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December 15, 2012

Jeffery Flier, M.D., Ph.D.
Dean of the Faculty of Medicine
Harvard Medical School
25 Shattuck Street
Boston, MA 02115

Re: Promotion of XXXX XXXX, M.D., Ph.D. to Professor of Anaesthesia

Dear Dr. Flier:

We write to propose with utmost enthusiasm the promotion of **XXXX XXXX, M.D., Ph.D.** from Associate Professor of Anaesthesia to Professor of Anaesthesia, full-time, at Harvard Medical School. Dr. XXXX's area of excellence is Investigation. He has a significant supporting activity of Clinical Expertise and Innovation.

Area of Excellence: Investigation

Dr. XXXX is a highly productive, creative, and well-recognized physician-scientist in the field of cardiovascular physiology, organ protection, and gas biology who has made numerous important original contributions to the field. He is recognized internationally as a leader in the translational research of gaseous signaling molecules, NO and hydrogen sulfide (H_2S). He established an innovative, well-funded, and highly recognized resuscitation science laboratory at MGH. His outstanding track record as a talented researcher and innovator in several areas of biomedical research is reflected by his consistent record of funding including three active NIH R01 grants.

1. Background and Training

Dr. XXXX was born and raised in Japan, and received his M.D. degree in 1988 from the Faculty of Medicine, The University of Tokyo. After completing a medical internship in 1989, Dr. XXXX started anesthesia residency at Teikyo University School of Medicine. He emigrated to the United States in April 1990, and completed his residency in Anesthesia in March 1993 at the Department of Anesthesia of Massachusetts General Hospital. Dr. XXXX then continued his postgraduate training as a Clinical and Research Fellow at MGH from April 1994 to March 1995, participating in the Cardiothoracic Anesthesia Fellowship and basic science research training in the laboratory of Dr. Warren M. Zapol. Dr. XXXX is a Diplomate of the American Board of Anesthesiology.

During the course of his research training under Dr. Zapol, Dr. XXXX made important contributions to the development of inhaled nitric oxide (NO) as a therapy for the treatment of babies and adults with pulmonary hypertension and acute lung injury. He examined the physiological and pathophysiological roles of NO, and utilized genetically-engineered mice to study the mechanisms controlling pulmonary vascular tone. These mouse models enabled Dr. Zapol's group to elucidate the role of NO synthases in vasomotor control. Dr. XXXX's accomplishments are all the more impressive in that they were achieved at a time when he had a 50% clinical commitment. Dr. XXXX had to return to Japan in 1995 to take care of his family following the sudden death of his father. During this difficult time, Dr. XXXX still managed to be extraordinarily productive. He continued his research, studying the impact of NO on the actions of general anesthetics, and he was appointed to a faculty position in the Department of Anesthesiology at Teikyo University School of Medicine. At the same time, he completed work on his Ph.D. in physiology, which was awarded in 1996 by the University of Tokyo. In December 1998, Dr. XXXX was able to rejoin Dr. Zapol's group and in 1999, he was appointed an Assistant Professor in Anaesthesia at HMS and Assistant Anesthetist at MGH. From 2003-2006, Dr. XXXX had further training in molecular biology and biochemistry under Dr. Kenneth Bloch and established an independent laboratory at MGH. In January 2007, he was promoted to Associate Professor in Anaesthesia at HMS and Associate Anesthetist at MGH.

2. Funding

Upon returning to Japan in 1995, Dr. XXXX created a well-funded anesthesia research laboratory at the Teikyo University School of Medicine. During the three years he spent there, he obtained 4 KAKEN grants-in-aid from the Ministry of Education, Science, Sports, and Culture of Japan, one as a Principal Investigator and three as a primary co-investigator. Dr. XXXX has obtained independent research support from NIH since 2004. His research funding has progressively increased, and three active R01 grants were awarded during the period 2007-2012. Dr. XXXX's research is also supported by foundations and industries. A detailed list of his awarded peer-reviewed grants is in his curriculum vitae.

