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# *Zeljko J. Bosnjak, Ph.D., Recipient of the 2008 Excellence in Research Award*

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EACH year, the American Society of Anesthesiologists Award for Excellence in Research is presented to an individual, in recognition of meritorious and original research that has led to the advancement of the science and clinical practice of anesthesiology. The 2008 designee is Zeljko J. Bosnjak, Ph.D. His research conducted over a span of 30 yr has continued to be productive, creative, and instructive as to basic cellular mechanisms of anesthetic action.

It is exceptional in that it has expanded the scientific foundation of our subspecialty in multiple ways. Zeljko's research is not only important for new discoveries but, because of his use of new approaches, methodologies and techniques, his research raises the bar for investigation in anesthesiology to a higher level. Finally, graduate students, postdoctoral fellows, residents, and junior faculty are involved in this work, ensuring that his research will be continued in the future. Zeljko published his first scientific article in ANESTHESIOLOGY in 1978. Since that time, his career has been characterized by nothing less than excellence in scientific investigation, and he has an international reputation based on his research.

Zeljko Bosnjak was born in Croatia in 1949. He and his family immigrated to the United States in 1970. Within 2 days of arriving in Milwaukee, Zeljko began working at a local tanning company, driving a cab on weekends, and taking English classes at night. He joined the Medical College of Wisconsin as a research technician a short time thereafter. In 1975, John P. Kampine, M.D., Ph.D., Professor of Anesthesiology and Physiology, convinced him to enter the Physiology Graduate Program at the Medical College of Wisconsin, and Zeljko started graduate school 2 days after he was married to his lovely wife, Mary. He received the Ph.D. degree in Physiology in 1979. He worked under the direction of John Kampine, Chairman of the Department of Anesthesiology, and John would be the first to state that much of his own success was due to the hard work, productivity, creativity, and dedication of Zeljko Bosnjak. Zeljko completed a postdoctoral fellowship in the Department of Anesthesiology in 1981. He remained on the faculty as an Assistant Professor and was promoted to Associate Professor and Professor of Anesthesiology and Physiology in 1984 and 1989, respectively. Zeljko was appointed Vice Chairman of Research in the Department of Anesthesiology in 2003.

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Investigations by basic scientists and physician scientists in the laboratory of Dr. Bosnjak are directed toward an understanding of the cellular mechanisms of volatile anesthetics. His more than 240 article published in peer-review journals can be summarized into three areas, all examining the cardiovascular response to anesthetic drugs: (1) impact of anesthetics on cardiac and vascular smooth muscle electrophysiology, (2) cardioprotection by volatile anesthetics, and (3) genetic basis for differences in the cardiovascular response to anesthetics. He is on the leading edge of research in anesthesiology, probing exciting areas and seeking answers to unique questions with state-of-the-art technologies, such as mitochondrial swapping, multiphoton confocal fluorescence microscopy, engineered heart tissue, identification of cardiac cells derived from human endothelial stem cells, channel/subunit knockouts, channel overexpression, and proteomics. He uses these techniques in a carefully orchestrated symphony to measure alterations in biologic function at nearly every level from single ion channel to the whole animal. Zeljko has been an important part of a group of talented scientists

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who have helped to identify a signaling cascade consisting of mitochondria, protein kinases, reactive oxygen species, adenosine triphosphate–dependent potassium channels, and the mitochondrial permeability transition pore involved in cardioprotection by volatile anesthetics against ischemia and reperfusion injury. This is critical information that in many ways has changed the practice of anesthesiology. What previously was avoided in the anesthesia of patients with coronary artery disease has now been proven to be beneficial. In a seminal investigation, Zeljko characterized the direct action of volatile anesthetics on adenosine triphosphate–dependent potassium channels in sarcolemmal and mitochondrial membranes using patch clamp techniques and inner mitochondrial membranes reconstituted in lipid bilayers, respectively. He was the first to provide direct evidence that administration of isoflurane can increase the open probability of adenosine triphosphate–dependent potassium channels in mitochondria.[1,2] A fascinating study conducted in his laboratory showed that overexpression of potassium channels in mitochondria can elicit cellular protection against hypoxia and reoxygenation.[3]

Zeljko Bosnjak's history of obtaining grant support is impressive. He received his first National Institutes of Health (NIH) grant—a New Investigator Award—in 1982 and since that time has had continuous funding from the NIH for 26 yr. His current R01 is funded through 2009, and he is the director of a Program Project Grant, the competitive renewal of which he learned at the time of this writing received a priority score of 120. Both of his grants are directed toward characterizing alterations in cardiomyocyte signal transduction produced by anesthetics. Zeljko's participation as a coinvestigator on 11 NIH grants has made a difference for other faculty, helping them to receive their own funding. The long history of peer-review funding is strong evidence that his investigative work is state of the art and leads the field in novel and new directions. Zeljko's research has been deemed meritorious by the International Anesthesia Research Society; he received the B.B. Sankey Anesthesia Advancement Award in 1986 and NIH Research Career Development Award in 1987. He is regularly asked to participate in the peer-review process by the NIH. His involvement in a variety of study sections and NIH committees, including Clinical Science Study Section II, Pharmacology Study Section II, and Surgery, Anesthesiology, and Trauma, attest to his scientific reputation. In fact, he has served as Chairman of the Surgery-Anesthesia-Trauma Study Section. Zeljko has also participated on a National Institute on Drug Abuse Special Review Committee, a National Institute on Drug Abuse Contract Review Committee, several *ad hoc* committees for a variety of study sections, and Chairman of site visit teams for the NIH National Heart, Lung, and Blood Institute and National Institute of General Medical Sciences.

