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2013 Association of American Physicians George M. Kober Medal
Introduction of John T. Potts Jr.

J. Larry Jameson

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AAP Kober Medal

It is a great honor to present the 2013 Kober Medal to my mentor and friend, John T. Potts Jr., for his outstanding contributions to medical science. John transformed the field of calcium metabolism by characterizing parathyroid hormone (PTH), documenting its exquisite regulation of serum calcium and developing a series of translational advances to improve the management of primary hyperparathyroidism and osteoporosis. In his role as Chief of Medicine at the Massachusetts General Hospital (MGH), John mentored a generation of physician-scientists and pioneered their training in molecular biology as a means to support their careers and catalyze breakthrough discoveries that have transformed medicine across multiple disciplines. Path to the calcium field As with most success stories, John followed a long and serendipitous path to arrive at this momentous day. He was raised in Moorestown, New Jersey. His mother had aspirations that he would become a priest, or, failing that, a doctor (Figure 1). After attending La Salle, John graduated from the University of Pennsylvania School of Medicine in 1957, where he was elected to the Alpha Omega Alpha Honor Medical Society. At Penn, John was influenced by faculty mentors, including Brooke Roberts, who ignited his interest in calcium metabolism. Like many other former Kober recipients, John journeyed to the MGH for training in Internal Medicine (Figure 2). This was a […]

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Path to the calcium field

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JTP in the JFK years: a scientific odyssey that begins at the NIH

It is not surprising, given this milieu at the MGH and his early interest in calcium metabolism, that John would migrate toward projects involving PTH and calcitonin when he joined the Anfinsen group as a research fellow at the NIH to learn protein chemistry techniques. Christian Anfinsen would later receive the Nobel Prize for his work on ribonuclease, which demonstrated how a primary amino acid sequence dictated tertiary protein conformation. This was one of many examples of John Potts's ability to recognize extraordinarily talented people and immerse himself in an environment where a fertile imagination, combined with data, leads to major discoveries. John subsequently accepted a leadership position in Donald Frederickson's group and initiated cross-institutional collaborations with Gerald Aurbach. Edman had pioneered new methods for protein sequencing, and John's group soon applied these to calcitonin and PTH. John led a dynamic team of protein chemists who were seeking to purify and sequence the calciotropic hormones, such as calcitonin and PTH (Figure 3).

In 1968, John heeded the call to return to the MGH to head the Endocrine Division. John's contributions to the field of endocrinology are enormous. In short, he and his collaborators transformed the field of calcium and bone metabolism. Generations of endocrine fellows at the MGH were taught in a conference room where two photos loomed large (Figure 4): a photograph of Fuller Albright, and giant poster of the amino acid sequence of PTH, which all of us were expected to have memorized — at least the highly conserved amino terminus!

It is only fitting that Potts's research group was able to solve many of the questions posed by Albright. John recognized

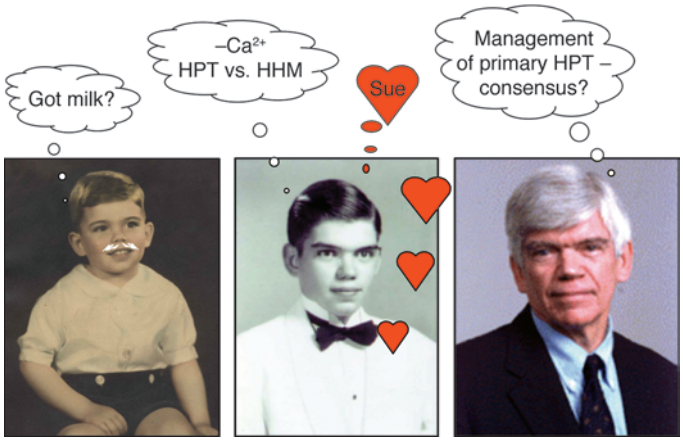

Figure 1
John Potts's path to the calcium field. Left: As a toddler, John foreshadowed later advertisement campaigns in which celebrities supported the dairy industry with "Got milk?" ads. Middle: As a student, John's interest in calcium metabolism was stimulated by Fuller Albright. Here we see him contemplating the differential diagnosis of hyperparathyroidism (HPT) versus humoral hypercalcemia of malignancy (HHM). Right: As a leader in the field, John has led several consensus conferences on the management of primary hyperparathyroidism.

