatment during cardiac catheterization and surgery.

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Focus On...



David R. Van Wagoner, Ph.D. received his Ph.D. in Pharmacology from the Thomas Jefferson University in Philadelphia in 1985. He currently holds the positions of Associate Staff at the Cleveland Clinic Departments of Molecular Cardiology & Cardiovascular Medicine, where he is the Director of the Cleveland Clinic Basic Cardiac Electrophysiology laboratory.

Dr. Van Wagoner is also an Associate Professor in the Department of Molecular Medicine of Case Western Reserve University Medical School. His research interests include cardiac arrhythmia mechanisms, atrial fibrillation, and ion channel pathophysiology.

Excerpt from <http://www.lerner.ccf.org/moleccard/vanwagoner/>:

"We have shown that markers of systemic inflammation such as C-reactive protein are elevated in many patients with AF, and that these markers tend to be more elevated in patients with persistent than with paroxysmal forms of AF. This suggests that inflammatory mechanisms may be related to remodeling of the atria associated with increased persistence and increased risk of complications."

continued on Page 16..

*ABOUT CBAC cont.***CBAC Faculty Members****Director - Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S.**

The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine, Radiology, and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC)

R. Martin Arthur, Ph.D.

Newton R. and Sarah Louisa Glasgow Wilson Professor of Engineering; Professor of Electrical and Systems Engineering; Professor of Biomedical Engineering

Philip V. Bayly, Ph.D.

Lilyan and E. Lisle Hughes Professor of Mechanical Engineering, Aerospace Engineering, and Biomedical Engineering

Sanjeev Bhalla, M.D.

Assistant Professor of Radiology; Assistant Radiology Residency Program Director, Mallinckrodt Institute of Radiology

John P. Boineau, M.D.

Professor of Surgery, Medicine, and Biomedical Engineering

Jane Chen, M.D.

Assistant Professor of Medicine

Jianmin Cui, Ph.D.

Associate Professor of Biomedical Engineering on the Spencer T. Olin Endowment

Ralph J. Damiano, Jr., M.D.

John M. Shoenberg Professor of Surgery; Chief of Cardiac Surgery

Victor G. Davila-Roman, M.D.

Associate Professor of Medicine, Anesthesiology, and Radiology; Medical Director, Cardiovascular Imaging and Clinical Research Core Laboratory

Igor R. Efimov, Ph.D., F.A.H.A., F.H.R.S.

The Stanley and Lucy Lopata Associate Professor of Biomedical Engineering, Cell Biology & Physiology, and Radiology

Mitchell N. Faddis, M.D., Ph.D.

Assistant Professor of Medicine, Radiology; Clinical Cardiac Electrophysiologist, Barnes Hospital

Richard W. Gross, M.D., Ph.D.

Professor of Medicine, Chemistry, and Molecular Biology & Pharmacology; Director, Division of Bioorganic Chemistry and Molecular Pharmacology (Joint Appointment with the School of Medicine), Department of Internal Medicine, Department of Molecular Biology and Pharmacology and Department of Chemistry, Washington University School of Medicine

Patrick Y. Jay, M.D., Ph.D.

Assistant Professor of Pediatrics and Genetics

R. Gilbert Jost, M.D.

Elizabeth Mallinckrodt Professor of Radiology; Chairman, Department of Radiology; Director, Mallinckrodt Institute of Radiology

Daniel Kelly, M.D.

Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Director of Cardiology; Co-Director, Cardiovascular Division, Department of Medicine, Washington University School of Medicine

Sándor J Kovács, Ph.D., M.D.

Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering

ABOUT CBAC cont.; CBAC Website

CBAC Faculty Members cont.

Bruce D. Lindsay, M.D.

Associate Professor of Medicine; Director, Clinical Electrophysiology Laboratory at Washington University

Achi Ludomirsky, M.D.

The Louis Larrick Ward Professor of Pediatrics and Biomedical Engineering; Director, Pediatric Cardiology, Washington University School of Medicine and St. Louis Children's Hospital

Arye Nehorai, Ph.D.

Chairman of the Department of Electrical & Systems Engineering; Eugene and Martha Lohman Professorship of Electrical Engineering

Jeanne M. Nerbonne, Ph.D.

Alumni Endowed Professor of Molecular Biology and Pharmacology

Colin G. Nichols, Ph.D.

Professor of Cell Biology and Physiology

Joseph A. O'Sullivan, Ph.D.

The Samuel C. Sachs Professor of Electrical Engineering; Professor of Radiology and Biomedical Engineering; Director of Electronic Systems and Signals Research Laboratory; Associate Director of Center for Security Technologies

Edward K. Rhee, M.D.

Assistant Professor of Pediatrics, Washington University School of Medicine; Director, Arrhythmia Services, St. Louis Children's Hospital

Jean E. Schaffer, M.D.

Associate Professor of Medicine, Molecular Biology & Pharmacology

Richard B. Schuessler, Ph.D.

Associate Research Professor of Surgery; Associate Research Professor of Biomedical Engineering; Director, Cardiothoracic Surgery Research Laboratory

Jinyi Shi, Ph.D.

Research Faculty, Biomedical Engineering

Gautam K. Singh, M.D., M.R.C.P.

Associate Professor, Department of Pediatrics, Director of Non-invasive Cardiac Imaging Research; Co-Director, Echocardiography Laboratory, Washington University School of Medicine

Timothy W. Smith, D.Phil., M.D.

Assistant Professor of Medicine

Jason W. Trobaugh, D.Sc.

Research Instructor in Medicine, Electrical and Systems Engineering

Lihong Wang, Ph.D.

Gene K. Beare Distinguished Professor; Department of Biomedical Engineering; Director, Optical Imaging Laboratory

Samuel A. Wickline, M.D.

Professor of Medicine; Adjunct Professor of Physics and Biomedical Engineering; Co-Director of Cardiology

Pamela K. Woodard, M.D.