3. Research programs

Overview: Dr. XXXX has a broad, innovative, and translational research focus on the organ protective role of nitric oxide (NO) and hydrogen sulfide (H_2S). He is an expert in murine cardiovascular physiology who has developed several unique models using genetically-modified mice that enable detailed characterization of organ dysfunction associated with critical illness. He has created innovative animal models of several clinical conditions, including sepsis and post-cardiac arrest organ dysfunction. Dr. XXXX has discovered previously unrecognized protective roles for NO and H_2S in major organs including brain, heart, and liver. At MGH, he now directs a highly productive basic and translational resuscitation science laboratory. This combined basic science and clinical research program currently employs 8 research staff.

Regulation of pulmonary vascular tone by NO and arachidonic acid metabolites

In order to investigate the protection or treatment of organs subjected to inflammation and ischemia, it is necessary to develop accurate measures of organ function in whole animals. Research using small mammals like the mouse has several advantages including cost and the

relative ease of obtaining genetically altered strains. Although genetically-engineered mice were becoming available as early as the 1990's, techniques to measure pulmonary vascular tone in 20-gram mice did not exist when Dr. XXXX began his research. He developed mouse models that were initially utilized in a number of seminal research projects coming from Dr. Zapol's laboratory. Specifically, they made it possible to elucidate the critical role of endothelial NO synthase (NOS3) in regulation of pulmonary vascular tone [*Circ Res* 1997;81:34-41] as well as the role of inducible NO synthase (NOS2) in the impairment of hypoxic pulmonary vasoconstriction (HPV) that occurs in sepsis [*J. Clin. Invest.* 1999;104:1421-1429].

Hypoxic pulmonary vasoconstriction is an intrinsic and ubiquitous pulmonary vascular response of mammalian lung to hypoxia, and as stated previously, NOS2 appears to be an important modulator of HPV during sepsis. Additional experiments using Dr. XXXX's mouse model demonstrated that NOS2 was required, but not sufficient, to impair HPV in septic mice. Dr. XXXX felt certain that some additional inflammatory mediator must be adding to the effect of NO and contributing to impairment of HPV during sepsis. After returning from Japan, he embarked on a series of studies to determine the nature of this factor. He ultimately discovered that cysteinyl leukotriene (cysLT), a potent lipid mediator of inflammation derived from the metabolism of arachidonic acid (AA) by 5-lipoxygenase (5-LO), is a critically important cause of decreased HPV and pulmonary injury during endotoxemia [*Circ Res.* 2001;88:832-838]. In a follow-up study, Dr. XXXX also found that HPV is absent in mice deficient for cytosolic phospholipase A2. (cPLA2 is a key enzyme that liberates AA from membrane phospholipids). Administration of AA to cPLA2 deficient mice restores HPV [*J. Clin. Invest.* 2002;109:1493-1500]. These observations suggest that AA and/or one of its eicosanoid metabolites must be important modulators of HPV. These studies suggest a potential role for treatment with selective inhibitors of the 5-LO pathway, especially cysLT1 receptor antagonists, in order to prevent the loss of HPV in patients with clinical sepsis. Dr. XXXX made important contributions to subsequent studies that confirmed the critical roles of 5-LO and cysLT in HPV using other models of acute lung injury [*Am J Resp Crit Care Med* 2005;172:334-43 and *Anesthesiology* 2011 Oct;115:804-811] and in human patients undergoing cardiac surgery [*J Thorac Cardiovasc Surg*. 2011 Jun;141:1496-502.e3]. The impact of this series of publications was recognized in an editorial appearing in one of the most highly cited journals of respiratory medicine: "*The effects of lipid mediators, including arachidonic acid metabolites appear to be greater than previously recognized and should stimulate renewed interest in 5-LO inhibitors for the treatment of acute lung injury*." (JA Frank and MA Matthay, Leukotrienes in Lung Injury. *American Journal of Respiratory and Critical Care Medicine* 2005)

