

HISTORY OF SCIENCE

A Golden Era of Nobel Laureates

Joseph L. Goldstein and Michael S. Brown

What conditions in the 1960s enabled nine physicians who trained at NIH to win Nobel Prizes?

The award of the 2012 Nobel Prize in Chemistry to Robert Lefkowitz brings to nine the number of Nobel laureates who trained in research at the United States National Institutes of Health (NIH) between 1964 and 1972—a remarkable outpouring over such a short period from a single biomedical institution (see the figure). Was there something particular about these recipients, the time, and the place that account for this unprecedented record?

We were among the nine, and the parallels in our experiences are striking. All of us graduated from medical school before entering NIH, and all (except Alfred Gilman) took residency training. Gilman and Ferid Murad were the only M.D.-Ph.D.s in the group. For the rest of us, NIH provided our first intense research experience. Some of our mentors were Ph.D.s and some were M.D.s, but they all worked in reductionist systems focused on fundamental mechanisms. The nine of us studied problems ranging from protein synthesis in bacteria to hormone receptors in animal cells. Despite our clinical training and the fact that some of us had patient care duties, our science was far removed from the bedside. The sharp contrast between the uncertainties of the bedside and the relatively “pristine” world of the laboratory provided the stimulus that drove us to pursue careers in fundamental research.

The research experience at NIH in the 1960s was intense. Distractions were few. Many of us knew each other, had heated discussions about our research, and wondered whether we had the ability to succeed in a laboratory-based career.

After finishing our training, it is surprising that none of us stayed at NIH. We either joined clinical departments or basic science departments in medical schools. Regardless, we all addressed fundamental problems that were relevant to medicine, making primary use of the tools of biochemistry, supplemented with molecular biology as those methods became available. It is noteworthy that four of us received our prizes for discovery of receptors [low-density lipoprotein

Nobel laureate	NIH mentor	Institute	Year of Nobel Prize	Discovery
Michael S. Brown	Earl Stadtman	NHLBI	1985	LDL receptors
Joseph L. Goldstein	Marshall Nirenberg	NHLBI	1985	LDL receptors
J. Michael Bishop	Leon Levintow	NIAID	1989	Cellular oncogenes
Harold E. Varmus	Ira Pastan	NIDDK	1989	Cellular oncogenes
Alfred G. Gilman	Marshall Nirenberg	NHLBI	1994	G proteins
Stanley B. Prusiner	Earl Stadtman	NHLBI	1997	Prions
Ferid Murad	Martha Vaughan	NHLBI	1998	Nitric oxide signaling
Richard Axel	Gary Felsenfeld	NIDDK	2004	Odorant receptors
Robert J. Lefkowitz	Jesse Roth and Ira Pastan	NIDDK	2012	G protein-coupled receptors

The Nobel nine. Listed are the Nobel Prize winners who trained at NIH in the years 1964 to 1972. NHLBI, National Heart, Lung, and Blood Institute; NIAID, National Institute of Allergy and Infectious Diseases; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases.

(LDL) receptors, G protein-coupled receptors, and odorant receptors], and two were honored for discovery of receptor-signaling mechanisms (G proteins and nitric oxide). In the nonreceptor arena, two laureates elucidated a basic mechanism of cancer, and one discovered a new form of infectious neurologic disease. Although none of us performed “translational research,” as currently in vogue, our discoveries influenced drug discovery, medical practice, and human health.

It is not a coincidence that the 1960s was the decade of the Vietnam War and the doctor draft. Service at NIH substituted for military service in Vietnam, which led some of us to apply to NIH instead of an academic institution. The draft exemption evoked a huge increase in the number of applicants for NIH fellowships. As a result, NIH had its pick of fellows with the strongest academic records. While these factors were important, they would have amounted to nothing if we had not encountered the excitement and rigor then in place at NIH.

As research fellows at NIH, we trained with brilliant scientists who had been appointed in previous years. Credit is due to the courageous leaders of the various institutes who chose to appoint basic scientists even when their work did not deal directly with the disease-oriented mission of the institute. Five NIH-career scientists have

been honored with Nobel Prizes: Marshall Nirenberg (1968), Julius Axelrod (1970), Christian Anfinsen (1972), D. Carlton Gajdusek (1976), and Martin Rodbell (1994). Four of them were Ph.D. basic scientists, and one (Gajdusek) was a physician-scientist. All five were dominant forces at NIH when we nine were there.

Scores of distinguished scientists were trained at NIH in the 1960s, including many who earned election to the U.S. National Academy of Sciences. Others achieved distinction in other ways. Indeed, a substantial portion of the faculties of American medical schools trained at NIH in this remarkable period.