Associate Professor, Diagnostic Radiology, Cardiovascular Imaging Laboratory, Mallinckrodt Institute of Radiology

Kathryn A. Yamada, Ph.D., F.A.H.A.

Research Associate Professor of Medicine

You can read more about the CBAC faculty members and their research interests on our website at <http://cbac.wustl.edu/pageFaculty.asp> and <http://cbac.wustl.edu/pageResearch.asp>.



CBAC Website

The **Cardiac Bioelectricity and Arrhythmia Center (CBAC)** website is located at <http://cbac.wustl.edu>.

The **CBAC website** has undergone a face-lift. In order to make the website more user-friendly and easier to navigate to important items, the website now displays the CBAC seminars and newsletters as main menu items.

The **CBAC** website now consists of the following sections and content: • **Overview** <CBAC Mission, Research Goals, Education and Training Goals, Support and Facilities, Center Directory, CBAC brochure (pdf); • **Director**; • **Faculty**; • **Research** <Research Areas, Representative Publications, Work in Progress (password required)>; • **Facilities**; • **Seminars** <CBAC Seminars, Seminar Video Archives, Research Retreat>; • **Newsletter**; • **Bulletin Board** <Announcements, News, Upcoming Events, Recent Events, Faculty Meetings>; • **Links**.



CBAC Video Archives of Past CBAC Seminars

The following are new seminar videos that have been added to the Video Archives section of the website along with the existing video archives for the Fall 2005 and Spring 2006 seminar sessions. The video archives can be found on the CBAC website at <http://cbac.wustl.edu/pageEducationVideo.asp>.

We offer both MPEG (lower quality video but accepted more by various browsers) and DIVX (higher quality video; needs to have a plug-in installed in order to view the file) formats for each seminar video to view or download. The remaining Fall 2006 and Spring 2007 seminar videos will be added to the website soon, so please check back.

John P. Boineau, M.D.

Professor of Surgery, Medicine, and Biomedical Engineering, Washington University School of Medicine, St. Louis, MO

Seminar titled "Arrhythmia Ablation - WPW and VTACH to Atrial Fibrillation: Personal reflections" given on October 9, 2006.

Edward Rhee, M.D.

Assistant Professor of Pediatrics, Washington University School of Medicine; Director, Arrhythmia Services, St. Louis Children's Hospital

Seminar titled "Device Therapy in Pediatrics: Millivolts to Kilovolts" given on October 23, 2006.

Achi Ludomirsky, M.D.

The Louis Larrick Ward Professor of Pediatrics and Biomedical Engineering; Director, Pediatric Cardiology, Washington University School of Medicine and St. Louis Children's Hospital

Seminar titled "Therapeutic Ultrasound: How to Create an Atrial Septal Defect?" given on October 30, 2006.

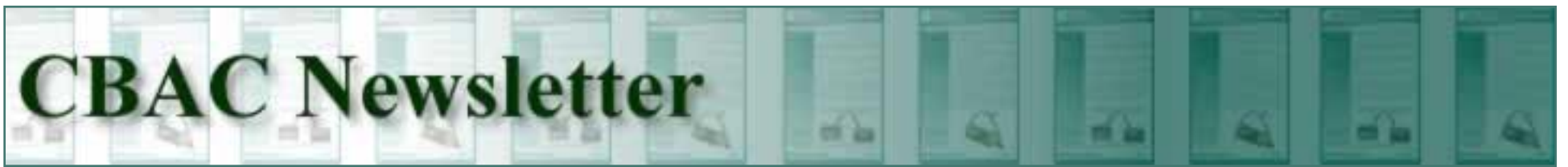
CBAC Website cont.

Bruce D. Lindsay, M.D.

Associate Professor of Medicine; Director, Clinical Electrophysiology Laboratory at Washington University

Seminar titled "Advances in Arrhythmia Ablation: What challenges lie ahead?" given on November 6, 2006.

Please note that each video comes with a strict Disclaimer: All material within each video file was filmed during a Cardiac Bioelectricity and Arrhythmia Center (CBAC) seminar at Washington University in St. Louis. It was made available on the website with permission from the speaker, who reserves and holds all rights. The video files are for educational purposes only and may not be reproduced, distributed or copied in any format.



PDF versions of current and past editions of the **CBAC Newsletter** can be viewed or downloaded from the CBAC website at <http://cbac.wustl.edu/pageNewsletter.asp>. You can also request a hard copy of the newsletter by emailing cbac@biomed.wustl.edu. Past editions of the newsletter include:

Issue #1, Spring 2006

Content:

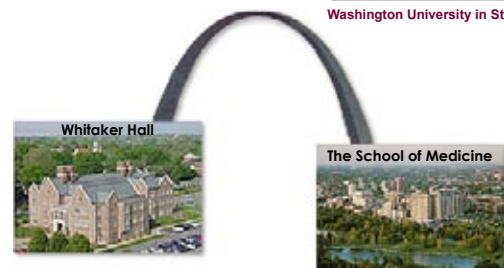
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- Spotlight On... Dr. Richard Schuessler

Cardiac Bioelectricity & Arrhythmia Center (CBAC)
Washington University in St. Louis



SPRING 2007 SEMINAR SCHEDULE

The Cardiac Bioelectricity and Arrhythmia Center (CBAC) seminars are held on Monday afternoons at 5:30 PM, with refreshments served beforehand from 5:00 PM - 5:30 PM, in room 218 of Whitaker Hall on the Washington University Danforth Campus.

Contact cbac@biomed.wustl.edu for more information, or visit the CBAC website at <http://cbac.wustl.edu/pageBulletinBoardClubs.asp>.

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**CBAC Seminar Series
Spring 2007 Schedule**



Date: January 22, 2007

Jean E. Schaffer, M.D.

Associate Professor of Medicine, Molecular Biology & Pharmacology, Washington University School of Medicine
"Lipotoxicity: Getting to the heart of the matter"

Date: January 29, 2007

Sándor J Kovács, Ph.D., M.D.

Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering, Washington University in St. Louis, Missouri

"How the Heart Must Work When It Fills", or "How Kinematic Modeling Can Elucidate Physiology"

Date: February 5, 2007

David Wilber, M.D.

Eisenberg Professor of Cardiovascular Sciences; Director of the Division of Cardiology and Cardiovascular Institute, Loyola University Medical Center, Maywood, Illinois

"Substrate-Based Approaches for the Ablation of Post-Infarction Ventricular Tachycardia"

Date: February 12, 2007

Craig T. January, M.D., Ph.D.

Professor of Medicine and Physiology; Vice-Chair for Research, Department of Medicine Department of Medicine Division of Cardiovascular Medicine School of Medicine and Public Health University of Wisconsin-Madison Madison, WI

"The hERG Potassium Channel in Cardiac Arrhythmias"

Date: February 19, 2007

John P. Boineau, M.D.

Professor of Surgery, Medicine, and Biomedical Engineering, Washington University School of Medicine

"Control of Normal Rate and Rhythm by a Widely Distributed, Functionally Differentiated and Integrated System of Atrial Pacemakers: The Pacemaker Complex"

Date: February 26, 2007

David R. Van Wagoner, Ph.D.

Associate Staff, Cleveland Clinic Departments of Molecular Cardiology & Cardiovascular Medicine; Associate Professor, Department of Molecular Medicine, Cleveland Clinic-Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio

"Inflammatory Pathways as Targets for the Treatment and Prevention of Atrial Fibrillation"

SPRING 2007 SEMINAR SCHEDULE cont.

Spring 2007 Seminar Schedule cont.

Date: March 5, 2007

Elliot R. McVeigh, Ph.D.

Principal Investigator, National Heart Lung and Blood Institute, NIH, Bethesda, Maryland

“Realtime MRI: Its applications for diagnosis and therapy”

Date: March 6, 2007

***Please note that this is a special seminar given on Tuesday, March 6*

Paul R. Volders, M.D. Ph.D.

Department of Cardiology, Academic Hospital Maastricht, Maastricht, Netherlands

“An In-Vivo Canine Model of Drug-Induced Long QT1 Syndrome”

Date: April 16, 2007

Bruno Taccardi, M.D., Ph.D.

Research Professor of Medicine, University of Utah School of Medicine; Associate Director, Cardiovascular Research and Training Institute (CVRTI), Salt Lake City, Utah

“Three-Dimensional Mapping of Intraventricular Repolarization”



Jennifer and Callum (the youngest CBAC member yet...)

Farewell to CBAC from Jennifer Godwin-Wyer (CBAC Coordinator and Webmaster)

Dear CBAC Faculty and Friends,

It is with great sadness that I say good-bye to the CBAC center, Dr. Rudy, and all of you. As most of you were aware of, I had been on maternity leave since the end of November 2006. While on leave and after the birth of my gorgeous little boy, Callum, my

husband, Dr. Paul Wyer, accepted a new position in Houston, Texas - hence my departure from CBAC at the end of February.

I have thoroughly enjoyed getting to know most of you personally or through email correspondences. My jobs of coordinating the seminars, writing and designing the newsletters, being the webmaster for the website, and working with Dr. Rudy were joys to me. You have all been very kind to me during my years at CBAC, and I appreciate all of your support and gracious comments to me about the work I produced.

I hope you all welcome the next Coordinator, whomever that will be, and that they will enjoy working for you and CBAC as much as I did. I will miss it very much. My plan for the year to come in our new home in Houston is to take the year off and just enjoy being a mom to my precious son.

Wishing you all the best for the future,
Jennifer Godwin-Wyer

NEWS AND ANNOUNCEMENTS

New Members:

CBAC would like to welcome four new faculty members, **Dr. Sanjeev Bhalla, Dr. Jane Chen, Dr. Gautam Singh, and Dr. Lihong Wang**. For more information on all of the CBAC faculty members please visit <http://cbac.wustl.edu/pageFaculty.asp> and <http://cbac.wustl.edu/pageResearch.asp>.



Sanjeev Bhalla, M.D.

Assistant Professor of Radiology; Assistant Radiology Residency Program Director, Mallinckrodt Institute of Radiology

Research Interests: Dr. Bhalla is expert in computed tomography of the chest, and is actively investigating the use of multi-detector array CT with 3-D reconstruction as an alternative to pulmonary angiography in the diagnosis of pulmonary arteriovenous malformations in HHT.



Jane Chen, M.D.

Assistant Professor of Medicine

Research Interests: My clinical interests involve all aspects of interventional arrhythmia therapy, including implantation of pacemakers, defibrillators, and biventricular systems, as well as ablative therapy for supraventricular and ventricular arrhythmias, and management of atrial fibrillation. My research interests are mainly clinical, and I participate in multicenter trials involving devices and new technologies to assess risks for sudden cardiac death. I also am very involved in community education to raise awareness of heart disease and SCD and in women.



Gautam K. Singh, M.D., M.R.C.P.

Associate Professor, Department of Pediatrics, Director of Non-invasive Cardiac Imaging Research; Co-Director, Echocardiography Laboratory

Research Interests: Cardiac mechanics in congenital heart disease particularly with single ventricular physiology by non-invasive cardiac imaging; non-invasive cardiac tissue characterization and cardiac kinematic in fetuses and children affected by cardiac disease, metabolic abnormalities and obesity; tissue characterization and cardiac mechanics in developing fetus in animal model.

Clinical Interests: Diagnosis, treatment and prevention of congenital heart disease, preventive pediatric cardiology, fetal cardiology, non-invasive cardiac imaging.



Lihong Wang, Ph.D.

Gene K. Beare Distinguished Professor; Department of Biomedical Engineering; Director, Optical Imaging Laboratory

Research Interests: Dr. Lihong Wang's group focuses on the research on non-ionizing biophotonic imaging. His group has made seminal contributions to ultrasound-modulated optical tomography, photoacoustic tomography, thermoacoustic tomography, modeling of light transport in biological tissue, and polarization-sensitive optical coherence tomography. In particular, his laboratory invented frequency-swept ultrasound-modulated optical tomography, dark-field confocal photoacoustic microscopy, exact reconstruction algorithms for thermoacoustic tomography, Mueller-matrix optical coherence tomography, and spectroscopic oblique-incidence reflectometry. His Monte Carlo model of photon transport in scattering media has been used worldwide.