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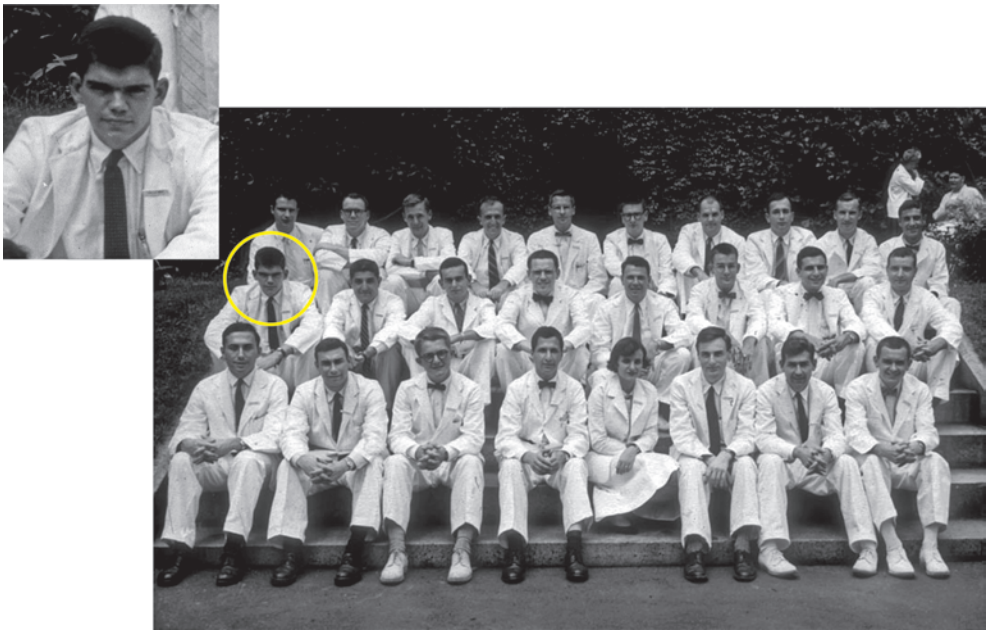

Figure 2
MGH residents in 1957 (Potts is circled).

early the incredible power of RIAs. In a characteristic collaborative style, he established interactions with Berson and Yalow, who received the Nobel Prize for developing RIAs. With this powerful tool in hand, John's group, still then at NIH, performed classic experiments demonstrating the physiologic role of PTH in the regulation of calcium homeostasis (1). When EDTA was administered to goats to lower serum calcium, PTH levels rose within minutes (Figure 5). Subsequent administration of i.v. calcium caused PTH levels to fall, only to rise again when EDTA was readministered. These experiments demonstrated the exquisite sensitivity of PTH to changes in calcium levels. Moreover, they laid the foundation for subsequent approaches to make the diagnosis of primary hyperparathyroidism. Later at MGH, together with Gino Segre, John developed a series of progressively more sensitive and specific immunoradiometric assays that allowed PTH to be measured more accurately, thereby helping to unravel the vexing clinical problem of determining whether patients had hypercalcemia from hyperparathyroidism or from humoral hypercalcemia of malignancy.

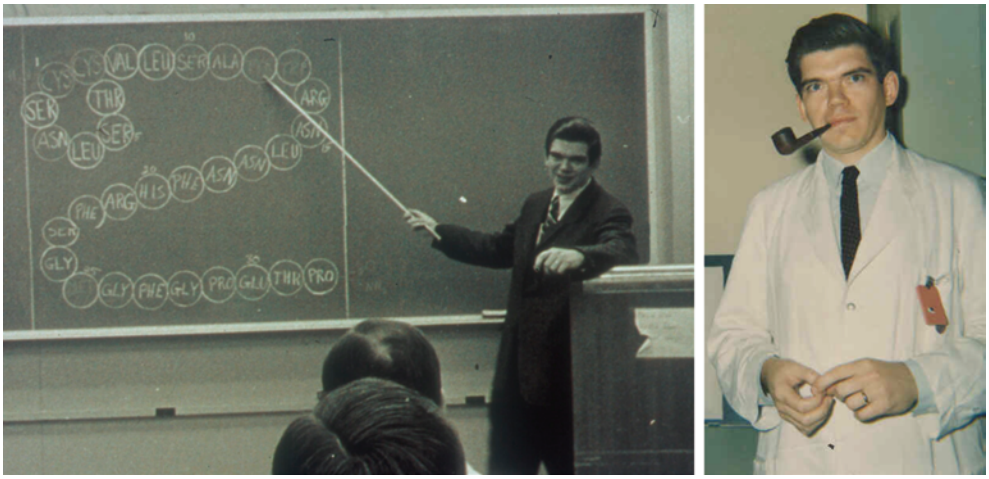

Figure 3
John T. Potts Jr., in the John F. Kennedy years. Right: JTP was a strong supporter of science and technology, but also influenced our culture, including the fashion and hairstyle of JFK. Left: This photo from the NIH archives depicts John in a classic "chalk talk," reviewing his latest work on the amino acid sequencing of porcine calcitonin.