Will a single biomedical institution ever again train nine Nobel laureates in a single decade? Under the current conditions, it seems unlikely. The focus of medical schools in the United States has changed. In the 1960s, basic science was at the core of medical education. The brightest graduates were expected to advance their discipline through scientific investigation. Today, medical school curricula tend to condense basic science teaching to a few months instead of the traditional two preclinical years, and the courses focus on a restricted set of disease-relevant “facts” with little to no discussion about where those facts came from or that facts will change as science advances. The

joy of finding new facts or overturning old ones is no longer transmitted to students.

As well, clinical departments have expanded geometrically as medical schools compete with private hospitals by amassing huge clinical programs. The few scientifically oriented faculty in clinical departments have been diluted to irrelevance by pure clinicians. No wonder that few medical students are choosing to follow paths in basic research.

The research emphasis of NIH has gradually shifted. The primary focus is no longer on acquisition of knowledge in basic bio-

logical mechanisms. Current emphasis on “translational research” relegates basic science to a back burner. What has been lost is the conviction that progress in medicine rests ultimately on a fundamental understanding of physiology. Individual curiosity-driven science has been replaced by large consortia dedicated to the proposition that gathering vast amounts of correlative data will somehow provide the answer to life’s fundamental questions.

Is it likely that the best and brightest medical students can be funneled into settings where they can reinforce each other

and be inspired by brilliant mentors? If it were to happen, it would require NIH to support teaching and research at a concentrated depth in the basic sciences to open the eyes of medical school graduates to the joy of scientific study.

There is a lesson from this golden era of NIH: Ambitious young physicians juxtaposed to cutting-edge basic scientists can themselves make fundamental discoveries. Hopefully, this lesson will help to reconfigure the future.

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AGRICULTURE

Carbon Storage with Benefits

Saran P. Sohi

Biochar is the solid, carbon-rich product of heating biomass with the exclusion of air (pyrolysis or “charring”). If added to soil on a large scale, biochar has the potential to both benefit global agriculture and mitigate climate change. It could also provide an income stream from carbon abatement for farmers worldwide. However, biochar properties are far from uniform, and biochar production technologies are still maturing. Research is beginning to point the way toward a targeted application of biochar to soils that maximizes its benefits.

Incentives for using biomass to mitigate climate change currently focus on replacing fossil fuels in combustion. Biochar production seeks a different route to carbon abatement. By stabilizing carbon that has already been captured by plants from the atmosphere into a form resembling charcoal, it can prevent the carbon from degrading and returning to the air. A key attraction of biochar is that it can enhance the fertility and resilience of crop land. If biochar production could be made profitable through its use in agriculture, this would distinguish it from costly geoengineering measures to mitigate climate change.

At least one-third of net plant growth globally is thought to be now managed by



Biochar variation. The diverse properties of biochar have led to widely varying results. A more systematic understanding is now emerging, helping to define its value in crop production and carbon storage.

humans (1). Diverting a few percent of this growth into biochar production could sustainably expand biosphere carbon stocks by a gigatonne [10^9 metric tons (t)] each year (2). In contrast, the addition of fresh or composted plant material would have a small effect on carbon storage: Only around 10% of the carbon becomes stabilized (3) and after reequilibration, higher levels of organic inputs to the soil are matched by more decomposition. Conversion of biomass to biochar through pyrolysis creates a product that is highly resistant to biological attack. The finite capacity of soils to store decomposing organic matter therefore does not apply to biochar. Exactly how long biochar remains stable in the soil is still not completely resolved, however.

Calculations show that cleanly creating biochar from diffuse, seasonal sources of biomass such as rice husk should provide a clear carbon benefit. However, biomass can often equally be used to create bioenergy

Biochar—a material related to charcoal—has the potential to benefit farming as well as mitigate climate change.

and displace the use of fossil fuel. For biochar to become the better option, the efficient stabilization of carbon into biochar must be combined with the recovery of energy from pyrolysis gases and residual heat (2, 4). Pyrolysis systems that connect continuous biochar production (for example, in rotating kilns) with power generation from coproducts remain scarce.

Without financial incentives for carbon abatement by stabilization, biochar has to be worth money in the soil. However, biochar materials are diverse (see the figure), and maximizing the benefits gained from their use depends on matching them to the right situation (5). This diversity is the reason for the startling variety of results from early observational studies that aimed to demonstrate benefits to plant productivity. Although one study reported an eight-fold increase in crop yield through the use of biochar (6), a meta-analysis of 16 glasshouse and field studies showed a mean impact of only 10 to 15% on plant productivity (7). The highest productivity increases were seen in soils of medium texture and low pH.

Many of these early studies used readily available charcoal, which is one form of biochar. Increasingly, biochar with particular properties is selected to address an identified soil constraint, such as water storage or flow, pH or retention of crop nutrients, or even a biological purpose (8). Suitable screening methods allow biochar to be compared for properties such as physical and material sta-

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