REVISITING THE VISION AND MISSION OF THE AUA

There was a strong view that there should be a shift in emphasis in the AUA’s Vision and Mission. The consensus was that the AUA should remain honorific, but that those becoming Members should expect to participate actively in activities designed to further the Mission of the AUA. The following are suggested amended Vision and Mission statements for the AUA.

The Association of Anesthesiology has as its Vision the furtherance of anesthesiology as a dynamic academic medical specialty, with a vibrant community of successful scientific, educational and medical leaders within the academic sector.

The Mission of the AUA is to bolster academic anesthesiology through:

- deliberate mentorship of academic anesthesiologists, under the rubric of faculty development;
- programmatic and ongoing career development of anesthesiology researchers, educators, and academic leaders throughout their careers;
- the organization of an outstanding annual academic meeting;
- targeted provision of networking opportunities to academic anesthesiologists.
In order to achieve these strategic Mission-based goals, the AUA must develop a tactical program with measurable outcomes. To this end, leadership development of academic anesthesiologists, and their engagement to achieve appreciable results to advance the Mission of the AUA was identified as a high yield investment. There are two components to the leadership Mission: (i) leadership development for academic anesthesiologists who are oriented towards scholarship, and (ii) leadership training for those Members of the academic community who may not aspire to substantial personal scholarly accomplishment, but who intend to advance scholarship in anesthesiology through their leadership. AUA Council Members recognized that this proposed change in Mission constitutes a major shift in emphasis for the AUA, and will need to be presented to the organization as a whole for endorsement.

The following action items were suggested as next steps:

1. The AUA Council will ensure that the broad Membership of the AUA is aware of the planned change in direction. This article is the first step to accomplishing this aim.

2. The Members of the AUA will have the ability to endorse, modify or reject the shift in the AUA’s Mission. In order to address this, the modified Vision and Mission statements will be presented at next year’s AUA business meeting. Following discussion and possible amendments, the Membership will have the opportunity to vote on the proposed changes.

3. We will consider forming a Leadership Development Taskforce within the AUA, with the specific mandate to conceptualize and beta test academic leadership development programs.

4. A meeting will be held, including the leadership of the AUA and other stakeholder organizations, to discuss how the various organizations can complement their various Missions, and how best to work together strategically.

5. We must redefine and refine the criteria for AUA Membership with more specific criteria, and now including three broad (and not mutually exclusive) categories: (i) researchers, (ii) educators and (iii) leaders at major academic anesthesiology departments, who have achieved outcomes that are in alignment with the Mission of the AUA.

6. In relation to leadership, we need to clarify that there are two key changes that are proposed, one of which is Mission related and one of which is Membership related.

   a. Regarding Membership, key leaders of major academic departments who have made modest personal contributions to scholarship (in research and education), but who have demonstrably promoted scholarship in anesthesiology in their capacity as leaders, might qualify for AUA Membership. As with all candidates for Membership, they would need to be nominated by an Active AUA Member, and their candidacy would be assessed by the AUA Council and the broad AUA Membership.

   b. Regarding Mission, the AUA will create leadership development programs at our meeting and potentially elsewhere. Such programs will be targeted at aspiring academic leaders who do not need to meet AUA Membership criteria. Hopefully many of them will become influential leaders in academic anesthesiology and will also become actively contributing AUA Members.

7. The EAB and SAB will consider how the meeting furthers the modified Mission of the AUA. If the change in Mission is adopted, there will potentially need to be a complete reappraisal of the annual meeting.

8. The AUA will solicit input from academic anesthesiology chairs regarding these proposed changes, and for practical advice on how to enhance leadership in the field in order to have outcomes that are in alignment with the Mission of the AUA.

9. The AUA must continue to provide guidance and mentorship to promising organizations representing future anesthesiology leaders, such as the Early Stage Anesthesiology Scholars. It was suggested that eSAS should have representation on the AUA Council, the SAB, the EAB, and possibly the Leadership Development Taskforce. These representatives must also be Associate Members of the AUA.

10. The AUA will continue to work with other organization on project-based initiatives, such as the Initiative for Multidisciplinary Pragmatic Anesthesiology Clinical Trials (IMPACT).

11. The AUA Council will create a working group with representation from the AUA Council, eSAS, EAB, SAB, and also the proposed Leadership Development Taskforce to plan strategically for the 2020 meeting and beyond. As mentioned previously, the eSAS representative must also be an Associate AUA Member.