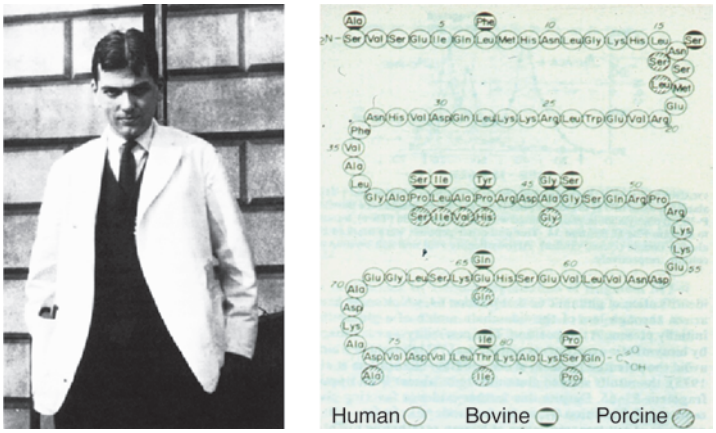

Figure 4
Symbols "haunting" the MGH Endocrinology Fellows' conference room. Each morning, endocrinology attending rounds occurred in the Albright conference room in the Bulfinch building. Looming above the group were photos of Fuller Albright (left) and the human PTH amino acid sequence (right), reminding the fellows of the giants who preceded them and the expectations going forward.

Partnerships and teamwork: the MIT effect

One of John's truly great talents is recognizing paradigm shifts in science. To this end, soon after arriving at the MGH, he established training relationships with Massachusetts Institute of Technology (MIT) and Harvard Medical School (HMS), including leading scientists such as Alex Rich, Phil Sharp, Phil Leder, and Richard Mulligan. John encouraged young physician-scientists like Joel Habener, Bill Chin, and Henry Kronenberg to perform postdoctoral training in this environment. In particular, John was keen to bring the tools of molecular biology to endocrinology. Moreover, recombinant DNA technology had not yet been approved at the MGH, whereas these protocols were approved at MIT, and the field was beginning to evolve rapidly. This training plan was a bold move for all involved — the postdoctoral fellows, straight from the clinical wards, were initially viewed with contempt and skepticism in the foreign basic science environment. However, they more than proved their skills, and used the new tools of molecular genetics to effectively tackle endocrine physiology. It was also a bold move for John, since it meant using valuable training grant slots outside of the institution. Examples of these collaborations are illustrated in Figures 6 and 7: these projects illustrate classic studies seeking to isolate PTH mRNA (2) and subsequently clone and sequence the cDNA (3). While we take these milestones for granted today, these were major breakthroughs in the late '70s and foreshadowed the powerful impact of recombinant DNA technology. These early successes by John's trainees led him to develop a robust NIH-funded physician-scientist program at the MGH. It was ultimately formalized as the MGH Society of Research Fellows, with more than 60 scholars, while John was Chief of Medicine between 1985 and 1996. Throughout his tenure as Chief of Medicine, John remained active in research, cultivating the careers of a talented and loyal team of scientists. Over decades, they shared a program project grant along with numerous individual grants. An example of the payoff from this long-term collaboration was the cloning of the PTH/PTHrP receptor (Figure 8 and ref. 4). In addition to this outstanding basic science work, there has always been a translational element to John's work. As one example, I cite an early idea that raised a paradox: hyperparathyroidism is characterized by bone loss. However, PTH is also anabolic — is it possible that short doses of PTH or its analogs could be used to treat osteoporosis? (Figure 9 and ref. 5). In some ways, John's research career has been a scientific odyssey that recapitulates