Unexpected cardioprotective effects of NO in sepsis

Although Dr. XXXX initially focused on the role of NO in pulmonary vascular function, since he is a cardiac anesthesiologist, he has always been interested in cardioprotection. Therefore, he obtained training in the relevant physiology with Dr. Kenneth D. Bloch, then collaborated with him on an independent line of research to study the role of NO in cardioprotection. Myocardial dysfunction contributes enormously to the high mortality of patients with septic shock. Starting with the discovery of NO as Endothelial Derived Relaxing Factor in 1988 until the early 2000's, NO, produced mainly from inducible NO synthase 2 (NOS2), was considered to be a primary cause of hypotension and cardiovascular dysfunction during sepsis. However, a multi-center clinical trial unexpectedly showed that a non-selective NOS inhibitor actually increased the mortality of septic patients, presumably by worsening myocardial dysfunction. Dr. XXXX's

studies of pulmonary vascular regulation demonstrated that the deleterious effects of inducible NOS2 were counteracted, to some extent, by the essential regulatory effects of endothelial NOS3. The role of myocardial NOS3 in sepsis had not been defined, but Dr. XXXX hypothesized that inhibition of NOS3 might have been responsible for the increased mortality seen in the clinical trial. Conversely, he proposed that augmentation of NOS3 might actually protect myocardial function during sepsis. Dr. XXXX demonstrated that mice with cardiomyocyte-specific NOS3 overexpression (NOS3TG) are indeed protected from myocardial dysfunction and death associated with endotoxemia [*Circ Res* 2007;100:130-9]. In a murine model of septic shock he demonstrated that increasing myocardial NO levels attenuates endotoxin-induced production of reactive oxygen species. Augmented myocardial NOS3 also increases the total sarcoplasmic reticulum Ca^{2+} load and increases myofilament sensitivity to Ca^{2+}, thereby improving myocardial function and reducing mortality during sepsis. An editorial by Dr. Berkowitz accompanying this paper stated that Dr. XXXX's work was important not only with respect to myocardial dysfunction in sepsis, but to our understanding of NO biology in general ["*Myocyte nitroso-redox imbalance in sepsis – NO simple answer*" *Circ Res* 2007;100:1-4]. Dr. XXXX subsequently conducted studies that used a reciprocal approach (i.e., using mice deficient for NOS3 or soluble guanylate cyclase [sGC], a NO receptor), and he was able to confirm that NOS3/NO-dependent signaling exerts salutary effects on myocardial function during sepsis [*Am J Physiol Heart Circ Physiol*. 2009 Aug;297:H654-663 and *Shock* 2010 Sep;34:281-90]. Dr. XXXX's results suggest the exciting possibility that therapeutic approaches to enhancing myocardial function (possibly by increasing cardiac NO levels) may improve survival in patients with cardiogenic shock induced by severe sepsis.

Improving outcomes after cardiac arrest and CPR using gaseous molecules

During the last few years, Dr. XXXX has also turned his attention to the preservation of brain and heart function following cardiac arrest and resuscitation. Sudden cardiac arrest is a leading cause of death worldwide. Despite advances in cardiopulmonary resuscitation (CPR) methods, fewer than 8% of adult out-of-hospital cardiac arrest victims survive to hospital discharge, and up to 60% of survivors have moderate to severe cognitive deficits 3 months after resuscitation. Poor outcomes after successful resuscitation from cardiac arrest are due to the "post-cardiac arrest syndrome" which includes ischemic brain injury, myocardial dysfunction, and "sepsis-like" systemic inflammation. No pharmacological agent is currently available to improve long term outcomes after cardiac arrest and CPR. While NO-dependent signaling may have a beneficial effect on ischemia-reperfusion injury, its ability to affect the outcome after cardiac arrest or CPR has not been determined. Based on the favorable effects observed in septic myocardial dysfunction, Dr. XXXX hypothesized that NOS3/NO-dependent signaling might protect organs following cardiac arrest. After developing a unique mouse model of cardiac arrest with CPR, Dr. XXXX was able to show that mice deficient in NOS3 or sGC exhibit poorer myocardial and neurological outcomes and lower survival rates than wild-type mice. Conversely, mice with cardiomyocyte-restricted overexpression of NOS3 have improved myocardial and neurological function and increased probability of survival [*Crit Care Med* 2009; 37:256–262]. These data suggest that manipulation of NOS3, NO, and sGC may improve clinical outcomes after cardiac arrest and CPR. The importance of this publication was highlighted in an accompanying editorial [*Crit Care Med* 2009; 37:368-367].

Another possible way to achieve organ preservation is the use of hydrogen sulfide (H_2S), a colorless gas with a characteristic rotten-egg odor found in various natural and industrial sources.