On Behalf of the AUA Council.
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University of California  
Los Angeles, California
**FUNDING OPPORTUNITIES**

- The 2019 Medical Student Anesthesia Research Fellowship (MSARF) Summer Program provides challenging and rewarding experiences in anesthesia research. Medical students who participate in the summer anesthesia research fellowship can expect:
  - Eight weeks of focused research related to anesthesiology
  - A dedicated mentor who will provide training in research techniques and scientific methods
  - The opportunity to make a scientific poster or oral presentation during the FAER MSARF Symposium held at the ASA’s ANESTHESIOLOGY® annual meeting
  - A $400 per week student stipend, ASA student membership dues, plus additional funds to help cover the costs of travel to the ANESTHESIOLOGY® annual meeting

The 2019 application website will open December 1, 2018 and will close January 31, 2019. Visit FAER.org to apply.

- The Anesthesia Patient Safety Foundation (APSF) and The Foundation for Anesthesia Education and Research (FAER) are now offering the joint APSF/FAER Mentored Research Training Grant (MRTG) to develop the next generation of perioperative patient safety scientists.
  - This two-year, $300,000 award aims to help anesthesiologists develop the skills and preliminary data they need to become independent investigators in the field of anesthesia patient safety.
  - Anesthesiologist faculty members who are within 10 years of their first faculty appointment are eligible.
  - The grant requires 60% of the grantee’s time will be dedicated to research.

The application is available at FAER.org. The deadline to apply is November 30th.

**SUPPORT OPPORTUNITIES**

- The Foundation for Anesthesia Education and Research is seeking volunteers to join its Development Committee. This is a unique opportunity to build a network of professionals committed to advancing innovation and scientific discovery in our specialty.

Volunteer roles and responsibilities include:
  - Serve as FAER ambassadors, believing and supporting FAER’s mission and vision for Research, Education, and Training/Mentoring within anesthesiology.
  - Solicit support for the Annual Appeal from a list of prospects.
  - Analyze relationships with current and prospective support and advise staff in developing individualized strategies to cultivate and strengthen these relationships.
  - Participate in quarterly conference calls (approximately 60 minutes) and provide updates on solicitation activities.
  - Review donor data and make recommendations for improvements for increasing donations.

The application is accessible on FAER.org. The deadline to apply is November 30th.

- FAER relies on the support of generous donors. Donate to FAER to support anesthesiology research and early physician-scientists. Visit FAER.org/donate to make your contribution to the field of anesthesiology today.

Contact faer@FAER.org with any questions or comments.
We are delighted to welcome 4 new members to the Education Advisory Board (EAB). In June of 2018 we issued a call for membership to the EAB. We received many applications from qualified candidates which made the decision to select only 4 new members quite challenging. Each new member has significant leadership experience and also has a long-term commitment to education. Our new members are Barbara G. Jericho, MD, DABPM, FASA, Cynthia A. Lien, MD, Susan Marie Martinelli, MD and Edward C. Nemergut II, MD. Each of these individuals will serve a 3-year term. Importantly, we will be issuing another call for membership in 2019.

Barbara G. Jericho, MD, DABPM, FASA
The University of Illinois Hospital and Health Sciences System
Chicago, Illinois

Cynthia A. Lien, MD
Froedtert & Medical College of Wisconsin Specialty Clinics
Milwaukee, Wisconsin

Susan Marie Martinelli, MD
The University of North Carolina School of Medicine
Chapel Hill, North Carolina

Edward C. Nemergut II, MD
University of Virginia Health Systems
Charlottesville, Virginia

IARS, AUA and SOCCA Annual Meetings
Montreal, May 16 – 20

All three meetings will be held at the historic Fairmont The Queen Elizabeth hotel in downtown Montreal. If you’ve never been to Montreal, now is your chance. One of the greatest cities in the world, Montreal offers incredible dining, a vivacious art and culture scene, and an infectious love of life. This is NOT an Annual Meeting you want to miss!
THE FLIPPED CLASSROOM: WHAT IS THAT?

In medical school and post-graduate training, most practicing anesthesiologists and intensivists learned through listening to lectures and reading textbooks. However, modern educational and neurobiological research is showing that these traditional approaches may not be nearly as effective as other modalities of learning. Traditionally, didactics were comprised of experts attempting to transfer knowledge to learners through lectures, a passive event for the learner. Then, learners were supposed to actively apply their new knowledge through assigned homework that was completed outside of class. Enter the Flipped Classroom (FC) model, where that traditional order is flipped, and the new knowledge content that would have been delivered in the lecture is consumed prior to class. Although the pre-class “homework” can take on many forms (i.e. readings, interactive modules, podcasts, etc.), it is most commonly delivered through brief 15-20 minute videos. Precious face-to-face class time is spent in active learning, applying and testing the new knowledge with the expert present to help facilitate the process. This active learning can be done through audience response questions, think-pair-share questions, case based learning, and educational games, just to name a few. In the FC model, the role of the educator changes from the “sage on the stage” to an active facilitator. For anyone beginning to use this method of instruction, it is important to note that the FC includes both the “homework” and the in-class portions of learning.