CBAC Alumni:

Amir A. Amini, Ph.D.

Kyongtae T. Bae, M.D., Ph.D.

Michael Cain, M.D.

Vladimir P. Nikolski, Ph.D.

Jeffrey E. Saffitz, M.D., Ph.D.

Faculty Honors:

We congratulate the following CBAC Faculty for their achievements and awards this year:

Jean E. Schaffer, M.D., Associate Professor of Medicine, Molecular Biology & Pharmacology, was appointed to serve on the Boards of the Sarnoff Cardiovascular Research Foundation and the Kern Aspen Lipid Conference.

Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S., The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine, Radiology, and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC), was elected President of the Cardiac Electrophysiology Society for a two year term (2006-2008). He was also inducted as a Fellow of the Academy of Science of St. Louis on Jan. 22, 2007 in a ceremony at the Donald Danforth Plant Science Center for his achievement in biomedical engineering.

Dr. Rudy received the Kazuo Yamada Lecture Award at the Japanese Society of Electrocardiology in Toyama, Japan, October 2006.

Sándor J Kovács, Ph.D., M.D., Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering, assumed the presidency of Cardiovascular System Dynamics Society (CSDS) in Sept. 2006 and will organize the XVIIIth International Symposium in St. Louis Sept. 27-30, 2008. See <http://csds.org/>.



Igor R. Efimov, Ph.D., F.A.H.A., F.H.R.S., the Stanley and Lucy Lopata Associate Professor of Biomedical Engineering, Cell Biology & Physiology, and Radiology, was elected Fellow of the Heart Rhythm Society, and was the Astor Visiting Fellow, University of Oxford, UK. He also gave the Doris J.W. Escher, MD Lecture in Medicine, Montefiore Medical Center, The University Hospital for the Albert Einstein College of Medicine, New York, NY.

Daniel Kelly, M.D., Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Director of Cardiology; Co-Director, Cardiovascular Division, Department of Medicine, Washington University School of Medicine, was appointed as the Director of Cardiology (Chief, Cardiovascular Division, Department of Medicine, Washington University School of Medicine) effective Monday, October 9, 2006. He also became a member of the Association of Professors of Cardiology, and gave the Blount Lectureship at the University of Colorado.

Colin G. Nichols, Ph.D., Professor of Cell Biology and Physiology, was elected President of the Society of General Physiologists for the term 2006-2007. He also became the Carl Cori Professor, Washington University School of Medicine in 2006.

Arye Nehorai, Ph.D., Chairman of the Department of Electrical & Systems Engineering; Eugene and Martha Lohman Professorship of Electrical Engineering, was selected to receive the 2006 Technical Achievement Award from the IEEE Signal Processing Society (SPS). This Award is the highest recognition for technical contributions within the scope of IEEE SPS, which has about 20,000 members worldwide. Dr. Nehorai will accept his award at the Society Awards Ceremony, during the 32nd International Conference on Acoustics, Speech, and Signal Processing (ICASSP), Honolulu, April 15-20, 2007.



Kathryn A. Yamada, Ph.D., F.A.H.A., Research Associate Professor of Medicine, has agreed to assume the position as Director of the Mouse Cardiovascular Phenotyping Core of the Center for Cardiovascular Research, effective October 1, 2006. See Page 20 for more details.

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*NEWS AND ANNOUNCEMENTS cont.***Faculty Research Support and Current Projects:**

▶ **Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S.**, The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine, Radiology, and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC), hosted a delegation from the national Cheng Kung University of Taiwan, headed by the Vice President of the University and Dean of the College of Medicine, and has started planning research collaborations between Cheng Kung University and our Cardiac Bioelectricity Center (CBAC) to be funded by the government of Taiwan.

▶ **Igor R. Efimov, Ph.D., F.A.H.A., F.H.R.S.**, the Stanley and Lucy Lopata Associate Professor of Biomedical Engineering, Cell Biology & Physiology, and Radiology, has been awarded \$143,000 from the American Heart Association to be the Principal Investigator for a project titled "Structure of the human AV junction".

He will also be Principal Investigator on one other project:

* "Low-energy implantable atrial defibrillator" funded by the Coulter Foundation (2006-2007); and Co-investigator on two other projects funded by the NIH:

* "Computational and Experimental Study of Early Cardiac" (2006-2010), and

* "Computational Modeling of Developmental Processes " (2006-2011).

▶ **Daniel Kelly, M.D.**, Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Director of Cardiology; Co-Director, Cardiovascular Division, Department of Medicine, Washington University School of Medicine, was awarded an NIH grant 2-R01 HL058493-09 titled "Probing the cardiac PGC-1 regulatory cascade" for the term 7/1/2006 – 6/30/2010.

▶ **Colin G. Nichols, Ph.D.**, Professor of Cell Biology and Physiology, is the Co-Principal Investigator for the Washington University Pfizer Biomedical Program project titled "Remodeling and novel biomarkers of cardiovascular disease in type 2 diabetes" for the term 5/1/2006-4/30/2008 (\$150,000 direct costs annually to Dr. Nichols). The PI for this project is **Jeanne Nerbonne, Ph.D.**, Alumni Endowed Professor of Molecular Biology and Pharmacology.

Invited Presentations / Lectureships:

Jean E. Schaffer, M.D., Associate Professor of Medicine, Molecular Biology & Pharmacology, was the speaker at the Society for Heart and Vascular Metabolism Meeting in Semiahmoo, WA in September 2006 and speaker at an NIH Workshop on Lipodystrophy and the Metabolic Consequences of Altered Fat Deposition in Bethesda, MD in November 2006. She was also the Organizer of the Metabolic Syndrome & Cardiovascular Risk Keystone Symposium that will be held in Steamboat Springs in March 2007.

Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S., The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine, Radiology, and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC), had several Invited Lectureships in late 2006:

* Workshop on Cardiac Electrophysiology and Arrhythmia, The Mathematical Biosciences Institute, Ohio State University, Columbus, Ohio, September 2006;

* A joint meeting of the International Dead Sea Symposium and the Rappaport Symposium "Consensus and Controversy in Cardiac Arrhythmias", Tel Aviv, Israel, October 2006;

* Fifth International Workshop on Computer Simulation and Experimental Assessment of Electrical Cardiac Function, Lausanne, Switzerland, December 2006;

* Institute of Physiology, University of Berne, Berne, Switzerland, December 2006.

*NEWS AND ANNOUNCEMENTS cont.***Invited Presentations / Lectureships cont...**

Sándor J Kovács, Ph.D., M.D., Associate Professor of Medicine, Physiology, Physics and Biomedical Engineering, was visiting professor at MAYO CLINIC in Rochester MN, Cornell University, UCSD, University of Memphis and Rutgers University.



Daniel Kelly, M.D., Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Director of Cardiology; Co-Director, Cardiovascular Division, Department of Medicine, Washington University School of Medicine, made several presentations at conferences in late 2006-early 2007:

- * 3rd Annual Symposium of the AHA Council on Basic Cardiovascular Sciences – Translational of Basic Insights into Clinical Practice, “Cardiac nuclear receptor signaling”, Keystone, CO, July 31-Aug. 3, 2006;
- * Kern Aspen Lipid Conference, “Regulation of energy metabolism by the PGC-1/PPAR axis”, Aspen, CO, Aug. 2006;
- * Cardiac Energy Metabolism in Heart Failure: From Concepts to Therapies Meeting, “PPAR regulation of metabolic phenotype”, Semiahmoo, WA, Sept. 2006;
- * Cold Springs Harbor Symposium on “Nuclear Receptors from Bench to Bedside”, Cold Spring Harbor, New York, Nov. 2006;
- * University of Louisville, Cardiology Grand Rounds, “PPAR signaling in the heart”, Louisville, KY, Jan. 2007;
- * Keystone Symposium on Molecular Pathways in Cardiac Development and Disease, “Metabolic Pathways for Cardiomyopathy”, Beaver Run Resort, Breckenridge, CO, Jan. 2007.

Igor R. Efimov, Ph.D., F.A.H.A., F.H.R.S., the Stanley and Lucy Lopata Associate Professor of Biomedical Engineering, Cell Biology & Physiology, and Radiology, gave several presentations and proceedings in 2006:

- * Glukhov AV, Fedorov VV, Egorov Y, Rosenshtraukh LV, Efimov IR, Electrophysiological mechanisms of resistance to hypothermic ventricular fibrillation in the heart of hibernator *Citellus undulatus*. *Heart Rhythm* 3(1S), Supplement, 2006: S221;
- * Fedorov VV, Dobrzynski H, Hucker WJ, Efimov IR. Postganglionic nerve stimulation induces temporal inhibition of excitability and unidirectional conduction block in the rabbit sinoatrial node. *Heart Rhythm* 3(1S), Supplement, 2006, S222;
- * Kuo S, Niwa N, Ashihara T, Nikolski VP, Fedorov VV, Efimov IR, Trayanova NA. Role of Electroporation in Initiation of Spontaneous Ectopic Postshock Activations. *Heart Rhythm* 3(1S), Abstr. Supplement 2006. S222-3;
- * Hucker WJ, Laughner JL, Fedorov VV, Efimov IR. Molecular Characteristics of the Rabbit Supraventricular Pacemaking and Conduction System. *Heart Rhythm* 3(1S): S311, 2006;
- * Hucker WJ, Sharma V, Efimov IR. Bypassing the Compact Atrioventricular Node in the Normal Rabbit Heart: Implications for Synchronized Ventricular Pacing. *Circulation*, 114(18): II-200. 2006;
- * McCain ML, Hucker WJ, Efimov, IR. Heterogeneity of Cell to Cell Communication in the Human Atrio-Ventricular Junction. *Circulation*, 114(18): II-291;
- * Hucker WJ, Laughner JI, Fedorov VV, Efimov IR. Autonomic Innervation and Coupling in the Rabbit Supraventricular Pacemaking and Conduction System. *Heart Rhythm* 3(5) (Supplement), S311;
- * Fedorov VV, Hucker WJ, Dobrzynski H, Efimov IR. Optical mapping of vagally-induced temporal inhibition of excitability and unidirectional conduction block in the rabbit sinoatrial node. *Heart Rhythm*, 3(5), Supplement, S222 2006.

NEWS AND ANNOUNCEMENTS cont.

Faculty News:

► **Daniel Kelly, M.D.**, Alumni Endowed Professor in Cardiovascular Diseases; Professor of Medicine, Pediatrics, and Molecular Biology & Pharmacology; Director, Center for Cardiovascular Research; Director of Cardiology; Co-Director, Cardiovascular Division, Department of Medicine, Washington University School of Medicine

Editorial and Peer Review Responsibilities:

- * 2006 Editorial Board, Genes & Development;
- * 2006 NHLBI Working Group on Mechanistic and Pre-Clinical Studies of Diabetic Macrovascular Complications;
- * 2007 Editorial Board, Journal of Clinical Investigation.

Professional Societies, Committees, Organizations, and Advisory Boards:

- * NIDDK Working Group, "Advances and Emerging Opportunities in Type 1 Diabetes Research" (2005 & 2006);
- * Internal Advisory Committee Washington University, NHLBI SCCOR on "Metabolic Syndrome and Vascular Disease" (P.I. Clay Semenkovich, M.D.) (2005-present);
- * Member, AHA Basic Cardiovascular Sciences Leadership Committee Meeting (2006);
- External Advisory Board, Clinical Nutrition Research Unit, Pennington Biomedical Research Center (2006);
- * External Advisory Board, Heart and Lung Institute, The Ohio State University (2006-present);
- * Chair, AHA Katz Basic Research Prize Selection Committee (2006-2007);
- * External Advisory Board – Pennington Center (2006-present).

