

Beverley A. Orser, M.D., Ph.D., F.R.C.P.C., F.C.A.H.S., Recipient of the 2018 Excellence in Research Award

Alex S. Evers, M.D.

EACH year, the American Society of Anesthesiologists Award for Excellence in Research recognizes a single individual for his or her outstanding achievements in research that have or are likely to have an important impact on the practice of anesthesiology. The requirements for this award can be fulfilled in many ways, but the ideal recipient will have one leg deeply embedded in science and the other in clinical care, recognizing that clinical practice informs research while research solves clinical problems and drives innovation. Dr. Beverley Orser, the recipient of the 2018 Excellence in Research Award, epitomizes the qualities of an ideal recipient. She has immersed herself in the fundamental science of ion channel biology and has applied it to gain an understanding of central problems in anesthesiology practice. Simultaneously, she has identified clinical problems in her practice and used her expertise in cellular physiology to identify their mechanism and develop therapeutic solutions. In addition to being one of anesthesiology's best physician-scientists, Bev Orser is an outspoken patient safety advocate in the areas of medication error and anesthesia awareness and an academic leader on the local, national, and international stage.

Dr. Orser is a lifetime Canadian. As a child, she lived in multiple cities in Ontario and Quebec, providing her with a sense of adventure, adaptability, and a passion for the outdoors. After receiving her medical education at Queen's University (Kingston, Canada), she was an intern at the Royal Columbian Hospital in British Columbia (New Westminster, Canada). While in medical school, she met Geordie Fallis, a family physician, and what followed was a 7-yr long-distance romance that spanned multiple continents and became a lifelong partnership. This perseverance is emblematic of Bev's determination and augured her scientific focus and ability to stick with a problem. Dr. Orser subsequently trained in anesthesiology at the University of Toronto (Toronto, Canada) and McMaster University (Hamilton, Canada) and then did research training with John F. MacDonald, Ph.D., F.R.S.C., University of Toronto (Toronto, Canada; deceased), leading to a Ph.D. in medical science. She has remained on the faculty of the University of Toronto in the Department of Anesthesia for her entire career and has been an active clinical anesthesiologist and educator at Sunnybrook Health Sciences Centre (Toronto, Canada).



Fig. 1. Beverly A. Orser, M.D., Ph.D., F.R.C.P.C., F.C.A.H.S., recipient of the American Society of Anesthesiologists 2018 Excellence in Research Award.

Dr. Orser's research focuses on the molecular mechanisms of anesthetic agents. Her seminal contributions have been in the area of anesthetic actions on γ -aminobutyric acid type A ($GABA_A$) receptors, the major inhibitory neurotransmitter receptor in the central nervous system. This work commenced in the late 1990s with her careful description of the electrophysiologic effects of propofol on $GABA_A$ receptors.¹ She subsequently made the critical observation that tonic $GABA_A$ currents in hippocampal neurons have distinct functional and pharmacologic properties.^{2,3} This dissection of γ -aminobutyric acid-mediated ($GABAergic$) neural inhibition into a tonic and a synaptic component has led to key insights into subunit-specific physiologic roles for $GABA_A$ receptors and to increased understanding of the pharmacologic specificity of anesthetics.

Dr. Orser has been a key leader in defining the role of tonic $GABA_A$ currents in the actions of anesthetics and other drugs. Her article showing that tonic $GABAergic$ currents in hippocampal neurons are uniquely sensitive to the inhalational anesthetic isoflurane provided the first clear evidence that tonic,

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rather than synaptic, GABAergic receptors might be the functional target for some effects of anesthetics.⁴ Her subsequent finding that the $\alpha 5$ subunit of the GABA_A receptor is specifically associated with tonic GABA_A currents in hippocampus⁵ and selectively mediates the amnestic, but not the sedative-hypnotic, effects of several anesthetic agents⁶ is a fundamental discovery. The identification of a specific molecular target for amnesia is profoundly important. It augers the possibility of drugs that will selectively produce amnesia without sedation, suggests that specific mutations of the $\alpha 5$ subunit could mediate individual susceptibility to anesthesia awareness, and provides a potential molecular target for prevention of post-traumatic stress disorder and/or memory enhancement.

Dr. Orser's studies have also focused on the properties of astrocytes, a critical supporting cell in the brain. She has shown that astrocytes express extrasynaptic GABA_A receptors and when anesthetics activate these receptors, they trigger release of soluble factors that cause persistent postanesthesia memory deficits.⁷ She has also shown that inflammation associated with surgery enhances $\alpha 5$ -GABA currents, increasing neuronal sensitivity to anesthetics and contributing to postsurgical memory impairment.⁸ These discoveries provide a likely explanation for the persistence of memory deficits after surgery.

Dr. Orser's impact as a researcher has not been limited to her scientific discoveries. She has trained numerous masters students, doctoral students, and fellows, many of whom have gone on to distinguished careers in academics and industry. Her students have been the recipients of numerous research prizes and awards. She has published more than 150 peer-reviewed articles and been the recipient of more than \$15 million in research grant funding. Dr. Orser's contributions to science and medicine have been recognized by the Gold Medal from the Canadian Anesthesiologists' Society (Toronto, Canada; 2017), the Peter Dresel Award in Pharmacology from Dalhousie University (Halifax, Nova Scotia, Canada; 2017), the first Canada Research Chair awarded to an anesthesiologist (2003), the first Frontiers in Anesthesia Research Award from the International Anesthesia Research Society (San Francisco, California; 1995), and recognition awards from the Australian and New Zealand College of Anaesthetists (Melbourne, Victoria, Australia) and the Association of Anaesthetists of Great Britain and Ireland (London, United Kingdom). In 2013, she was inducted as a fellow of the Canadian Academy of Health Sciences (Ottawa, Canada). Dr. Orser is also a leader of academic anesthesiology, serving as a trustee of the International Anesthesia Research Society and as chairperson of the Department of Anesthesiology at the University of Toronto.

As is apparent from all the above, Beverley Orser is a person of incredible drive, perseverance, and accomplishment. She is also a person of incredible generosity and warmth. Dr. Orser is talented at solving differences of opinion because, despite being strong-minded, she exudes integrity and inspires trust and confidence. Her dedication and warmth

extend to her husband Geordie and her three very successful children, Kevin (age 31), Becky (28), and Sarah (25), who share her love for outdoor adventure.

Dr. Beverley Orser is a role model physician-scientist whose research contributions, mentorship, and leadership will greatly impact the future practice of anesthesiology and the careers of a generation of physician-scientists. I am profoundly gratified that the American Society of Anesthesiologists has wisely chosen my very deserving friend and esteemed colleague, Beverley Orser, for the 2018 Excellence in Research Award.

Competing Interests

The author declares no competing interests.

Correspondence

Address correspondence to Dr. Evers: Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri 63110. eversa@wustl.edu. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

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