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ASCi Presidential Address

2015 American Society for Clinical Investigation Presidential Address

Advancing the mission

Mukesh K. Jain

Introduction

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Having succumbed to the power of tradition, I set out to develop thoughtful remarks. Over the past few weeks, my children, who are both here today, watched me struggle at the keyboard. They observed with amusement but not surprise as I attempted to illuminate previously unappreciated philosophical insights. I say “without surprise” because like most young people they concluded some years ago that their father lacks a deep understanding of frankly anything, a view reaffirmed for them by my continued struggle.

I sought inspiration by reading previous presidential addresses. As I reviewed, it became clear that, while the elocutionary approach varied, recurrent themes dominated the discussion — reflective of the importance of some issues across generations. David Ginsburg, in his 2002 presidential address, provided quantitative data that the most common topics include (a) the future of the physician-scientist, (b) clinical investigation, (c) ASCI state of the union, (d) research funding, and (e) education/mentoring (2).

Conflict of interest: The author has declared that no conflict of interest exists.

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The Council’s reflections on career life cycle dynamics led us to forge initiatives that support the physician-scientist’s scientific efforts and educational needs. We focused in large part on the earlier phases of the life cycle — from medical student to junior faculty, where (to continue the analogy) birth rates are low and fall out is high. I will highlight three specific initiatives related to Strategy number 2.

Howard Hughes Medical Institute Medical Research Fellows Program. The first is a collaboration with the Howard Hughes Medical Institute (HHMI) and relates to the medical student phase of the life cycle (Figure 1). The recruitment and retention of aspiring medical trainees in research has been and remains a constant challenge. Evidence has suggested that early exposure to research enhances a rising physician’s interest in pursuing a research career. A major effort to address this issue began decades ago in the 1950s with the establishment of dual degree MD-PhD programs. Additionally, prestigious fellowship programs instituted by the HHMI, Sarnoff Cardiovascular Research Foundation, NIH, and the Doris Duke Charitable Foundation have been effective. A 2003 review of the effect of two HHMI programs concluded that “one-year intensive training offered an effective imprinting experience on medical student research careers” (4).

Knowing this, the American Physician Scientists Association (APSA) and ASCI/AAP forged an important partnership nearly a decade ago. In addition to enhancing the vitality of the meeting, this partnership has strategically engaged dual-degree students and provided them an opportunity to interact with and learn from role-model physician-scientists. The Council recognized the value of such engagements and sought to develop a complementary new program that helps increase the supply of physician-scientists. I am very pleased to announce the establishment of a collaboration with the HHMI Medical Research Fellows Program that will provide talented MD students who have scientific aspirations with an opportunity to engage with the ASCI/AAP (Figure 1). This new program is spearheaded by ASCI Vice President and HHMI investigator, Dr. Vivian Cheung, in close collaboration with Melanie Daub, Program Officer for the HHMI Medical Research Fellows program, who has kindly joined us today. This year, a small contingent of students from the program is attending our meeting, and participation will expand in future years. We are excited about this program, and we hope these talented students benefit from the program and engagement.

Young Physician-Scientist Award Program. Another critical phase of the life cycle is the junior faculty phase. Members of this group are vulnerable for manifold reasons, some of which include a long training path, stagnant or declining federal funding, the demands of delivering health care, and dual-occupation families. The fact that we lose highly trained, talented, and committed individuals when they are most productive poses problems not only for the future of science but also for our economy and society.

In the mid-1990s, Dr. David Nathan led an NIH-sponsored committee to evaluate clinical problems will ever be available by a complete reduction to chemistry and physics, I feel it essential, for this reason as well as others, to cultivate clinical investigation as a basic research activity of practicing clinicians and teachers” (3).
Recognizing the need to enhance engagement of individuals at this phase of their career life cycle, we established the Young Physician-Scientist Award (YPSA) program in 2013 (Figure 1). This program recognizes young investigators who at the time of their nomination are supported by an NIH K award or equivalent, are early in their first faculty appointment, and have made notable achievements in their research. The ASCI set aside funds to support up to 40 of these individuals to attend the annual meeting. Since inception, the number of applicants has increased beautifully (Figure 2). Because these young investigators are so critical to the future of ASCI, we are delighted to see such growth.

Seeing the success of the program, we established in 2014 a committee of ASCI members to evaluate YPSA applicants and to help plan this annual meeting (Figure 2). The committee established a separate poster session for YPSA on Saturday night and invited Dr. Griffin Rodgers, Director of the National Institute of Diabetes and Digestive and Kidney Diseases, to share reflections prior to launching the inaugural Young Physician-Scientist award. This award recognizes the need to enhance engagement of individuals at this phase of their career life cycle, we established the Young Physician-Scientist Award (YPSA) program in 2013 (Figure 1). This program recognizes young investigators who at the time of their nomination are supported by an NIH K award or equivalent, are early in their first faculty appointment, and have made notable achievements in their research. The ASCI set aside funds to support up to 40 of these individuals to attend the annual meeting. Since inception, the number of applicants has increased beautifully (Figure 2). Because these young investigators are so critical to the future of ASCI, we are delighted to see such growth.