Dr. Bosnjak's professional service to the American Society of Anesthesiologists is extensive. He has served on the Subcommittee on Anesthetic Action and Biochemistry, on the Subcommittee on Experimental Circulation, and as a session moderator at a large number of American Society of Anesthesiologists meetings. He has been a member of the International Anesthesia Research Society Frontiers in Anesthesia Research Award External Advisory Board and acted as Chairman of that committee as well. Zeljko is an editor of ANESTHESIOLOGY and an *ad hoc* reviewer for a number of journals, such as the *American Journal of Physiology*, *Brain Research*, the *British Journal of Anesthesia*, and *Anesthesia & Analgesia*. Finally, he has been a member of the Scientific Advisory Board of the Association of University Anesthesiologists and the Foundation for Anesthesia Education and Research Academy of Research Mentors. Any one of these endeavors requires an extraordinary amount of energy and effort. His professional service to a wide variety of organizations directly and indirectly advances the scientific basis of our subspecialty. He has already successfully accomplished this during his career.

Zeljko Bosnjak has been an advisor to numerous postdoctoral fellows, graduate students, medical students, and residents. He has mentored faculty in the Department of Anesthesiology, Medical College of Wisconsin, that have gone on to be successful in their own careers, *e.g.*, David Stowe, M.D., Ph.D., Tom Stekiel, M.D., Quinn Hogan, M.D., and Harvey Woehlck, M.D. The fellows and visiting professors whom he has attracted to his laboratory now include individuals who have become chairs of departments in different institutions in many other countries, including Sumio Hoka, M.D. (Department of Anesthesiology, Kitasato University School of Medicine, Kitasato, Japan); Mitsuaki Yamazaki, M.D. (Department of Anesthesiology, Toyama Medical and Pharmaceutical University, Faculty School of Medicine, Toyama, Japan); Noel Flynn, M.D., B.Sc., F.F.A.R.C.S.I. (Department of Anesthesiology, Galway University Hospitals, Ireland); Mladen Boban, M.D. (Department of Pharmacology, University of Split Medical School, Split, Croatia); Zeljko Dujic, M.D., Ph.D. (Department of Physiology, Vice Rector, University of Split Medical School, Split, Croatia); and Bernard Graf, M.D. (Universitätsmedizin-UMG, Georg-August-Universitaet Goettingen, Zentrun Anaesthesiologie, Goettingen, Germany). The numbers of graduate students and fellows he has trained is very large, and many receive funding from their home institutions or governments to study in his laboratory at the Medical College of Wisconsin. The most important product of Zeljko's investigative work may not necessarily be specific results of studies contributing to the scientific foundation of anesthesiology at this moment. Instead, it may be the impact that his former trainees will continue to have well into the future. Few scientists can claim such a legacy.

In 1970, Zeljko and his family escaped a communist-controlled country that had literally seized all they owned. He, his sister, and parents came to the United States with little more than the clothes on their backs. His homeland of Croatia was destined to be ripped by war and genocide. His subsequent successes as a scientist have been enjoyed by colleagues at our institution and also have been shared with those who remained in his beautiful homeland, which his heart has never left behind. His only passion greater then the country of Croatia is his family. Mary and Zeljko have three absolutely wonderful grown children. One of Zeljko's personal and professional objectives has been to enhance the Croatian medical and scientific communities. Over the past 20 yr, his participation in the organization and planning of various congresses and symposia in Croatia, establishing an international Ph.D. program, and education of Croatian physicians have been unparalleled. Although not a physician himself, it is significant that he served as president of the World Association of Croatian Physicians. His involvement in the research training of Croatian physicians is a passion, and he has been awarded the highest honor from the Croatian government, the Presidential Medal "Northern Star," for this. What is even more remarkable is that he has been awarded this honor twice. The latter instance began with the Bosnjak home phone recently ringing at 3 AM. He and his wife thought someone had dialed the wrong number, or worse. Instead, it was a call from the Office of the President of the Republic of Croatia, informing him that the President of Croatia would appreciate his presence in Zagreb the following week to receive the honorable Katarina Zrinska National Decoration for Humanitarian Services to his native country. The humanitarian work included organizing relief efforts during the war in the early 1990s, including several shiploads with medical supplies and hospital equipment, providing emergency drugs in very short supply or nonexistent to hospitals in Zagreb at the height of the aggression against Croatia, and finally organizing organ transplants in the United States for patients in Croatia, the latter of which he continues to do until this very day. This is truly humanitarian effort on a grand scale—the Croatian who came to America never left Croatia behind.

The Excellence in Research Award of the American Society of Anesthesiologists recognizes accomplishments in science. The scientific accomplishments of Zeljko J. Bosnjak, Ph.D., in research have had an important impact on the scientific foundation of anesthesiology. In addition, his efforts have enhanced the level of sophistication of medical sciences in another country, Croatia.

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