Along with NO and CO, H_2S is now considered a third "gasotransmitter" that exerts a host of biological effects on various targets. In 2008, Dr. XXXX and colleagues showed that inhalation of H_2S reduces the metabolic rate of mice without changing body temperature or blood pressure [*Anesthesiology* 2008 Apr;108:659-68]. Since reducing cellular metabolic expenditure is known to improve cellular survival during anoxia or ischemia, Dr. XXXX hypothesized that H_2S might also be beneficial in cardiac arrest and CPR. He used his mouse model to demonstrate that administration of Na_2S (an H_2S donor) at the initiation of CPR markedly increased survival rate and improved both neurological and myocardial function after 8 min of cardiac arrest followed by CPR. Similar results were produced in mice that had cardiomyocyte-restricted overexpression of the H_2S producing enzyme, cystathionine γ-lyase [*Circulation* 2009; 120:888-896, *Resuscitation*. Epub 2012 Feb 24]. Of equal importance, Dr. XXXX demonstrated that these beneficial effects of H_2S are mediated via NOS3 and NO-dependent mechanisms. This is the first time such an interaction has been demonstrated for these two gaseous molecules. The possibility that H_2S could improve the outcome after cardiac arrest is certainly provocative, and this can actually be tested because Na_2S is easily administered intravenously. The results not only demonstrate neuroprotective effects of H_2S but also reinforce Dr XXXX's contention that NOS3 and NO-dependent signaling plays a critical role in recovery from anoxic injury of brain and heart.

If NOS3 and NO-dependent signals are the ultimate mechanism for the improvements in function and survival, it would be logical to use a NO-based therapy in this clinical setting. Unfortunately, intravenous administration of NO-donor compounds induces systemic vasodilation, and the resulting hypotension precludes their use in patients following cardiac arrest, when blood pressure may be low and unstable. Although inhaled NO was originally developed as a selective pulmonary vasodilator, it has since been shown in a variety of pre-clinical and clinical studies to produce systemic effects without causing systemic vasodilation. Dr. XXXX conducted a study with his mouse model in which he administered a low concentration of inhaled NO starting 1h after successful CPR and continued it for 23h. Systemic blood pressure did not change, but long-term neurological and cardiac outcomes and survival were markedly improved [*Circulation* 2011 Oct 11;124(15):1645-53]. If these findings can be confirmed clinically, the fact that inhaled NO improves outcomes even when started after CPR makes it a practical therapeutic approach that can be initiated after patients are transferred to hospital. Prevention of ischemic brain injury in mice is an intriguing finding, and Dr. XXXX is hopeful that the well-established safety profile of inhaled NO will allow rapid translational studies in patients at risk for the post-cardiac arrest syndrome. There was great interest in this article. It was selected by the editors of Circulation as one of the most important and most read articles published in *Circulation* in 2010-2011 (*Circulation* Editors' Picks. *Circulation*. 2012;125:e274-e286). Dr. XXXX's group, in collaboration with a group in Belgium, have already initiated a large animal study to confirm the effects of NO inhalation after cardiac arrest and CPR. They are also currently planning a clinical outcomes trial in which the effects of NO inhalation will be examined in patients successfully resuscitated from sudden cardiac arrest.

Neuroprotective effects of H_2S

The beneficial neurological effects of H_2S observed in the course of the cardiac arrest studies prompted Dr. XXXX to look further into its neuroprotective properties. Dr. XXXX and colleagues demonstrated that breathing low levels of H_2S prevents neurodegeneration and movement disorder in a mouse model of Parkinson's disease [*Antioxid Redox Signal.*

2011;15:343-52]. Gaseous H_2S may be difficult to use clinically due to its unpleasant odor, and it may possibly be toxic to neurons, particularly at high concentrations. To reduce the possibility of toxicity while improving the clinical acceptability of H_2S, Dr. XXXX and colleagues recently synthesized a novel H_2S-releasing NMDA receptor antagonist, S-memantine. They chemically combined an experimental, slow H_2S releasing agent, ACS48, with memantine, an NMDA antagonist that is already FDA-approved for treating Alzheimer's disease. In both in vitro and in vivo models of neuronal ischemia-reperfusion, they found that S-memantine exhibits markedly more potent neuroprotective effects than its parent compounds, with minimal toxicity to neurons [*J. Biol. Chem.* 2012 Epub 2012 Jul 19]. Based on these promising effects they have filed a patent application on the composition and synthesis of sulfide-releasing NMDA receptor antagonists. They are currently testing the effects of S-memantine in mouse models of Alzheimer's disease.