WHAT ARE THE PURPORTED BENEFITS?

There are many suggested benefits of the FC. First, it allows for asynchronous learning, meaning that learners can choose the pace, place, and time in which they learn foundational concepts. Second, learners are more engaged by nature of the problem-solving exercises in class (Sait). Third, the FC model promotes teamwork, which also holds learners accountable to do the “homework” so they are prepared in class. Fourth, the educator has a better opportunity to understand and teach to knowledge gaps as learners are working through problems.

IS THERE QUANTITATIVE DATA?

However, these are qualitative outcomes. What about quantifiable results? A number of studies, largely from pharmacy graduate education, demonstrated improvements in knowledge gain and learner preference for FC compared to traditional lectures (Wong, McLaughlin, Pierce). In the setting of undergraduate medical education, there have been mixed results with knowledge and skill acquisition compared to traditional methods, but learners prefer the FC approach. (Chen) Recently, there have been several studies published within graduate medical education (GME). A FAER-sponsored multi-institutional study compared FC to traditional lectures for CA-1 residents preparing for the American Board of Anesthesiology BASIC Examination. There was a trend toward greater knowledge acquisition with the FC at baseline and significantly greater knowledge retention after 4 months compared to traditional lectures. Additionally, the residents preferred the FC model to traditional lectures. (Martinelli JGME) These findings were similar to those reported in a recent study evaluating FC for internal medicine resident quality improvement education. (Bonnes) In addition, a neurosurgery residency program showed an improvement in board scores when FC was utilized. (Girgis)

Most of the FC studies have used multiple choice questions (MCQs) to assess knowledge. As MCQs often fall toward the base of Miller’s pyramid (Miller), this type of assessment may underestimate the value of FC. As one of the goals of active learning and FC is to improve learners ability to problem solve and...
apply knowledge, it could be posited that this could translate into higher areas of Miller’s pyramid. To test this, Objective Structured Clinical Examinations (OSCEs) were utilized in two prospective controlled studies to assess knowledge application and use of skills in an OB/GYN medical student clerkship (Gillespie) as well as a pharmacy graduate school course (Lockman). Both studies reported significantly greater learning benefits with FC as compared to traditional lectures. This suggests that it might be beneficial for future work on FC in GME to assess with OSCE as well as MCQs.

**IF THE FC IS SO GOOD, WHY ISN’T EVERYONE USING IT?**

Most of the potential barriers to implementing the FC come from the faculty. Academic anesthesiologists were surveyed about this teaching method and the most common concerns were that: 1) learners would not come to class prepared or participate in class, 2) faculty were more comfortable with lecture-based teaching, 3) it would take too much time to prepare, and 4) the use of technology (e.g. recording a video) was intimidating. (Martinelli JEPM) The experience of programs utilizing FC demonstrate that learners come prepared and are more engaged to learn, train the educator seminars can readily train faculty to be facilitators rather than lecturers, and technology hurdles are minimal and overcome with a short orientation to available resources. Finally, some detractors will note that further research is needed in order to fully demonstrate the efficacy of the FC and to clarify which aspect of active learning is most important. While we agree that future research is needed, the evidence is clear that traditional passive learning through lectures needs to be supplanted with evidence-based methods based on the neurobiology of learning.

In summary, the FC is an emerging and increasingly evidence-based educational method that encourages application of foundational material and problem-solving in the classroom.

**References:**


Gillispie V. Using the flipped classroom to bridge the gap to generation Y. Ochsner J. 2016; 16(1):32-36.


The flipped classroom (FC) format contrasts with “traditional” didactic formats in two ways: 1) the FC format is necessarily preceded by assigned self-directed learning (the “flipping”), and 2) traditional formats do not necessarily include interactive discussion. The FC format is gaining popularity and the subject of increasing amounts of medical education research.

**ISSUES WITH CURRENT FC STUDIES IN MEDICAL EDUCATION**

Published interventions that assess FC in medical education 1) are often part of larger curriculum redesign efforts that change many factors in addition to “flipping the content” and 2) do not track important confounders. Specifically, in addition to the FC format, comparator groups have differed from intervention groups in important ways, including total study time, expectations for didactic attendance, solicitation and response to student feedback, and streamlining of content. Thus, we cannot ascribe causality to the “flipping” per se.

This is not to say that FC does not or cannot work in medical education. It simply means that current studies do not seem to be designed to answer that question.

Setting this aside, let’s look at the literature.