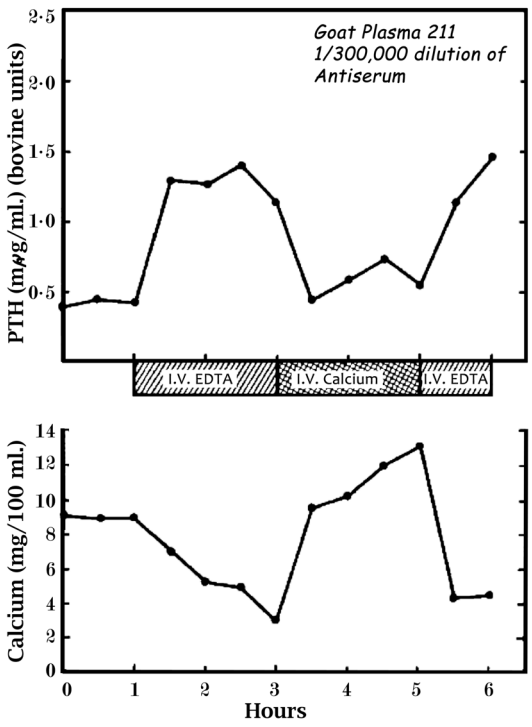

Figure 5
Translation to physiology. This classic study by Sherwood, Potts, Care, Mayer, and Aurbach demonstrated the physiologic interrelationship between serum calcium and PTH. The advent of a RIA for PTH allowed the first quantitative studies showing that when calcium falls, PTH rises, and vice versa. Reproduced with permission from *Nature* (1).

Figure 6
The MIT link. A classic study by Kemper, Habener (left), Mulligan, Potts (right), and Rich sought to isolate PTH mRNA (2).

Figure 7
The MIT link. A classic study by Kronenberg (left), McDevitt, Majzoub, Nathans, Sharp, Potts (right), and Rich sought to clone and sequence the cDNA of PTH (3).

Figure 8
An example of the payoff from long-term collaboration: the cloning of the PTH/PTHrP receptor (4). Clockwise from top left: Harald Jüppner, Abdul Abou-Samra, Mason Freeman, Ernestine Schipani, Gino Segre, Henry Kronenberg, John Potts.

Figure 9
The translational element. The study by Reeve, Meunier, Parsons, Bernat, Bijvoet, Courpron, Edouard, Klenerman, Neer (left), Renier, Slovik (middle), Vismans, and Potts (right) raised a paradox (5). Hyperparathyroidism is characterized by bone loss, yet PTH is also anabolic — is it possible that short doses of PTH or its analogs could be used to treat osteoporosis?

the key features in modern textbooks of biochemistry and molecular biology. Moreover, his fundamental research has informed new approaches to managing patients (Figure 10). In addition to his own research, John has chaired numerous conferences, including a series of consensus conferences on the management of asymptomatic hyperparathyroidism.

Leading the MGH to new frontiers

In addition to his scientific impact on the field of endocrinology, John had an enormous impact on the Department of Medicine and the MGH more broadly. He was an early champion of expanding the research enterprise. As noted above, he played a key role in bringing molecular biology to the MGH. He also catalyzed industry relationships, including the recruitment of Howard Goodman to lead the newly created Hoescht laboratories, as well as partnerships with Bristol-Myers Squibb, among others. He fostered the development of a cadre of Howard Hughes Medical Institute (HHMI) investigators at the MGH. He was a critical visionary and catalyst for the development of MGH East in Charlestown — a bold step that geographically separated the campus, but enormously expanded the research space. This expansion enabled development of the MGH Cancer Center (directed by Kurt Isselbacher) and the Cardiovascular Research Institute (directed by Mark Fishman). Despite early timidity about moving from the mother campus, MGH East is now a fully integrated component of the MGH research enterprise.

An enduring legacy for John was his early focus on diversity and inclusion. He created a Minority Recruitment Committee to identify a pipeline of talented underrepresented minorities (Figure 11 and ref. 6). Soon, the ranks of underrepresented minorities swelled, and John's mentoring skills found yet another dimension of influence. Not surprisingly, many of the MGH recruits have emerged at leaders in science, industry, policy, and education. John describes his focus on attracting minority students into medicine as a blend of "educated altruism and common sense . . . ." Though this reasoning is obvious to John, few people have exhibited his passion and commitment to mentoring and opening doors for those historically excluded from opportunity. Of his many accomplishments, I believe this ranks among his most important as a leader in academic medicine.