4. Research productivity

Dr. XXXX has been highly productive as a physician-scientist despite his substantial clinical commitment to the MGH Cardiothoracic Anesthesia Group. He has published over eighty peer-reviewed original articles in prestigious journals such as the *Journal of Clinical Investigation*, *Circulation*, *Circulation Research*, and *Critical Care Medicine*. Dr. XXXX is either the first or senior author on 35% of these publications, reflecting his leading role in this research. During just the past three years, he has published twenty-three (23) peer reviewed original articles in high profile journals including *Circulation*, *Antioxidant & Redox Signaling*, *and Journal of Biological Chemistry* as senior author, confirming his role as an important independent investigator in our department. Dr. XXXX has also published over a dozen invited reviews in peer-reviewed journals, such as *Circulation*, *Cardiovascular Research*, and *Trends in Cardiovascular Medicine*, as well as seven book chapters, and a book.

Dr. XXXX seeks to translate his basic science studies on the organ protective effects of NO and H_2S into clinical applications. He was awarded two US patents as a co-inventor on the method to enhance effects of inhaled NO. Since 2008, Dr. XXXX filed 5 more patents on the systemic effects of NO inhalation, anti-inflammatory effects of sodium thiosulfate, and neuroprotective effects of H_2S-releasing NMDA receptor antagonists.

It is worth mentioning that Dr. XXXX has collaborated frequently with Drs. Zapol and Bloch, two of the strongest and most productive researchers at MGH, and added luster to their programs. This has not prevented him from developing quite independent lines of research, obtaining independent funding, and engaging in independent collaborations. There is no doubt that he has met the criteria for "independence."

5. Honors and awards

Dr. XXXX was selected as a finalist in the Cournand and Comroe Young Investigator Award of the American Heart Association in 2000 and in the New England Cardiovascular Research Competition and Award in 2001. He was elected to the *Association of University Anesthesiologists* in 2003 and was named a *Fellow of the American Heart Association* in 2009. He was a plenary session or keynote speaker for a number of national and international conferences including the International Conference of Hydrogen Sulfide in Biology and

Medicine, Shanghai, China and the International Conference on the Biology, Chemistry, and Therapeutic Applications of Nitric Oxide, Kyoto, Japan.

6. National and international committees

Dr. XXXX has served as a regular member of the Lung, Resuscitation, and Respiration Grant Review Committee of the American Heart Association since 2008 and has recently been appointed as the Co-Chair of this Review Committee. He has also served on three NIH study sections as an ad hoc reviewer since 2006. Dr. XXXX was recently selected to serve as a reviewer for the American Society of Anesthesiologist's Foundation for Anesthesia Education and Research. He has also served as an ad hoc reviewer for international grant-awarding agencies including the Fund for Scientific Research, Flanders, Belgium, The British Heart Foundation, and the Erwin Schroedinger Program of the Austrian Science Fund, demonstrating the international reach of his research and reputation. Dr. XXXX has been a member of the Subcommittee on Experimental Circulation (since 2006) and Committee of Research (since 2011) of the American Society of Anesthesiologists. He also serves as a member of the Program Committee (since 2008) and Leadership Committee of the Council on Cardiopulmonary, Perioperative, and Critical Care (since 2011) of the American Heart Association. Since 2011, Dr. XXXX has served as the Vice-Chair of the Scientific Sessions Program Committee of the American Heart Association. He is a Founding Member and serves as an Organizing Committee Member of the International Conference on Hydrogen Sulfide in Biology and Medicine since 2009, and he has been a member of the International Advisory Committee of the European Conference on the Biology of Hydrogen Sulfide since 2012.

7. Other national and international recognition

Dr. XXXX is a member of numerous professional societies including American Society of Anesthesiologists, Association of University Anesthesiologists, American Heart Association, American Physiological Society, International Anesthesia Research Society, and Society of Cardiovascular Anesthesiologists. He has chaired a number of symposia, workshops, and courses on behalf of these organizations. Dr. XXXX serves as the Vice-Chair of the Committee for Scientific Sessions Program of American Heart Association. He serves on the editorial board of the *American Journal of Physiology-Lung, Cellular, and Molecular Physiology* and *the Journal of Anesthesia*. Since 1995, Dr. XXXX has served as a regular reviewer for some 30 professional journals in the field of pulmonary and circulatory physiology, neurology, and anesthesiology. In the past three years he has been an invited speaker or seminar organizer for over 30 national and international seminars and societal annual meetings, and has held nine Visiting Professorships in the USA and overseas.