► **Igor R. Efimov, Ph.D., F.A.H.A., F.H.R.S.**, the Stanley and Lucy Lopata Associate Professor of Biomedical Engineering, Cell Biology & Physiology, and Radiology, became a Fellow of the Heart Rhythm Society in 2006, and a Member of the Industry-Foundations Liaison committee, American Physiological Society for the term 2006-2009.



Yoram Rudy, Ph.D., F.A.H.A., F.H.R.S., The Fred Saigh Distinguished Professor of Engineering; Professor of Biomedical Engineering, Cell Biology & Physiology, Medicine, Radiology, and Pediatrics; Director of the Cardiac Bioelectricity and Arrhythmia Center (CBAC), was elected a member of the Board of Directors of the International Society for Computerized Electrocardiology (ISCE) for the term 2006 - 2007.

In 2006, **Dr. Rudy** was appointed by Chancellor Wrighton to be the Ambassador to Technion- Israel Institute of Technology for the McDonnell International Scholars Academy. The academy is a unique global education and research initiative that partners with universities and corporations around the world to provide the scholars with an extraordinary educational experience.

Charu Ramanathan and Ping Jia, both former Ph.D. students of **Dr. Yoram Rudy**, established CardioInsight Technologies, Inc., a startup company for developing Electrocardiographic Imaging (ECGI) as a clinical diagnostic tool for cardiac arrhythmias. Charu Ramanathan will run CardioInsight's technology development, and Ping Jia will be in charge of its clinical development.

Excerpt from The Plain Dealer, "Heart-imaging firm gets seed money", Wednesday, August 23, 2006 (Mary Vanac, Plain Dealer Reporter, <http://www.cleveland.com/business/plaindealer/>):

"Cleveland medical device start-up CardioInsight Technologies Inc. has received an investment of \$750,000 to develop a new type of heart imaging device. The money came from Draper Triangle Ventures, JumpStart Inc. and Case Western Reserve University's technology transfer office. Each investor contributed \$250,000, said Thom Ruhe, chief marketing officer for JumpStart, the Cleveland nonprofit group that invests money and expertise in local start-ups that have substantial growth potential."

"Using technology developed by Case researcher Yoram Rudy during the last 18 years, CardioInsight is aiming at commercializing a device that generates a detailed, three-dimensional image of a heart's electrical activity without invading the body with instruments."

Focus On...Dr. David Van Wagoner cont.

“To better understand the mechanisms that underlie AF, we have been studying the cellular and biochemical properties of atrial tissues. We are evaluating the expression and function of ion channels that are responsible atrial excitation-contraction coupling. We are utilizing microarray techniques to evaluate the biochemical signaling pathways that are altered in AF, and perhaps that lead to AF. We are also evaluating the links between systemic inflammation and atrial histology.”

“We are exploring the distribution of inflammatory mediators, inflammatory cellular infiltration, and the links to altered atrial architecture (dilatation, myocyte loss, accumulation of fibroblasts and interstitial fibrosis). In addition to characterizing the phenotype of surgical tissues, animal models are used to explore the impact of high rate activity and / or inflammation subsequent to cardiac surgery on the electrophysiologic, biochemical and functional properties of the atria in relevant animal models. Using this combination of approaches, we are attempting to identify and evaluate novel pathways for pharmacologic intervention, in an effort to decrease the incidence and the complications associated with AF.”

Excerpt from <http://www.clevelandclinic.org/heartcenter/pub/staff/biography.asp>:

“Dr. Van Wagoner does not treat patients, but works closely with Heart Center physicians to research the mechanisms underlying atrial fibrillation, and to develop and assess new techniques for treating atrial fibrillation and other cardiovascular conditions. Dr. Van Wagoner’s specialty is cellular electrophysiology research.”

“Dr. Van Wagoner’s cardiac electrophysiology research program is primarily funded by the National Institutes of Health, but has also received support from the American Heart Association and several pharmaceutical companies. His research focused on human atrial fibrillation is highly collaborative and translational, with extensive interactions both with the cardiac surgeons in the Department of Cardiothoracic Surgery and the cardiologists in the Section of Electrophysiology in the department of Cardiovascular Medicine. Recent studies have examined the role of oxidative stress in the electrophysiological remodeling associated with atrial fibrillation, the mechanisms underlying post-operative atrial fibrillation, and the relationship between the systemic inflammatory response and the persistence of atrial fibrillation.”

Dr. Van Wagoner will give the February 26, 2007 **CBAC Seminar** titled “**Inflammatory pathways as targets for the treatment and prevention of atrial fibrillation**”.

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[Reference Cut-off Date: 08/01/2006 - 01/31/2007; References received by author]

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CONTACT INFORMATION

Kathryn Yamada Promotion cont.

Email announcement from 2006:



Dr. Kathryn Yamada has agreed to assume the position as Director of the Mouse Cardiovascular Phenotyping Core of the Center for Cardiovascular Research, effective October 1, 2006. Given the growth of the Core services and user base over the past several years, I believe it is necessary for the Core Director to bring significant expertise in animal physiology and research, a "hands-on" approach to the general operations of the Core, and a vision for future development of Core services including pioneering approaches aimed at further enhancing our ability to define the cardiovascular phenotype of genetically-modified mice and other small animals. As you know, in addition to being involved with the Core since its inception, Kathryn is an outstanding cell biologist and physiologist with a broad background in cardiovascular investigation utilizing in vivo systems. This research expertise coupled with her efficient management style will serve Kathryn well as she assumes this position. Carla Weinheimer will continue to serve as the Core Supervisor and Chief Animal Surgeon. Attila Kovacs will continue to oversee and develop new pioneering approaches to ultrasonic imaging of the heart and vasculature in small animals. Indeed, Carla, Attila, Michael Courtois, and Carrie Gierasch comprise a nationally-recognized Core facility that has and will continue to provide a key resource for investigators at Washington University, and several other collaborating institutions, and for our industry partners."