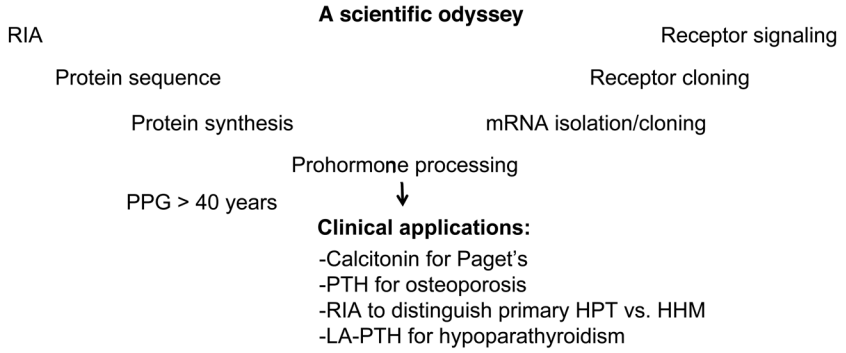

Figure 10
A scientific odyssey. John's research in calcium metabolism spans fundamental protein biology, including the development of RIAs, protein sequencing and synthesis, mechanisms of prohormone processing, and the use of recombinant DNA tools to allow cloning of hormones and receptors. Importantly, this research has spun off clinical applications including the use of calcitonin for Paget's disease, the use of PTH analogs for osteoporosis, the application of RIAs to distinguish primary hyperparathyroidism from humoral hypercalcemia of malignancy, and the development of long-acting forms of PTH (LA-PTH) for hypoparathyroidism.

The Potts family

At NIH, John was intensely focused on his work. Nonetheless, after an introduction to Susanne by a friend, he worked up the nerve to ask her out for a date to a concert. Thinking nothing out of order, John later called her to cancel the date because of an important lecture at the NIH. After some negotiation, Susanne agreed to attend the lecture, which both found to be quite boring. Remarkably, given this bumpy start, their relationship blossomed (Figure 12). John and Susanne share a passion for art, architecture, music, tennis, and philosophy, and they enthusiastically support a variety of social issues. Their home in Newton was a nerve center for the Department of Medicine. A typical week might include receptions or dinner parties on two or three nights. The various events would range from a reception for residents or physician-scientists returning to share their progress; to gatherings of faculty, unit chiefs, or academic leaders from around the Boston area; to political fundraisers. During these events, the Potts children were ever-present, and always engaging and charming. Not surprisingly, John's focus on his family was the foundation for the values and skills he brought to mentoring. Despite his hectic schedule, John has been a devoted father to his three children. The image of John shielding his daughter, Martha, from the rain at her graduation from Harvard (Figure 13) is symbolic of his protection of family, friends, and colleagues. When a colleague faced a crisis, John was typically the first to offer help and remain steadfast until the storm clouds cleared. John now has the privilege of supporting a new generation of grandchildren (Figure 14).

Potts's pearls for success

As one reflects on John's success as a scientist, leader, mentor, and family man, it is useful to extract a few pearls of wisdom that can be used by other members of the academic medicine community. Below, I list four pearls that permeate John's success.

Science will transform medicine. Throughout his career, John had a remarkable ability to identify disruptive technologies and outstanding people to work with as collaborators. It is one thing to recognize these opportunities; it is another to bring them to fruition. The latter characteristic results from John's enthusiasm, warmth, and willingness to share credit. Beyond his own research, his deep commitment to science is also reflected in his advice to trainees and faculty as well as his strategic guidance to the MGH. His vision is bold and penetrating.

Teams. It is evident from John's approach to science that he attracts and sustains creative and effect research teams. It is particularly remarkable that these teams are enduring. Among others, Henry Kronenberg, Gino Segre, Robert Neer, and Henry Keutmann have been close colleagues for decades. However, his emphasis on teams goes well beyond the laboratory. In the Endocrine Division, John identified extraordinarily talented Unit Chiefs, including Joel Habener, Bill Crowley, and Chip Ridgway, allowing these leaders to direct flourishing subspecialty groups, several the size of many endocrine divisions. I am proud to be included among this group, succeeding Chip Ridgway as Chief of the Thyroid Unit. John led the Department