Dr. XXXX has been invited to speak at over sixty national and international conferences including invitations to give plenary session talks by overseas professional organizations including those from Denmark, Belgium, China, Korea, and Japan. He also has been invited to lecture by many academic institutions in the U.S and abroad. The details of these talks are covered in his curriculum vitae.

In conclusion, Dr. XXXX's activities admirably fulfill the metrics specified for promotion to Professor using Investigation as his area of excellence. He has a substantial record of conducting

exceptional basic and translational research on the role of gaseous signaling molecules in cardiovascular physiology and neuroprotection that has had a major impact on the field, and he has gained international recognition for his exceptional scholarship.

Teaching and Education Contributions

1. Advisory and supervisory role

Over the years, Dr. XXXX has advised over 40 graduate and undergraduate students, post-doctoral research fellows and international visiting professors. Dr. XXXX has also advised a number of former and current faculty members from the MGH Department of Anesthesia, Critical Care and Pain Medicine (DACCPM), including Drs. Wolfgang Steudel (Assistant Professor of Anesthesia, HMS), Oleg Evgenov (Instructor in Anesthesia, HMS), Ion Hobai (Instructor in Anesthesia, HMS), Binglan Yu (Instructor in Anesthesia, HMS), and Hae-Sook Shin (Instructor in Anesthesia, HMS). A number of Dr. XXXX's former international trainees have achieved successful academic careers after returning to their home countries. These individuals include Dr. Roman Ullrich (Associate Professor of Anesthesia, Vienna General Hospital, University of Vienna), Dr. Pietro Caironi (Assistant Professor of Anesthesia, the Istituto di Anestesiologia e Rianimazione, Università degli Studi di Milano), and Dr. Manabu Kakinohana (Associate Professor at the University of Ryukyus).

Dr. XXXX is skilled and sought-after scientific collaborator. He is currently a co-investigator on awarded R01 grants by Drs. Klaus Van Leyen (Assistant Professor of Radiology, MGH/HMS) and by Wei Chao (Associate Professor of Anesthesia, HMS, MGH) and a pending R01 grant by Dr. David Sosnovik (Assistant Professor of Medicine, HMS, MGH). Dr. XXXX serves as a member of the Scientific Advisory Committees on awarded K08 grants to Drs. Ion Hobai (Instructor in Anesthesia, MGH HMS) and Koichi Yuki (Assistant Professor of Anesthesia HMS, Children's Hospital Boston). He is a sponsor for a pending American Heart Association Postdoctoral Research Fellowship Award to Drs. Patrick Sips (Research Fellow, MGH DACCPM) and Kotaro Kida (Research Fellow, MGH DACCPM) and a Shock Society Research Fellowship Award to Dr. Lin Zou (Research Fellow, MGH DACCPM). Dr. XXXX served on Ph.D. Dissertation Committees for the University of Gent (Belgium). He has been elected as a member of the MGH DACCPM Research Council by his colleagues and serves as the Chair of the MGH DACCPM Pilot Clinical Research Grant Program since its inception in 2011 and leads grant review committee meetings 4 times a year.

As an attending physician working in the MGH Cardiothoracic Anesthesia Group, Dr. XXXX annually supervises over 30 MGH DACC anesthesia residents, 5-6 MGH cardiac anesthesia clinical fellows, 8-12 medical students from Harvard Medical School, and 3-5 international visiting physicians. These extensive mentoring and supervising responsibilities are listed in his curriculum vitae.

2. Clinical and laboratory teaching

Each year, Dr. XXXX provides lectures to Harvard Medical students, anesthesia residents, clinical cardiac anesthesia fellows, ICU fellows, and other healthcare professionals. He also moderates a weekly journal club for his post-doctoral research fellows. As described previously, Dr. XXXX has been invited to give numerous grand rounds.

