

# Peter Nagele, M.D., Recipient of the 2012 Presidential Scholar Award

Alex S. Evers, M.D.\*

**N**OTHING is more gratifying to a department chair than to celebrate the academic success and recognition of a young faculty member or trainee. I thus relish this opportunity to introduce you to Peter Nagele, the recipient of the 2012 Presidential Scholar Award, and to share with you his accomplishments and how and why they have occurred. From my first acquaintance with Peter, it was clear that he had the “phenotype” of a successful academic physician: He was smart, passionate about research, driven to succeed, and had “new ideas” about most topics in science and medicine. Like many physician-scientists who go on to success, Peter was also strong-minded, impatient, and occasionally contentious! I have come to recognize that these are also characteristics of success, provided that the strong-mindedness is not a manifestation of closed-mindedness and that impatience is coupled with perseverance. As I have come to know Peter as a friend and colleague, I have learned that he is a generous and kind man who embraces advice and has unlimited stamina to pursue every project to completion. In hindsight, it is no surprise that Peter Nagele’s career has been one of continuous ascent!

Dr. Nagele received his medical education at Leopold-Franzens University in Innsbruck, Austria and completed his residency in anesthesiology and critical care medicine at the University of Vienna. From the inception of his clinical training, he sought out both clinical and laboratory research experiences. As a resident he was a participant and coauthor on a landmark study of the role of supplemental oxygen in the incidence of surgical wound infections in patients undergoing colectomy that was published in the *New England Journal of Medicine*.<sup>1</sup> He was subsequently an investigator on the first human safety and efficacy study examining xenon as an anesthetic in humans.<sup>2</sup> Peter then interrupted his clinical training to spend 2 yr with Michael Crowder, M.D., Ph.D., at Washington University in St. Louis, Missouri, learning to use genetic techniques to study mechanisms of anesthetic action in the model organism, *Caenorhabditis elegans*. In the Crowder laboratory, he completed a project using <sup>19</sup>F- nuclear magnetic resonance spectroscopy to measure the direct binding of isoflurane to presynaptic SNARE proteins,<sup>3</sup> and then brought his own “new ideas” to the laboratory, convincing Mike Crowder to investigate the mechanisms of action of



Peter Nagele, M.D., recipient of the American Society of Anesthesiologists 2012 Presidential Scholar Award.

nitrous oxide and xenon. In a series of elegant experiments using glutamate-receptor null mutants and genetic rescues, Dr. Nagele’s work provided the first *in vivo* evidence for the molecular mechanisms of xenon and nitrous oxide. This work was published in the *Proceedings of the National Academy of Sciences (USA)*<sup>4</sup> and *ANESTHESIOLOGY*,<sup>5</sup> completing a remarkable record of ten first author publications (including five original research studies) during clinical training. In 2002, Dr. Nagele returned to Austria to complete his clinical training and his habilitation. Habilitation is the equivalent of a research doctoral degree and is the highest academic qualification one can achieve for his or her own pursuit in Austria. Peter’s habilitation was awarded the Otto-Kraupp Prize as the single best habilitation in any medical discipline in the nation of Austria.

In 2005 Dr. Nagele joined the anesthesiology faculty at Washington University, splitting his time between research and clinical work. He decided that his true passion was for translational research (rather than model organism genetics) and with the advice and guidance of Michael Crowder and Evan Kharasch he sought to combine his clinical interests with his knowledge of genetics. In characteristic fashion, Peter recognized that to become a principal investigator in clinical/translational research he would need additional training and he matriculated in and completed a National Institutes of Health-sponsored Master’s degree program in clinical research (K30). He then initiated his clinical research, first under the auspices of a Foundation for Anesthetic Education

\* Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri.

Submitted for publication July 2, 2012. Accepted for publication July 6, 2012.