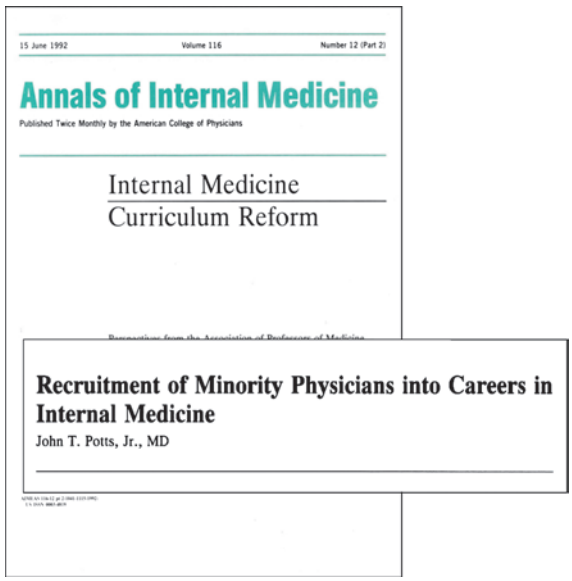

Figure 11
Mentoring. John created the Minority Recruitment Committee in the Department of Medicine at the MGH. Chairs of this committee included Juanita Merchant (1987–1989), Tony Coles (1989–1991), and Win Williams (1991–2005). His efforts were highlighted in a review in the *Annals of Internal Medicine* (6).

Figure 12
John and Susanne at their wedding.

Figure 13
John and his daughter, Martha, at her graduation.

of Medicine by "distributed governance," granting significant autonomy to the Division Chiefs. In turn, this group shared an enduring commitment to the institution and to John's standards of excellence and collaborative style. Finally, the MGH residency program took great pride in the "team system" for patient care, a model in which every member of the clinical team shared equal responsibility for all patients on the service, independent of who admitted the patient. The team system preceded John, but he championed it during a time when the clinical mission residency program expanded dramatically. This culture of "all for one" permeated the department and created a wonderful esprit de corps.

Recognize and support talent. Without question, remarkably talented people are attracted to the MGH at every level — students, residents, and faculty. That said, John exhibited an uncanny ability to identify the strengths, interests, and passions of individuals, and he directed them accordingly. This ability predominantly reflects his careful listening and observation skills. Many a person has been drawn into the mind meld with John — he asks penetrating, sometimes uncomfortable questions, and then follows up after a period of self-reflection. When you are with John, you feel that you are the only person in the room and your issue is the only topic on his mind.

Lead with vision, values, and trust. Leadership is earned. John's ability to engender loyalty reflects trust and his deeply held values. His ability to motivate people and shift their directions reflects his bold vision and ability to "think different" — before this phrase was popularized by Steve Jobs. More than one faculty member exited John's office with a different agenda than from when they entered it.

It is not surprising that John has been recognized by other Societies for his many accomplishments. He received the Ernst Oppenheimer Award from The Endocrine Society and later served as President of this group during a critical transition — he masterfully retained the bonds that linked the basic scientists and clinicians during a time when the Society was at great risk of being splintered. John also received the Fred Conrad Koch Award, the highest recognition by the Endocrine Society. He is a member of the ASCI and AAP, an elected Fellow of the American Academy for Arts and Sciences, and a member of the National Academy of Sciences as well as the Institute of Medicine and the American Academy of Arts and Sciences.

Figure 14
Teaching the next generation: John with his grandchildren.

Figure 15
Chiefs of Medicine at the MGH bicentennial. Left: John Potts (1981–1996). Middle: Alexander Leaf (1965–1981). Right: Dennis Ausiello (1996–2013).

Figure 16
The unveiling of John's portrait (middle) captures the "gaze and glow" he bestows on those around him. Left: John Potts. Right: Dennis Ausiello.

Legacy of leadership

The hallways of the MGH are graced by portraits of its Chiefs of Medicine — surprisingly few in number, reflecting long terms of leadership. Over the last century, these chiefs have included James Howard Means, Walter Bauer, Alex Leaf, John Potts, and Dennis Ausiello. The latter three are captured in this photograph from the MGH bicentennial celebration, held in 2011 (Figure 15). Finally, John's portrait captures his intense gaze and glow when he engages you in conversation (Figure 16).

John, for those of us fortunate to work with you or to be trained by you, we are deeply grateful for your mentorship. On behalf of patients, physicians, and scientists, we are grateful for your contributions to the field of calcium metabolism. Congratulations on receiving the Kober Medal. I now present to you Dr. John T. Potts Jr.

Address correspondence to: J. Larry Jameson, University of Pennsylvania, Perelman School of Medicine, 295 John Morgan Building, 3630 Hamilton Walk, Philadelphia, Pennsylvania 19104, USA. Phone: 215.898.6796; Fax: 312.926.7260; E-mail: ljameson@mail.med.upenn.edu.

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