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I am pleased today to officially announce the establishment of the Donald Seldin-Holly Smith Award for Pioneering Research (Figure 1). For this award, the ASCI will call for nominations of physician-scientists who are early in their faculty appointments and who are on a particularly promising trajectory in their research careers. From these nominations, a panel of ASCI presidents, guided by a senior advisory board, will select the recipient (Figure 4).

The recipient will (a) receive an unrestricted award to advance her or his academic efforts, (b) be provided with a mentoring team to advise on career development, and (c) have an opportunity to speak at the Joint Meeting.

Through this award we hope to recognize the country’s most promising young physician-scientists, connect them to later-phase physician-scientists mentors, hear about their accomplishments, and celebrate the legacies of Drs. Seldin and Smith. The Society has set aside $1.2 million, and we will seek over the next several years to build a multimillion-dollar endowment to support the country’s most promising young individuals. We have high hopes that the individuals selected and supported by this program will become the next physician-scientist leaders in academic medicine.

Although today marks our official announcement, we celebrated the establishment of this award in San Francisco late last year and Dallas earlier this year (Figure 5). All of us at ASCI are deeply grateful to Dr. Vivian Cheung and Dr. Helen Hobbs, who tirelessly contributed their time and effort to make these events and this award possible. We are also grateful to those friends, admirers, and colleagues of Drs. Seldin and Smith who gave generously to enhance the endowment. And finally, we are grateful to Drs. Seldin and Smith themselves for providing the inspiration that has spanned many academic generations and advanced our mission. Would you please join me in thanking Drs. Donald Seldin and Holly Smith?

Strategy number 3: advance the clinical aspirations of physician-scientists

Our third strategy related to the clinical aspirations of physician-scientists to translate fundamental discovery at the bench to impact patients by the bedside (Figure 1). In Dr. Smith’s 1970 presidential address, which I referenced at the outset of my remarks, he identified a challenge connected to the “outflow pathway from medical science to its final application in health care” (1). He noted, “…the thrust of this criticism is that the biomedical scientist pursues his research as an intellectual game, hermetically sealed off from the real problems of society, indifferent to the ultimate utility, or even lack thereof, of his discoveries. The spin-offs may be there but they come grudgingly from a process with a rather low angular velocity.”

You heard beautiful remarks a few minutes ago from Drs. Michael Brown and Warner Greene about two paragons of academic medicine. Drs. Donald Seldin and Holly Smith have for decades provided exemplary leadership in science, medicine, and education. Both shepherded once fledgling institutions to greatness and in so doing left an indelible mark on hundreds of trainees and faculty, their respective institutions, and the profession as a whole. Both also served as ASCI presidents and remain staunch supporters of this Society, as exemplified by their attendance at nearly every meeting over the past half-century, including today (Figure 3).
In the 45 years since these remarks, we have witnessed remarkable progress in basic biomedical research, fueled by powerful technologies and fundamental insights into the biologic basis for disease. Strikingly, despite this progress, we have not witnessed a correponding increase in the number of FDA-approved drugs in recent years. Many refer to this as the “Valley of Death” (Figure 6). This famed metaphorical chasm — this gap located between fundamental discovery by the public sector and commercialization of that discovery by the private sector — has clearly damaged a real core aspiration of the physician-scientist to change standard of care.

The reasons for this chasm are numerous. Major participants in the health care industry — the biomedical research enterprise in universities, the clinical research engine in hospitals, and drug development efforts in the pharmaceutical industry — face numerous challenges. Additionally, traditional partners, such as venture capital firms, have reduced their support of therapeutic products that lack demonstrated human clinical proof of concept. An Institute of Medicine report noted grimly that “... without mechanisms and infrastructure to accomplish this translation in a systematic and coherent way, the sum of data and information produced by basic research enterprises will not result in tangible public benefit” (7).

This translational productivity “gap” is a serious problem. Not to be misunderstood, I wish to emphasize my staunch advocacy for fundamental discovery — this is the foundation on top of which all therapies rest. The purpose of my following comments is to emphasize that we may not be realizing the full promise of these discoveries. If we don’t leverage our scientific insights maximally, we risk a negative impact in public trust, economic growth, and most importantly human health. And I can think of no better group of individuals than members of this Society who ought to be at the forefront, leading efforts to address this productivity gap.

Fortunately, awareness of this issue has increased in recent years, with promising efforts at the local and national levels. Some institutions are dedicating significant energy and resources to support and incentivize their faculty to traverse the so-called valley. These efforts typically involve assistance for lead optimization, preclinical development, and commercialization. I have seen a deep commitment to such efforts by leadership at my own university, and, happily, parallel efforts are developing or have been established across the land.