Copyright © 2012, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins. Anesthesiology 2012; 117:714–6

and Research mentored-research training grant and subsequently a National Institutes of Health mentored patient-oriented career development award (K23). Evan Kharasch served as Peter's mentor for both of these grants and Peter strongly believes that Evan's guidance and mentorship have been pivotal to his success. Indeed, Peter was one of several mentees who nominated Evan Kharasch for his 2010 Foundation for Anesthetic Education and Research Mentoring Excellence in Research Award. Dr. Nagele subsequently completed a second Master's degree program in genetic epidemiology to enable him to fully pursue his interests in perioperative pharmacogenomics.

Peter's clinical research interests are broad. A major focus of his work has been perioperative pharmacogenomics, an area poised at the intersection of clinical outcomes, pharmacology, and genetics. His first pharmacogenomics study examined the effect of nitrous oxide on homocysteine levels in patients with mutations in the gene for methylene tetrahydrofolate reductase, a key enzyme in folate metabolism. This is an important area because nitrous oxide has been implicated in adverse cardiac outcomes.<sup>6,7</sup> In an initial study, Peter showed that nitrous oxide exposure resulted in higher plasma homocysteine levels in patients with methylene tetrahydrofolate reductase mutations.<sup>8,9</sup> He has recently completed a 625-patient randomized clinical trial (the VINO study) examining the effects of nitrous oxide on perioperative myocardial infarction in patients with and without methylene tetrahydrofolate reductase mutations. The important results of this trial will be published shortly and presented at this year's American Society of Anesthesiologists meeting; I will refrain from "spilling the beans." Dr. Nagele has also taken a strong interest in the genomics and pharmacogenomics of perioperative myocardial infarction,<sup>10,11</sup> with particular interest in pharmacogenomic influences on patient response to perioperative  $\beta$ -blockers. A more recent interest in the genetic cause of hidradenitis suppurativa, was spurred by Peter's recurrent contact with patients (and their family members) with this disease requiring urgent surgery.

Dr. Nagele's research interests stem from his prowess as an active and vibrant clinical anesthesiologist. He has a long-standing interest in prehospital care and trauma anesthesiology, and is the head of our department's section of trauma anesthesiology. His long-term involvement in trauma anesthesiology has also sustained his interest in resuscitation research. He has several significant publications in this area,<sup>12</sup> including an influential meta-analysis published in *Lancet* examining the efficacy of chest compression only *versus* standard cardiopulmonary resuscitation.<sup>13,14</sup>

Although the Presidential Scholar Award recognizes Peter Nagele's research accomplishments, it is important to note that he is also a contributor to a wide array of activities in our specialty. He is the recipient of multiple federal and foundation grants and has received several major prizes, including the Elmer-Zsigmond award from the International Society for Anesthetic Pharmacology and the Billroth Prize from the

Vienna Medical Society. He also serves on the Scientific Advisory Board of the Association of University Anesthesiologists and reviews for multiple anesthesiology and general medical journals. Recently, he has been appointed as an associate editor of *ANESTHESIOLOGY*.

Over the past 7 yr, I have watched Peter Nagele mature from a person of energy, passion, and potential into a mature academic physician who now provides advice and mentoring for trainees and junior faculty. This year I proudly observed as Peter mentored a senior resident with no previous research experience to complete and publish a study in *ANESTHESIOLOGY*.<sup>15</sup> He is developing a following among our trainees and I would not be surprised to see one of Peter's mentees receive the Presidential Award in years to come. It is a pleasure to see Peter Nagele receive this recognition for his scholarly achievement. However, it is even better to watch close-up as my friend and colleague, Peter Nagele, inexorably expands his intellectual reach, his research skills and his accomplishments. Peter has continued to have a multitude of "new ideas" and they are clearly getting better with time. I applaud Peter for his accomplishments and for this award, but stay tuned ... the best is yet to come from Peter Nagele.