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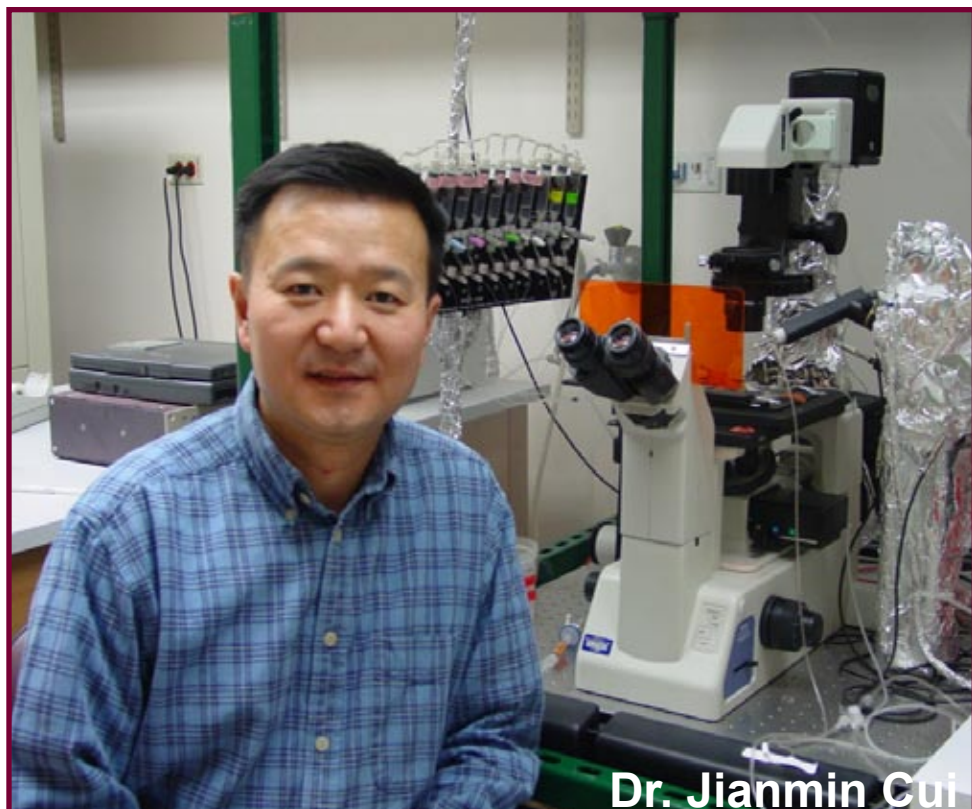
This newsletter is produced on behalf of the Cardiac Bioelectricity and Arrhythmia Center (CBAC) by the CBAC office. Editors: **J. Godwin-Wyer** <jennilynng@netscape.net> and **Y. Rudy** <rudy@wustl.edu>.



Olin Library on the Danforth campus

*SPOTLIGHT ON...**DR. JIANMIN CUI*

Dr. Jianmin Cui is an Associate Professor of Biomedical Engineering on the Spencer T. Olin Endowment at Washington University, St. Louis, Missouri. He received his Ph.D. in 1992 from the State University of New York. Dr. Cui, along with Dr. Igor Efimov, Dr. Jinyi Shi (his wife who is a Research Faculty member in Biomedical Engineering and works alongside Dr. Cui in his laboratory located in Whitaker Hall), and Dr. Yoram Rudy, relocated from Case Western Reserve University in Cleveland, Ohio to Washington University in 2004, and was one of the first faculty members to join CBAC. Dr. Cui works collaboratively with many other faculty, several of which are also CBAC members. His laboratory focuses on studying ion channels and his research interests focus on the mechanisms underlying conformational changes that occur as the channels open and close and on the interaction of ion channels with other molecules during cellular electrical activity. The approach in his research is to use a combination of molecular biology, protein biochemistry, patch clamp techniques, and biophysical analysis and kinetic modeling. This approach allows him to manipulate channel protein structure, estimate the number of distinct conformational states of the channel protein, and determine the energy associated with the transitions among these states.



Dr. Jianmin Cui

“There is a Chinese saying: ‘In a 7 year old child you can see his/her life’s destination.’ When I was 7 years old, China was in the heat of the Culture Revolution. Schoolteachers and parents were busy in political meetings and could not pay much attention to children. I lived in the suburbs of Nanjing and spent most of my afternoons and evenings with friends roaming in fields, hills, and woods. The nature’s wonders fascinated me, I had spent hours in bushes watching spiders weaving their web, or under the moon observing cicadas transforming from their pupa. Of all those things, the most memorable was a pond that I went to day after day, from winter to spring, waiting for toads to spawn eggs, and for the eggs to become tadpoles. At that time, I had no idea that, one day, biomedical research would become my career.”

“By the end of Culture Revolution, the traditional value of education revived in China. In 1977, universities reopened to admit students through entrance exams. I entered Peking University in 1979 and majored in physics. In my junior year, I took a class “Quantum Mechanics” and read the book “What is life?” authored by one of the founding fathers of quantum physics, Erwin Shrodinger. The book was the topic of many discussions among several classmates, which renewed my fascination about the secrets of life. A year later, I joined the master’s program in the Department of Biology at Peking University to study the neural basis of behavior in silkworms. In 1986, I was admitted to the Ph.D. program of Physiology and Biophysics at the State University of New York in Stony Brook. Dr. Ira Cohen introduced me to the study of ion channels that are important for cardiac functions, which has remained my research focus till today. After receiving the Ph.D. degree in 1992, I had postdoctoral trainings first with Drs. Ira Cohen and Gail Mandel in Stony Brook, and then with Dr. Richard Aldrich at Stanford University. I became an assistant professor in 1999 at Case Western University, and joined faculty of the Department of Biomedical Engineering at Washington University in St. Louis in 2004.”