Further, leaders at disease-specific organizations, such as the Cystic Fibrosis Foundation and the Leukemia & Lymphoma Foundation, have increasingly focused their organizations on supporting translational opportunities in their respective areas of interest. These efforts have enjoyed palpable success.

Figure 6. The Valley of Death. The gap located between fundamental discovery by the public sector and commercialization of that discovery by the private sector.

Figure 7. The Harrington Project for Discovery and Development. A dedicated initiative to ensure physician-scientists have the resources they need to accelerate the development of medical breakthroughs into medicines that benefit society.
The effort has earned great interest from investigators around the globe — including many members of this Society (Figure 8) who are supported by Harring-
ASCI PRESIDENTIAL ADDRESS

- ASCI Council & Administrative Team, 2012-2015
- Scientific Mentors
  - Edgar Haber
  - Mu-En (Arthur) Lee
- Mentors & Colleagues (Boston & Cleveland):
  - Peter Libby
  - Patrick O’Gara
  - Thomas M. Michel
  - Victor J. Dzau
  - Daniel I. Simon
  - Jonathan S. Stamler
  - Marco A. Costa
  - Richard A. Walsh
  - Fred C. Rothstein
  - Jeffrey H. Peters
  - Pamela B. Davis

Figure 9. Acknowledgments. A special thank you to the ASCI Council and administrative team and scientific mentors Edgar Haber and Mu-En (Arthur) Lee as well as mentors and colleagues from Boston and Cleveland over the years.

Although this effort is housed at my home institution, I believe (and hope) this does not diminish the fact that the project offers a significant opportunity for our Society’s members to advance the mission. In fact, several years ago, the ASCI engaged with the Harrington Project in a specific way, namely through the ASCI-Harrington Project programs — as well as from prominent disease foundations, academic institutions, philanthropic thought leaders, countries, and global pharmaceutical companies.

Although this effort is housed at my home institution, I believe (and hope) this does not diminish the fact that the project offers a significant opportunity for our Society’s members to advance the mission. In fact, several years ago, the ASCI engaged with the Harrington Project in a specific way, namely through the ASCI-Harrington Prize for Innovation in Medicine. This prize has allowed the Society to recognize annually a physician-scientist whose translation of a discovery has positively impacted human health. This year’s recipient, Dr. Douglas Lowy, is exemplary.

Conclusion
As I enter the blissful phase of retirement commonly referred to as past president, I am confident that the three strategies I have discussed — first, putting ASCI’s mission into words; second, programmatically supporting the scientific and educational needs of our members throughout their life cycle; and third, advancing the clinical aspirations of our mission-driven and productive community — will advance to great success under the leadership of Drs. Levi Garraway, Vivian Cheung, and Benjamin Ebert and the entire ASCI Council.

Over the upcoming year, in my capacity as past president, I plan to cultivate interactions of the ASCI with like-minded organizations internationally. The Council made this request of me because it rightly believes that engagement with the broad ecosystem of physician-scientists across the globe will benefit us all. As one example, you may be aware that the UK has a parallel society to the AAP, namely the Association of Physicians of Great Britain and Ireland. Founded on the urging of Sir William Osler in 1909, this organization bears striking similarity to the ASCI/AAP. I am very pleased that the Association’s secretary, Professor Salim Khakoo of Southampton General Hospital, has joined us this year to learn a bit more about our meeting and Society. I will be attending next year’s Association of Physicians meeting in the UK with the hope of codifying transatlantic collaborations, perhaps initially in the areas of training and education.

Figure 9. Acknowledgments. A special thank you to the ASCI Council and administrative team and scientific mentors Edgar Haber and Mu-En (Arthur) Lee as well as mentors and colleagues from Boston and Cleveland over the years.

Figure 10. Acknowledgments. (A) Jain family reunion July 2014. (B) From left to right, Nisha Jain (daughter), Mukesh K. Jain, Rachana Jain (wife), and Kavi Jain (son).
I wish to conclude by thanking you, our members, my colleagues on the Council, and our administrative team (Figure 9). It has been my great privilege to work with you over these three years. I wish also to thank the enormous number of individuals, organizations, and institutions that have provided support for this meeting and ASCI initiatives, in particular the Seldin-Smith Award. A complete listing of supporters can be found in the ASCI annual report. Finally, I would like to thank those people who have supported my personal efforts in my own career life cycle: (a) my scientific mentors (Figure 9), (b) institutional leaders and colleagues in Boston and Cleveland for their continued and unwavering support (Figure 9), and (c) my own family, seen here in the Outer Banks at a recent reunion: two wonderful kids and my wife, who remains the wind beneath my wings (Figure 10).

Thank you.

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