**DOES THE FC FORMAT INCREASE LEARNING IN MEDICAL EDUCATION?**

Unfortunately, systematic review of the FC format in medical education failed to show a consistent empiric learning benefit of the FC format in medical education. This is a surprising finding, because the FC format includes active learning strategies that should work. By its nature, the FC format includes some of the most highly effective learning techniques that have been studied: the spreading out of study activities over time (spacing), active recall of previously studied material (retrieval), explaining why something might be true (elaboration), and relating learning to other knowledge (self-explanation). When compared to more passive learning strategies these active strategies dominate. Consequently, we should expect that the FC format affords substantial gains for learners. That we do not see a consistent learning benefit is puzzling.

**WHY DO FC STUDIES FAIL TO SHOW CONSISTENT LEARNING BENEFIT IN MEDICAL EDUCATION?**

How could it be that a format that employs high-yield strategies and requires additional self-directed learning has no impact on learning?

Maybe it’s a problem in the methods

If we take the optimistic view, it may be that studies, even systematic reviews, have simply been underpowered. Power is a major issue for medical education research, where “dilution” of observed effects is possible owing to many other factors. It may also be that researchers are looking at the wrong outcomes. Most studies of FC have looked at short-term retention of learned material. Perhaps longer-term retention or transfer of learned materials to new areas would be more successful in demonstrating an effect.

Maybe “flipping” is not practical for medical education

On the other hand, it may be that the FC format does not work as well in medical education for other reasons. One of the greatest and most practical threats to the FC format is when learners do not do the pre-work. When this happens, the learner does not encode the information before the session, and (because the session is focused on using the information, not acquiring it) they do not encode it then either. This subgroup of learners
would greatly decrease any observed effect in studies (and in practice). In published accounts of FC in medical education, compliance with pre-work is disappointing: 25-69% of medical education learners complete the pre-work, even when the pre-work only requires watching a 10-minute video.\textsuperscript{5,6} Learners in medical education have extensive competing responsibilities, and attempting to force learners to do the pre-work is challenging, to say the least.

Moreover, while the active learning components of FC have substantial theoretical and empiric grounding, the “flipping” itself has little laboratory evidence. Although the “FC” name suggests that the temporal “flipping” is an important element, proponents of the FC format justifiably argue that it is the active learning techniques that are more important.\textsuperscript{7} Continuing to emphasize the pre-work “flipping” component, instead of focusing on active learning during didactics, may be the Achilles heel of it all.

**BOTTOM LINE**

Studies of FC in medical education have been heavily confounded, limiting our ability to ascribe causality. Even disregarding this, evidence does not yet support a learning benefit of the FC content in medical education. Future studies must employ adequate controls and should focus on longer term learning outcomes. To find success in medical education, the FC format may benefit from “re-branding” that focuses more on active learning components and less on the pre-work that is often not done by medical learners. 

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**References**


Michael Andreae, MD, is Associate Professor of Anesthesiology and holds the Donald E. Martin Professorship in Anesthesia and Pain Medicine at Penn State College of Medicine. He is an anesthesiologist and data scientist interested in health service science, in particular how to leverage clinical data registries to address healthcare disparities and measure individual provider performance and how to synthesize the evidence on long-term pain outcomes.

Meghan Lane-Fall, MD, MSHP, is Assistant Professor of Anesthesiology and Critical Care and Co-Director of the Center for Perioperative Outcomes Research and Transformation at the University of Pennsylvania. She is an implementation scientist whose work focuses on perioperative handoffs and other strategies to improve the quality and safety of acute care.

Christine Sang, MD, MPH is Associate Professor of Anesthesiology at Harvard Medical School and the founding director of the Translational Pain Research Program at Brigham and Women’s Hospital. Her program systematically evaluates novel potential analgesics in Phases Ia (First-in-Man) through Ila clinical trials to target selective mechanisms of pain by optimizing efficient designs, endpoints (including biomarkers), and execution.

Niccolò Terrando, BSc (hons), DIC, PhD, is Associate Professor in Anesthesiology at Duke University, North Carolina. His laboratory studies the pathogenesis of perioperative neurocognitive disorders, with emphasis on the mechanisms whereby surgery affects brain function and how regulation of neuro-immune processes can be targeted to develop safer mitigation strategies to prevent these common postoperative complications.