“Ion channels are proteins spanning the cell membrane that allow ions to flow into or out of cells. These exquisite molecules open and close in response to stimulations such as the membrane voltage and messenger molecules, thus generating electrical signals for neural transmission, heart beating, and muscle contraction. In a nutshell, ion channels are vital for our existence. Ion channel studies have been very exciting in the last two decades because of

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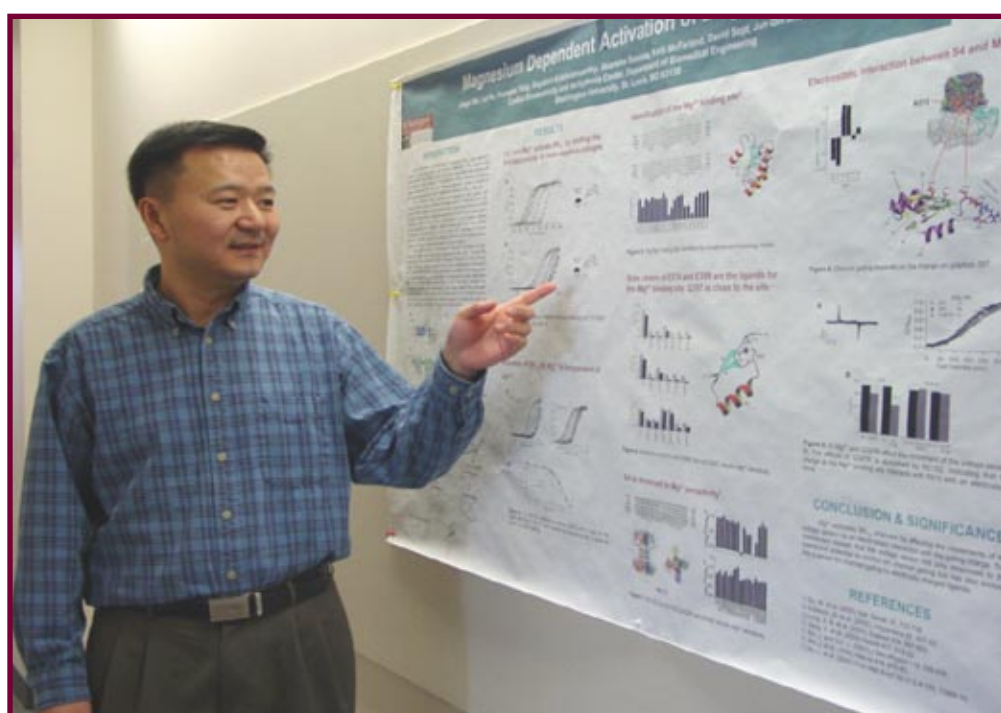
*SPOTLIGHT ON... cont.**DR. JIANMIN CUI*

the rapid progress with a breath-taking speed. Since the cloning of the acetylcholine receptor in 1982, the molecular identities of virtually all known ion channels have been elucidated. In 1998 the first crystal structure of an ion channel was published, and since then the list of solved ion channel structures has been steadily increasing. These results have helped us to understand how ions flow through the pore and how the voltage sensor and the activation gate move during channel activation. These progresses have also set up the stage for studying the energetic coupling between the movements of the sensors in response to stimulation and the opening of the channel gate, a question that is arguably the last frontier in understanding the molecular mechanisms of ion channel function. My lab has been focusing on this important question by studying the BK-type, voltage, calcium, and magnesium activated potassium channels. BK channels are particularly suited for such studies because the sensors of the three stimuli open the same activation gate, enabling us to compare different mechanisms of sensor-gate coupling in the same channel. I started studying BK channels when I was in Dr. Richard Aldrich's lab at Stanford, where we demonstrated that calcium and voltage activate the channel with distinct molecular mechanisms. At Case Western Reserve University, my lab revealed that the mechanisms for calcium and magnesium dependent activation are also distinct. Thus, the three stimuli open the activation gate by perturbing different sets of amino acids in the channel protein; and these sets of amino acids form distinct intra-molecular paths connecting the voltage sensor, the calcium and magnesium binding sites to the activation gate. Currently, we have identified some amino acids in each of the activation paths. In collaboration with Dr. David Sept's lab, we have begun to understand the interaction among these amino acids that leads to channel opening. Our goal is to understand important steps along these paths of channel activation. We believe that these studies will reveal the general principles that govern the sensor-gate couplings in ion channels."

"Electrical excitation leads to muscle contraction in the heart, for it to pump blood. Thus, it is no surprise that abnormal ion channel function or distribution is associated with arrhythmias. Another research focus of my lab is to study the molecular mechanism of the IKs channel that is important for the repolarization of ventricular action potentials. The IKs channel is composed of two types of subunits, and the interaction between them determines the properties of the channel. So far, nearly 300 different mutations of the two subunits have been associated with the long Q-T syndrome. To explain how these mutations compromise IKs functions, it is essential to understand the fundamental structure-function relations of the channel. Recently, in the study of a mutation associated with the long Q-T syndrome, we discovered that the voltage sensor is involved in the interaction between the two types of subunits. This result provides a mechanistic basis to explain how some of the mutations affect channel function. This work is done in collaboration with Dr. Yoram Rudy's laboratory. Together with Dr. Rudy's lab we hope that by integrating the molecular mechanism of ion channel function into the cellular context we can unveil the secret of how a single mutation of amino acid leads to arrhythmias. Someday, such understandings will lead to the discovery of drugs or therapies

for the treatment of these diseases. Much like the pond in my childhood, this fascinating prospect attracts me back to the lab day after day."

Dr. Cui presented a **CBAC seminar** during the Fall 2005 session on October 10, 2005 titled "**Ca²⁺-Activated K⁺ Channels: Structure, Function and Disease**".



Dr. Jianmin Cui (left) outside his office located in Suite 290, Whitaker Hall.