## References

- Greif R, Aka O, Horn EP, Kurz A, Sessler DI, Outcomes Research Group. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med* 2000; 342:161-7
- Rossaint R, Reyle-Hahn M, Schulte Am Esch J, Scholz J, Scherpereel P, Vallet B, Giunta F, Del Turco M, Erdmann W, Tenbrinck R, Hammerle AF, Nagele P, Xenon Study Group. Multicenter randomized comparison of the efficacy and safety of xenon and isoflurane in patients undergoing elective surgery. *ANESTHESIOLOGY* 2003; 98:6-13
- Nagele P, Mendel JB, Placzek WJ, Scott BA, D'Avignon DA, Crowder CM: Volatile anesthetics bind rat synaptic snare proteins. *ANESTHESIOLOGY* 2005; 103:768-78
- Nagele P, Metz LB, Crowder CM: Nitrous oxide (N<sub>2</sub>O) requires the N-methyl-D-aspartate receptor for its action in *Caenorhabditis elegans*. *Proc Natl Acad Sci USA* 2004; 101: 8791-6
- Nagele P, Metz LB, Crowder CM: Xenon acts by inhibition of non-N-methyl-D-aspartate receptor-mediated glutamatergic neurotransmission in *Caenorhabditis elegans*. *ANESTHESIOLOGY* 2005; 103:508-13
- Leslie K, Myles PS, Chan MT, Forbes A, Paech MJ, Peyton P, Silbert BS, Williamson E: Nitrous oxide and long-term morbidity and mortality in the ENIGMA trial. *Anesth Analg* 2011; 112:387-93
- Myles PS, Leslie K, Chan MT, Forbes A, Paech MJ, Peyton P, Silbert BS, Pascoe E, ENIGMA Trial Group. Avoidance of nitrous oxide for patients undergoing major surgery: A randomized controlled trial. *ANESTHESIOLOGY* 2007; 107:221-31
- Nagele P, Zeugswetter B, Wiener C, Burger H, Hpfl M, Mittlbck M, Fdinger M: Influence of methylenetetrahydrofolate reductase gene polymorphisms on homocysteine concentrations after nitrous oxide anesthesia. *ANESTHESIOLOGY* 2008; 109:36-43
- Nagele P, Zeugswetter B, Eberle C, Hpfl M, Mittlbck M, Fdinger M: A common gene variant in methionine synthase reductase is not associated with peak homocysteine concentrations after nitrous oxide anesthesia. *Pharmacogenet Genomics* 2009; 19:325-9

10. Nagele P, Liggett SB: Genetic variation,  $\beta$ -blockers, and perioperative myocardial infarction. *ANESTHESIOLOGY* 2011; 115:1316-27
11. Vascular Events In Noncardiac Surgery Patients Cohort Evaluation (VISION) Study Investigators, Devereaux PJ, Chan MT, Alonso-Coello P, Walsh M, Berwanger O, Villar JC, Wang CY, Garutti RI, Jacka MJ, Sigamani A, Srinathan S, Biccard BM, Chow CK, Abraham V, Tiboni M, Pettit S, Szczeklik W, Lurati Buse G, Botto F, Guyatt G, Heels-Ansdell D, Sessler DI, Thorlund K, Garg AX, Mrkoprada M, Thomas S, Rodseth RN, Pearse RM, Thabane L, McQueen MJ, VanHelder T, Bhandari M, Bosch J, Kurz A, Polanczyk C, Malaga G, Nagele P, Le Manach Y, Leuwer M, Yusuf S: Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012; 307:2295-304
12. Hpfl M, Duma A, Uray T, Maier C, Fiegl N, Bogner N, Nagele P: Over-the-head cardiopulmonary resuscitation improves efficacy in basic life support performed by professional medical personnel with a single rescuer: A simulation study. *Anesth Analg* 2005; 101:200-5
13. Hpfl M, Selig HF, Nagele P: Chest-compression-only *versus* standard cardiopulmonary resuscitation: A meta-analysis. *Lancet* 2010; 376:1552-7
14. Nagele P: Augmented CPR: Rescue after the ResQ trial. *Lancet* 2011; 377:276-8
15. Nagele P, Pal S, Brown F, Blood J, Miller JP, Johnston J: Postoperative QT interval prolongation in patients undergoing noncardiac surgery under general anesthesia. *ANESTHESIOLOGY* 2012; 117:321-8