A very warm welcome to our new SAB members, and a heartfelt thank you to the many highly accomplished AUA members who submitted their CVs, but were not selected this year. I encourage everyone to please reapply next year.
The mitochondrion is a dynamic organelle that maintains cellular homeostasis by generating high-energy phosphates, buffering intracellular calcium, and modulating oxidative stress (1). However, mitochondria are also capable of mediating programmed cell death and necrosis (1). Central to many of these regulatory functions is the mitochondrial permeability transition pore (mPTP). Mounting evidence suggests that permeability transition (opening of the pore) within mitochondria plays a pathological role in a variety of cardiac disease processes and neurodegenerative states while physiological regulation of the mPTP has recently been shown to be important for cellular development and differentiation (Figure)(2). Thus, the mPTP plays a dichotomous role in health and disease.

The mPTP is a voltage-gated, non-specific, non-selective mega-channel present on the inner mitochondrial membrane (2, 3). Although the presence of the pore and its functional importance have been well established, its exact proteinaceous molecular identity remains elusive. Our understanding of the components that make up the mPTP has evolved over time and genetic-based studies have helped to better define the pore-forming structures and pore regulators (4). Currently, the ATP synthase (Complex V of the electron transport chain [ETC]) is believed to form the putative core component of the mPTP while the adenine nucleotide translocator (ANT), the mitochondrial phosphate carrier (PIC), and cyclophilin D (CypD) are believed to serve as pore regulators (4). Some have proposed that the c-subunit ring of the ATP synthase is the pore while others have suggested that the mPTP forms between ATP synthase dimers (3, 5). CypD, a mitochondrial matrix protein with peptidyl-prolyl cis-trans-isomerase activity, promotes mPTP opening by facilitating a calcium-triggered conformational change in the pore (6). Calcium and reactive oxygen species (ROS) facilitate pore opening while adenine nucleotides, low pH, magnesium, cyclosporine A (CsA) and sanglifehrin A ([CypD] inhibitors) inhibit the mPTP (4).

High-conductance opening of the mPTP permits molecules of up to ~1.5 kD in size to pass into the mitochondrial matrix while low-conductance opening restricts permeability to molecules with a molecular mass of < 0.3 kD (2, 7). The resultant inner membrane permeability can have consequences for the mitochondrial membrane potential, calcium handling, superoxide production, ATP synthesis, and cell viability (2). Uncontrolled, high-conductance opening of the mPTP causes collapse of the mitochondrial membrane potential, rapid uncoupling of oxidative phosphorylation, swelling of mitochondria, and ultimately leads to apoptosis or necrosis (2, 3, 7). This pathological mPTP opening is thought to underlie ischemia-reperfusion injury in the heart and other organ systems and contributes to the mitochondrial dysfunction and oxidative stress seen in neurodegenerative disorders such as Huntington’s, Alzheimer’s, and Parkinson’s disease (Figure) (2). Furthermore, mPTP opening is known to play a role in the pathophysiology of traumatic brain injury (TBI) (2). Thus, the mPTP represents an important therapeutic target for a wide variety of disease processes.

In contrast to pathological opening, physiological opening of the mPTP is a regulated and controlled process important for homeostasis and cellular maturation (Figure)(2). Transient, low-conductance opening of the pore has been shown to result in calcium efflux, suggesting a role in calcium regulation (2). In addition, controlled mPTP opening has been shown to result in physiological ROS signaling (2). Transient pore opening results in proton leak, a brief decline in mitochondrial membrane potential, an increase in electron

**THE PATHOPHYSIOLOGICAL AND PHYSIOLOGICAL ROLES OF MPTP OPENING**

From Kwong and Molkentin, Cell Metab 2015.
flux through the ETC and a short burst or “flash” of superoxide (2). These superoxide flashes are thought to be important during cellular maturation and may mediate the metabolic switch from aerobic glycolysis to oxidative respiration in differentiating stem cells (8). Closure of the mPTP also appears to be an important process in developing cells. In embryonic cardiomyocytes, the ETC is immature and energy is known to be produced primarily via anaerobic glycolysis (2, 9). During this developmental period, the cardiomyocyte mPTP is wide open, mitochondrial membrane potential is low, and ROS levels are high (2, 9). Closure of the mPTP couples oxidative phosphorylation, increases the mitochondrial membrane potential, reduces oxidative stress, and induces cardiomyocyte differentiation and mitochondrial maturation (10). In the developing nervous system, neural progenitor cells also undergo a metabolic switch from glycolysis to aerobic respiration during differentiation (11). Emerging evidence suggests that the mPTP plays a role in metabolic reprogramming to suppress neural progenitor cell proliferation and promote differentiation (8). Further evidence suggests a role for the mPTP in the differentiation of other types of cells, such as hematopoietic and vascular progenitor cells and natural killer cells (10). Therefore, developmental regulation of the mPTP is important in a variety of cells, tissues, and organ systems.

