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## The Role of the NIH in Nurturing Clinician-Scientists

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The awarding of the 2012 Nobel Prize in Chemistry to Robert Lefkowitz and Brian Kobilka, both M.D.s trained in cardiology, for their work on characterizing the structure and function of beta-adrenergic receptors, should remind us of the critical role that clinician-scientists have played in formulating the seminal concepts that govern modern biomedical science. Much has been written since the 1970s about the demise of the physician-scientist<sup>1,2</sup> — as evidenced by the declining share of RO1 grants that the National Institutes of Health (NIH) awards to physicians — and the economic factors that have driven physicians away from the laboratory and research clinic into more remunerative clinical practice. Even as the reasons for this shift are debated, physician-scientists continue to make critical contributions to biomedical research; indeed, in the past 2 years, three researchers with medical degrees have won the Nobel Prize in Physiology or Medicine — Shinya Yamanaka (2012), Bruce Beutler (2011), and Ralph Steinman (2011). Considering that less than 2% of physicians conduct research as their primary profession,<sup>3</sup> this is an impressive showing for physician-scientists competing with a much larger pool of Ph.D.s.

Nevertheless, we at the NIH share the concern that some of the best, most creative clinically trained scientists are shying away from research, and we want to work with the broader research community to help reverse this trend. The profound effect that clinically trained scientists have had on our understanding of basic human biology argues that we must sustain the flow of such scientists into research careers. To do so, we must surmount two barriers: an apparently decreasing interest by medical and dental students in establishing research careers and the increasing difficulty that research-oriented physicians and dentists face in pursuing their research interests full time without the distractions of clinical practice.

The NIH is addressing the former problem — getting students, particularly from underrepresented minorities, hooked on clinical research — through year-off research programs for medical and dental students (and in some cases students of veterinary medicine), including two programs that have been consolidated as the Medical Research Scholars Program. These programs complement long-standing research training programs at U.S. medical schools, as well as the Medical Research Fellows Program of the Howard Hughes Medical Institute.

After a student's graduation, NIH K-award programs (K08 and K23) have traditionally provided research and salary support, along with mentoring and graduated independence. But until recently, the NIH had not addressed the need for sustained, 100% research support for the time it takes to establish a research career. So in 2011, the NIH-Lasker Clinical Research Scholar Program was created.

Two NIH-trained physician-scientists, Joseph Goldstein and Michael Brown, both 1985 Nobel laureates, recently noted that the special environment at the NIH in the 1960s and 1970s — including a talented group of senior scientists and a dedication to supporting

research to uncover basic principles of biology — provided ambitious physician-scientists with fertile ground for success.<sup>4</sup> The new NIH-Lasker program builds on this legacy.

This collaboration with the Lasker Foundation aims to attract a new generation of medical researchers to continue their training at the NIH for 5 years or longer; here, they will be able to take advantage of the NIH Clinical Center and our community of more than 1100 principal investigators and 6000 trainees. The hope is to expand the pool of talented clinically trained researchers at both academic institutions and the NIH by providing substantial and protected full-time support for medical and dental scientists for up to 12 years. The program combines 5 to 7 years of independent research as a principal investigator in the NIH Intramural Research Program with the opportunity for either additional years at the NIH or independent financial support of up to \$500,000 per year (plus indirect costs) for 5 years at a clinical research institution.

The NIH has already begun recruiting for this program. We now have two researchers on our Bethesda campus, and we envision a steady state of at least 20 researchers at various stages in their careers benefiting from the proximity to our laboratory facilities, mentors, and role models (free from the conflict-of-interest issues that arise from industry funding). Candidates must have an M.D., M.D.–Ph.D., D.O., D.D.S., D.M.D., or equivalent clinical doctoral degree from an accredited domestic or foreign institution and a professional license to practice in the United States.

The NIH's Intramural Research Program has a long history of training clinicians as scientists. Lefkowitz did his postdoctoral research with Ira Pastan, M.D., and Jesse Roth, M.D., at the NIH, where they developed the original concept of cell-surface receptors. Richard Axel (2004 Nobel winner) trained with Gary Felsenfeld in the field of DNA and chromatin structure. Arvid Carlsson (2000) studied serotonin with Bernard Brodie. The list goes on. NIH trainees from the past three decades are now leading scientists at clinical institutions worldwide. Yet the number of physicians applying for research positions at the NIH has been dropping since the 1970s. The majority of NIH trainees are Ph.D.s, and many of our outstanding physician-scientists are nearing retirement age.

A second major approach we're taking to enhancing clinical research training is the opening of the NIH Clinical Center to extramural investigators. A new grant program, Opportunities for Collaborative Research at the NIH Clinical Center, is aimed at established physician-scientists and was a venture recommended by a congressionally mandated Scientific Management Review Board. The Clinical Center has resources such as pharmaceutical development capabilities, a world-class metabolic unit, and advanced research-related radiology imaging services. This opportunity for extramural researchers will enhance clinical research both within and beyond the NIH and, we hope, be a wellspring for future collaborations with trainees and early-career clinical scientists. Further incentives to encourage M.D.-, D.D.S.-, and D.V.M.-scientists will be considered by a subcommittee of the Advisory Committee to the NIH Director.

The shortfall of new physician-researchers is a national, if not global, concern, and its remedy requires a coherent and cooperative approach among biomedical research and teaching institutions. We hope that our actions will help to recreate the environment of the 1960s and 1970s that Goldstein and Brown describe, in which so many physician-scientists (many of whom came to the NIH as officers in the U.S. Public Health Service Commissioned Corps to fulfill their Selective Service obligation) were trained and developed scientific maturity and independence before pursuing research careers.

The best attraction to a clinical research career may be the promise to a physician of committed funding to conduct the clinically oriented or basic research of his or her choice.

Goldstein and Brown argue that the best science done by physician-scientists occurs in an atmosphere that is not oriented to clinical outcomes but seeks only to elucidate basic biologic processes.<sup>4</sup> Jeffrey Flier, dean of the Faculty of Medicine at Harvard Medical School, notes that it's the confluence of talented individuals and "magical" research opportunities at the NIH that enables success.<sup>5</sup> The major contributions that clinically trained scientists have made to our understanding of human biology have come not from anything unique about their research skills, but rather from their perspective derived from clinical experience or training that enables them to define and pursue important problems in human biology, especially in a highly supportive research environment.

The NIH hopes to serve as a catalyst for a national effort to nurture clinician-scientists by providing such varied opportunities in an incubator-like environment, by demonstrating the value of investing in protected research time, and by inspiring partnerships and complementary clinically oriented research programs at major institutions.

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