We wish to emphasize that Dr. XXXX's knowledge of basic cardiovascular physiology and gas biology, neuroprotection, and clinical management of patients undergoing cardiac surgery enables him to bridge many clinical and preclinical disciplines as few others are able to, and make his talks particularly informative. He stimulates provocative discussions during conferences and journal clubs. Our residents and cardiac anesthesia fellows consider him an outstanding physician and scientist, which is repeatedly reflected in their very positive anonymous faculty evaluations such as: "XXXX has a very reassuring air to his presence. He made the experience in the OR extremely enjoyable and educational", "Very nice and considerate to residents. Great teaching", and "Handles resident involvement extremely well. Able to teach about mistakes without being condescending. Overall just extremely pleasant to work with. Great attending". In addition, Dr. XXXX has spent countless hours advising staff physicians inside and outside the DACC on preparing IRB proposals, designing and conducting basic science studies, writing scientific articles, and writing and submitting NIH grants. He is a highly respected staff member and a valuable collaborator to the MGH Heart Center, DACCPM, MGH, and the Harvard community. He also has been very helpful in counseling clinical fellows and residents in their search for posts and is a frequent writer of numerous requested recommendation letters.

Significant Supporting Activity

Clinical Expertise

Dr. XXXX formerly spent half time and still spends one full day each week providing care to patients as an attending anesthesiologist in the cardiac surgery operating rooms, electrophysiology laboratory, cardiac ultrasound laboratory, and Knight Cardiac Catheterization unit at MGH. He takes 25 first calls and 20 second calls and 11 full weekend calls per year. Dr. XXXX is an expert in perioperative transesophageal echocardiography whose American Society of Echoccardiography Certification is currently pending. He is highly regarded by colleagues and patients as an outstanding cardiothoracic anesthesiologist. Dr. XXXX is an exceptionally dedicated clinician who always keeps his beeper on and is therefore constantly accessible to his patients and colleagues including surgeons, and cardiologists. He is an excellent "team player" whose ethics are beyond reproach. He is well liked and respected by physician colleagues, supporting staff, clinical fellows, residents and patients. Dr. XXXX was a recipient of the *Partners in Excellence Award* in 1999, 2002, and 2011 for exceptional patient care in the ECT clinic and cardiac operating room at MGH, nominated by his clinical colleagues and supporting staff. As a clinical expert on inhaled NO therapy especially during perioperative period, Dr. XXXX has written a number of review articles on the clinical use of inhaled NO in adult and pediatric patients [*Circulation* 2004;109:3106-3111, *Int Anesthesiol Clin.* 2004 Fall;42(4):93-100, *Cardiovascular Research* 2007 Jul 15;75(2):339-48]. Dr. XXXX contributed the chapter on "Nitric oxide and inhaled vasodilators" in the 7th and 8th editions of *Anesthesia,* R.D. Miller, editor, the most highly-cited reference text in anesthesia. .

Review of Solicited Letters

To be added

X. SUMMARY

Dr. XXXX XXXX's achievements in his area of excellence of Investigation, his Teaching and Education activities and significant supporting activity of Clinical Expertise surpass the requirements for promotion to Professor of Anaesthesia. He admirably fulfills the metrics defined in each of these categories. Dr. XXXX has an exemplary record of basic and translational research accomplishments broadly focusing on organ protection utilizing gaseous molecules. He is a central and contributory staff member of the MGH Department of Anesthesia's research, educational and clinical missions, and he is a highly-respected cardiothoracic anesthesiologist. He has achieved international recognition as an independent investigator who heads a productive research laboratory. Dr. XXXX has received uninterrupted and generous extramural NIH research funding, achieved teaching and mentoring excellence, national and international recognition and has demonstrated clinical expertise in cardiothoracic anesthesia. His candidacy was unanimously and enthusiastically endorsed by the Harvard Medical School Department of Anaesthesia Executive Committee on xx yy 20zz. We forward this application to you with our strongest and most enthusiastic support for his promotion and look forward to the outcome of your deliberations.

Sincerely yours,

Carl E. Rosow, M.D., Ph.D., Provost
Department of Anesthesia
and Critical Care

Jeanine Wiener-Kronish, M.D.
Henry Isaiah Dorr Professor of Research
and Teaching in Anaesthetics and Anaesthesia