With regard to anesthetics, a number of the agents we commonly use in daily practice have been shown to impact open probability of the mPTP. Most studies have evaluated the effect of anesthetics on the mPTP in the context of ischemia-reperfusion in a variety of different cell and tissue types. Propofol, for example, has been shown to prevent reperfusion injury by inhibiting mPTP opening and calcium-induced permeability transition in rodent brain, cardiomyocytes, and hepatocytes (12-14). Isoflurane prevents permeability transition during the reperfusion phase (postconditioning) in the rodent heart and brain, conferring cytoprotection following ischemia-reperfusion (15-17). Interestingly, anesthetic preconditioning has also been shown to promote cellular survival by preventing subsequent activation of the mPTP (18). A number of potential mechanisms of anesthetic-mediated cellular protection have been proposed by investigators and include roles for CypD, calcium, and ROS signaling (19). However, the exact mechanisms remain elusive. Importantly, detailed rigorous investigation of how various anesthetics interact with the mPTP is also lacking. An obvious barrier to our full understanding is the fact that the exact proteinaceous molecular identity of the mPTP channel is unknown. These gaps, however, represent opportunities for anesthesiologist-scientists to contribute to the literature and enhance our knowledge. Thus, future investigation should focus on attempts to identify the molecular components of the mPTP, determine if anesthetic agents bind to and modulate the pore itself, and develop novel therapeutics that target the mPTP in various disease processes. Anesthesiologists and intensivists should be aware of this channel’s biological activity and recognize that mPTP research is a fertile area for basic scientific investigation. Because the mPTP is important in health and disease, future research is likely to shed greater light on the pathophysiology of permeability transition in many different disease processes relevant to our field and elucidate the role of the pore in development and aging.
References:


During embryonic development, primitive yolk sac myeloid progenitors enter the brain and differentiate into microglial cells. It is usually estimated that around 10% of the adult brain cells are microglia cells. Microglia can develop into proinflammatory/classically activated M1 or anti-inflammatory activated M2 phenotypes depending on the signals present at different stages after brain lesions. M1/proinflammatory microglia produces proinflammatory mediators and ROS that exacerbate neuronal death. Alternatively, M2/immunoregulatory microglia induce brain repair and regeneration, produce growth factors and anti-inflammatory cytokines to protect neurons and resolve inflammation. Several subclasses of M2/immunoregulatory activation have been identified. The M2a activation state has a main function of suppression inflammation. A second state of alternative activation is classified as M2c, which has been suggested to restore the tissue after the inflammatory process has been attenuated. M2b has been involved in both pro- or anti-inflammatory responses and related to memory immune responses. Collectively, M2 phenotype cells are involved in anti-inflammatory, debris clearance, extracellular matrix deposition and angiogenesis functions in the brain. Progression from the proinflammatory /M1 to immunoregulatory/M2 phenotype is necessary to efficiently counteract brain lesions. However, when this process is dysregulated, the persistent release of inflammatory cytokines and ROS induces neuron death and enhances brain damage. Persistently proinflammatory M1 microglia in the brain is the key factor for the development of neurodegenerative disorders like multiple sclerosis, Alzheimer’s disease and Parkinsonian disease. Of note, the FDA-approved drug glatiramer acetate (GA) for multiple sclerosis treatment, works by inducing Th1 to Th2 shift, resulting in the production of anti-inflammatory cytokines like IL-4 that polarize the microglia into M2 anti-inflammatory phenotype.

Cytokines like TNF-α, IL-6, IL-1β and interferon-γ (INF-γ) and several chemokines, in addition to the level of microglia NADPH-oxidase activation are essential to shift the microglia to pro-inflammatory type M1. Ang-II via its AT1 receptor, is a major activator of the NADPH-oxidase complex, leading to pro-oxidative and pro-inflammatory effects resulting in the shift to M1 type. However, the anti-inflammatory cytokines like IL-4, IL-10 and peroxisome proliferator activated gamma receptor (PPAR γ) agonists are polarizing the microglia towards the anti-inflammatory M2.

The angiotensin receptor blocker (ARB) group is heterogenous, with some members notably Telmisartan and to lesser extent Candesartan, exhibiting a pleiotropic profile, not only blocking AT1 receptor but also activating PPARγ an anti-inflammatory, and pro-metabolic nuclear receptor thereby helps in shifting the microglia cells towards the anti-inflammatory M2 type.

