

SNM Members Elected to IOM

At its annual meeting in Washington, DC, on October 13, the Institute of Medicine (IOM) of the National Academies announced the names of 65 new members and 5 foreign associates. Among the newly elected scientists are SNM members Sanjiv Sam Gambhir, MD, PhD, head of the Division of Nuclear Medicine, director of the Molecular Imaging Program, and a professor in radiology and bioengineering at Stanford University (CA); and Helen S. Mayberg, MD, a professor of psychiatry, behavioral sciences, and neurology and Dorothy C. Fuqua Chair in Psychiatric Neuroimaging and Therapeutics at Emory University School of Medicine (Atlanta, GA). Election to the IOM is among the highest honors in the fields of health and medicine and recognizes individuals who have demonstrated outstanding professional achievement and commitment to service.

Gambhir trained at the University of California Los Angeles (UCLA) Medical Scientist Training Program, where he obtained both an MD and PhD. He completed his medicine and nuclear medicine training at UCLA and was a professor of molecular pharmacology, vice-chair of molecular and medical pharmacology, and director of the Crump Institute for Molecular Imaging before moving to Stanford in 2003. His translational laboratory focuses on merging advances in molecular biology with those in biomedical imaging to advance the new field of molecular imaging. Among his many areas of interest are new probe development for PET, multimodality molecular imaging including the use of optical imaging, and the integration of nanotechnologies into both imaging and therapy. His laboratory has developed methods to image gene/cell therapy in both animals and humans. He has developed numerous strategies for imaging basic cell/molecular events, including signal transduction, gene expression, and cell trafficking. He also has extensive experience with clinical ¹⁸F-FDG PET imaging and has developed many routinely used management algorithms and cost effectiveness models for cancer patients.

Gambhir oversees the activities of more than 20 graduate students and postdoctoral fellows in his own lab and more than 100 scientists and staff in the Molecular Imaging Program at Stanford. He received the 2008 Tesla Medal from the United Kingdom Royal College of Radiologists, the 2006 Paul C. Aebersold Award from SNM, the 2006 Hounsfield Medal from the Imperial College of London, the 2004 gold medal from the Society of Molecular Imaging, the 2004 distinguished scientist award from the Academy of Molecular Imaging, and the 2003 Holst Medal for his contributions to the field of molecular imaging. He is a past president of the Academy of Molecular Imaging and in 2007 was cohost of the Nobel Symposium on Molecular Imaging.

Mayberg received her medical degree from the University of Southern California (Los Angeles). She completed residency training at the Columbia University Neurological Institute (New York, NY) and a research fellowship at the Johns Hopkins University PET facility (Baltimore, MD). Before going to Emory, she held faculty positions at the Rotman Research Institute at Baycrest Centre (Toronto, Canada) and was a professor in the departments of psychiatry and neurology and chair of neuropsychiatry at the University of Toronto. Her research focuses on the use of functional neuroimaging to characterize neural systems mediating mood and emotions in health and disease. One goal of this research is to define brain mechanisms underlying major depression, with an emphasis on development of algorithms that will discriminate patient subgroups, optimize treatment selection, and provide markers of disease vulnerability. Her work on the first pilot study of deep brain stimulation has been widely praised. She has delivered numerous prestigious named lectures and received many awards and honors, including the 2002 Distinguished Investigator Award from the National Alliance for Research on Schizophrenia and Depression and the 2001 Arnold Pfeffer Prize from the *Journal of Neuropsychanalysis*.

In recognizing the newly elected members, IOM President Harvey V. Fineberg, MD, PhD, said, "It is a great pleasure to welcome these distinguished and influential individuals to the Institute of Medicine. Members are elected through a highly selective process that recognizes people who have made major contributions to the advancement of the medical sciences, health care, and public health." A diversity of talent in the IOM membership is assured by the organization's charter, which stipulates that at least 25% of the membership is selected from outside the health professions, for example, from such fields as the natural, social, and behavioral sciences; law; engineering; and the humanities. Current active members elect new members from among candidates nominated for their outstanding accomplishments. The newly elected members raise total active membership to 1,576 and the number of foreign associates to 89. With another 71 members holding emeritus status, the IOM's total membership is now 1,736.

The IOM is unique for its structure as both an honorific membership organization and an advisory organization. Established in 1970 by the National Academy of Sciences, the IOM has become recognized as a national resource for independent, scientifically informed analysis and recommendations on human health issues. With their election, members make a commitment to volunteer a significant amount of time as members of committees that engage in a broad range of studies on health policy issues. Studies
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Molecular Imaging Technologies and Translational Medicine

Throughout the decade since the National Institute of Biomedical Imaging and Bioengineering was established, molecular imaging has continued gaining acceptance as a successful component of translational research. Before molecular imaging is employed routinely in clinical trials, however, the need remains for biomarker validation and proof-of-concept studies.

Molecular imaging's reach has expanded in parallel with the recognition of its potential role as a biomarker in the drug discovery process. In 2001, the Biomarkers and Surrogate Endpoint Working Group developed a classification system for biomarkers: type 0 (markers of the natural history of disease), type 1 (markers of the mechanism of drug action), and type 2 (markers used as surrogate endpoints when the marker predicts clinical outcome). Molecular imaging plays a role in all these areas.

Molecular imaging has been applied to natural history experiments in atherosclerosis, including the characterization of inflammatory atheroma. Several techniques have been applied, including carotid ^{18}F -FDG PET. Results suggest cathepsin B and other proteases may serve as type 0 biomarkers for predicting high-risk plaque.

Type 1 biomarker studies include pharmacokinetic evaluation of activity-based probes (ABP) for proteases. Two main techniques to image proteolytic activity *in vivo* have been employed: a reporter substrate that emits a fluorescent signal when processed by a protease, and fluorescently labeled ABPs that indicate active proteases. Potential applications to visualize proteases in intact cells include ABPs to monitor

caspace activity after induction of apoptosis and papain-family cysteine protease in a mouse model for pancreatic cancer.

Finally, molecular imaging elucidates ways to measure the concentration of a drug within the tumor as well as the biological response. The first PET pharmacokinetic study of an antiangiogenic agent illustrated this technique well. The inhibition of vascular endothelial growth factor (VEGF) was assessed using ^{124}I -HuMV833 PET, visualizing radioligand uptake and subsequent clearance by both normal tissue and dysplastic cells. MR imaging algorithms measured the vascular permeability surface area product, which is controlled by VEGF. The findings suggested tumor response varied by anatomic area, supporting the contention that molecular imaging allows for *in situ* biological response assessments.

The momentum to bring molecular imaging from bench research to the clinical trials arena must continue. Success with this integration will require flexibility of regulatory agencies and collaboration among sites, drug sponsors, and imaging laboratories.



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completed in the past year include: *Retooling for an Aging America: Building the Health Care Workforce*, which calls for bold initiatives to ensure the availability of sufficient adequately trained health care workers to tend to the expanding population of older patients; *Cancer Care for the Whole Patient: Meeting Psychosocial Health Needs*, a blueprint for ways in which cancer care providers can address patients' psychological, emotional, and social needs in addition to their physical ailments; *Treatment*

of Posttraumatic Stress Disorder: An Assessment of the Evidence, which found that research to determine the effectiveness of various treatments is urgently needed in light of uncertainties about most therapies and growing patient needs; and *Knowing What Works in Health Care: A Roadmap for the Nation*, which provides a vision and roadmap for improving the ways in which the nation uses scientific evidence to identify the most effective clinical services.

Institute of Medicine