Alzheimer’s disease is the most common form of dementia and is characterized by the presence of neurofibrillary tangles of hyperphosphorylated Tau and extracellular deposits of the peptide amyloid β (Aβ), forming neuritic plaques. Another key feature of Alzheimer’s disease is the presence of prominent neuroinflammation. There are several ways for Aβ clearance from the brain. Amyloid β can be directly shuttled out of the brain via protein complexes such as LRP1 and apolipoprotein E, which can bind extracellular Aβ and transport them to the blood brain barrier, where they are then shuttled to the

continued on page 15
other side. Extracellular Aβ in CNS interstitial fluid is moved into the CSF via the newly discovered glymphatic pathway. Finally, Aβ can be cleared via phagocytosis and degradation by resident CNS immune cells, such as microglia, astrocytes and possibly neurons. M2 type is the key player in the process of phagocytosis and clearance of Aβ from the brain. 

The treatment of ARB with their ability to shift the microglia towards M2 type has improved the cognition in many rodent models of Alzheimer’s disease in doses that did not significantly lower blood pressure. Therefore, administration of ARBs to hypertensive patients, reduced the risk not only of Alzheimer’s disease but also for vascular dementia. In controlled clinical trials, several ARBs not only limit stroke-induced damage, protecting executive function and cognition, but also reduce hypertension and diabetes, major risk factors for stroke.

Parkinson’s disease is characterized by enhanced NADPH-oxidase activity, enhanced uncontrolled inflammatory processes, increased TNF-α production, regulation of α-synuclein, reduction of brain neurotrophic factors and decreased activation of PPARγ. The use of most potent ARBs Candesartan and Telmisartan is considered among the new treatments for Parkinson’s disease.

In vivo and vitro studies revealed that the ARB Olmesartan increased neurite outgrowth and acetyltransferase activity in primary cultures of ventral spinal cord and enhanced survival of motor neurons after unilateral section of the sciatic nerve. Therefore, Olmesartan is considered as a possible therapeutic agent in disorders leading to degeneration of motor neurons, such as amyotrophic lateral sclerosis.

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The American Society of Anesthesiologists (ASA) recently presented Alex Macario, M.D., M.B.A., with its 2018 Excellence in Education Award in recognition of his outstanding contributions to resident and graduate education in anesthesiology. The award is presented annually to an ASA member who has made significant contributions to the specialty through excellence in teaching, development of new teaching methods, or the implementation of innovative educational programs in anesthesiology.

Dr. Macario is vice-chair for education and professor in the Department of Anesthesiology, Perioperative and Pain Medicine at the Stanford University School of Medicine, California, where he is also professor by courtesy in the Department of Health Research and Policy. "Dr. Macario is an exceptional professor of anesthesiology who deserves this award for his outstanding contributions to graduate medical education," said ASA President James D. Grant, M.D., M.B.A., FASA. "His drive and passion for teaching, mentoring and creating innovative educational programs for young physicians is not only essential, but unparalleled."

A member of the faculty at Stanford for 23 years, Dr. Macario established early in his career an internationally recognized academic program in operating room (OR) management, including creating the Management of Perioperative Services Fellowship, before transitioning to an interest in medical education. In 2006, he assumed the position of director of the anesthesiology residency program at Stanford, where he transformed the program into a national leader in graduate medical education. Over the past 12 years, Dr. Macario has led the training of approximately 250 graduates who are now practicing physician anesthesiologists.

Dr. Macario has been instrumental in creating and leading innovative educational programs and tracks for residents at his institution, including the Stanford Fellowship in Anesthesia Research and Medicine track for anesthesia residents who want to pursue research-intensive careers, many of whom have gone on to obtain National Institutes of Health (NIH) funding. He also serves as program director for the Combined Residency in Internal Medicine and Anesthesiology and is associate program director for the Combined Residency in Pediatrics and Anesthesiology. These and other programs offer individualized training and learning pathways for residents that allow for more informed career choices (e.g., investigator, specialty clinician, educator, etc.).

Additionally, Dr. Macario was founder and served as director of the Stanford Anesthesia Faculty Teaching Scholars Program, which launched a structure for department faculty to obtain education in teaching, curriculum development and assessment.

Dr. Macario is a member of ASA’s Committee on Research and serves as director at the American Board of Anesthesiology. In 2019, he will also begin a six-year term on the Accreditation Council for Graduate Medical Education (ACGME) Review Committee for Anesthesiology. Dr. Macario received his medical degree from the University of Rochester, New York, and completed his residency in anesthesia and a postgraduate fellowship in health services research at Stanford University, Palo Alto, California.

A champion for education throughout his career, Dr. Macario has received numerous awards, including being the inaugural recipient of the Outstanding Contribution to Graduate Medical Education as Program Director Award for Stanford University Medical Center in 2015. His research on the economics of health care, management of the OR suite, and medical education have been published in numerous publications and cited more than 8,000 times.
The National Academy of Medicine (NAM) today announced the election of 75 regular members and 10 international members, including George Mashour, M.D., Ph.D.

George Mashour, M.D., Ph.D., associate dean for clinical and translational research, Bert N. La Du Professor of Anesthesiology, and director, Center for Consciousness Science and Michigan Institute for Clinical and Health Research, University of Michigan, Ann Arbor.

For research informing current clinical practice in monitoring general anesthesia and leading to the identification of a common neural correlate of anesthetic-induced unconsciousness across diverse drug classes.

Election to the Academy is considered one of the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service.

“This distinguished and diverse class of new members is a truly remarkable set of scholars and leaders whose impressive work has advanced science, improved health, and made the world a better place for everyone,” said National Academy of Medicine President Victor J. Dzau. “Their expertise in science, medicine, health, and policy in the U.S. and around the globe will help our organization address today’s most pressing health challenges and inform the future of health and health care. It is my privilege to welcome these esteemed individuals to the National Academy of Medicine.”

New members are elected by current members through a process that recognizes individuals who have made major contributions to the advancement of the medical sciences, health care, and public health. A diversity of talent among NAM’s membership is assured by its Articles of Organization, which stipulate that at least one-quarter of the membership is selected from fields outside the health professions — for example, from such fields as law, engineering, social sciences, and the humanities. The newly elected members bring NAM’s total membership to 2,178 and the number of international members to 159.

Established originally as the Institute of Medicine in 1970 by the National Academy of Sciences, the National Academy of Medicine addresses critical issues in health, science, medicine, and related policy and inspires positive actions across sectors. NAM works alongside the National Academy of Sciences and National Academy of Engineering to provide independent, objective analysis and advice to the nation and conduct other activities to solve complex problems and inform public policy decisions. The National Academies of Sciences, Engineering, and Medicine also encourage education and research, recognize outstanding contributions to knowledge, and increase public understanding. With their election, NAM members make a commitment to volunteer their service in National Academies activities.

For more information and the full list of newly elected members, visit NAM.
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### SUBMISSION GUIDELINES

Are you interested in contributing an article to AUA Update? Please familiarize yourself with the submission guidelines before you proceed. Thank you for your interest and contact Dr. Lisa Wise-Faberowski, MD, lwf1212@stanford.edu with any questions.
FUNDING OPPORTUNITIES

• The 2019 Medical Student Anesthesia Research Fellowship (MSARF) Summer Program provides challenging and rewarding experiences in anesthesia research. Medical students who participate in the summer anesthesia research fellowship can expect:
  – Eight weeks of focused research related to anesthesiology
  – A dedicated mentor who will provide training in research techniques and scientific methods
  – The opportunity to make a scientific poster or oral presentation during the FAER MSARF Symposium held at the ASA’s ANESTHESIOLOGY® annual meeting
  – A $400 per week student stipend, ASA student membership dues, plus additional funds to help cover the costs of travel to the ANESTHESIOLOGY® annual meeting

The 2019 application website will open December 1, 2018 and will close January 31, 2019. Visit FAER.org to apply.

• The Anesthesia Patient Safety Foundation (APSF) and The Foundation for Anesthesia Education and Research (FAER) are now offering the joint APSF/FAER Mentored Research Training Grant (MRTG) to develop the next generation of perioperative patient safety scientists.
  – This two-year, $300,000 award aims to help anesthesiologists develop the skills and preliminary data they need to become independent investigators in the field of anesthesia patient safety.
  – Anesthesiologist faculty members who are within 10 years of their first faculty appointment are eligible.
  – The grant requires 60% of the grantee’s time will be dedicated to research.

The application is available at FAER.org. The deadline to apply December 14, 2018.

SUPPORT OPPORTUNITIES

• The Foundation for Anesthesia Education and Research is seeking volunteers to join its Development Committee. This is a unique opportunity to build a network of professionals committed to advancing innovation and scientific discovery in our specialty.

Volunteer roles and responsibilities include:
  – Serve as FAER ambassadors, believing and supporting FAER’s mission and vision for Research, Education, and Training/Mentoring within anesthesiology.
  – Solicit support for the Annual Appeal from a list of prospects.
  – Analyze relationships with current and prospective support and advise staff in developing individualized strategies to cultivate and strengthen these relationships.
  – Participate in quarterly conference calls (approximately 60 minutes) and provide updates on solicitation activities.
  – Review donor data and make recommendations for improvements for increasing donations.

The application is accessible on FAER.org. The deadline to apply is November 30th.

• FAER relies on the support of generous donors. Donate to FAER to support anesthesia research and early physician-scientists. Visit FAER.org/donate to make your contribution to the field of anesthesiology today.

Contact faer@FAER.org with any questions or comments.