Genetic Revolution

DNA - By Robert A. Weinberg Last edited April 6, 2024

Through no fault of our own we were born precisely at the right time to experience the 20th century revolution that changed the face of biology. In addition, MIT had made a strategic decision in the mid-1950s that the then-new field of molecular biology should represent the future trajectory of the Institute's Biology Department. At the time, biological sciences at the Institute had been dominated by research into diverse areas that could best be summarized as applied biological research, including work on nutrition, food preservation, bacteriology, public sanitation and public health. Recognizing that biological research was about to undergo a revolution, the Institute separated the more traditional lines of research into the Nutrition and Food Science Department, leaving behind a core of faculty who became founders of the modern Department of Biology.

The roots of the revolution can be traced directly back to Watson and Crick's 1953 discovery that the genetic material inside all living organisms was borne by DNA molecules. From this flowed the notion that DNA somehow influenced the ways that diverse organisms developed and functioned. This simple idea could explain almost the entirety of the biosphere (the exceptions being viruses).

The mid-1950s decision about MIT's future involvement in biological research led the Biology Department to bring in Salvador Luria in 1959, who a decade later won a Nobel Prize for his work on bacterial genetics. (Among Luria's doctoral students before his arrival at MIT was Watson.) Others included Boris Magasanik, recruited from Harvard in 1960, who served as Department Head that resulted in even more recruits in the then-exploding field of molecular biology.

I was thunderstruck by a lecture given in 1963 by the late Maurice Fox. (Imagine how infantilizing it was for me to work as a colleague of his for the first 45 years of my tenure as a faculty member of the Course VII Biology Department!) What he preached at the time was truly extraordinary: That one could now understand all biological function – all of it– in terms of a simple information hierarchy: DNA makes RNA which makes proteins, where the DNA served as the genetic repository, the RNA carries information from the DNA in the nucleus of the cell to protein factories in the cell cytoplasm; the latter, in turn, do the work to create biological form and function.

I thought then and still believe that this doctrine, first enunciated in 1961, was by any measure as important as Newton's description of his laws of mechanics and Darwin's description of his theory of evolution. There we were as MIT undergraduates, learning from faculty who were in direct contact with the developers of these ideas! And there was more that happened while we were undergraduates: between 1961 and 1966 the genetic code was deciphered, that is the rules dictating how sequences in DNA could be translated into the sequences of amino acid that formed proteins. The Morse code of the genome. Wow! What a time that was, and we undergrads at the Institute had a front-row seat for viewing the action!

After those years the life sciences at the Institute went from strength to strength, and there were times over the past decades that our Biology Department ranked among the country's top five university biology faculties. During our time at Tech, the Course VII bio majors numbered about 30 – a beleaguered 3% of our undergraduate class. Nowadays, almost one-third of the Institute and its students are working in areas that have some connection with the "life sciences", many being enrolled in the relatively new Bioengineering Department.

Figure 1 – North of the MIT campus circa 1975.

Actually, there was another factor in the Institute's rise as a world center of the new biotechnology. This one was traceable to the 1963 assassination of President Kennedy. Starting soon after he ascended to the presidency, the decision was made to locate NASA's Electronics Research Center in the midst of an almost-30 acre plot of Cambridge land that was being cleared as part of a massive urban renewal project. Much of the site was occupied by 19th century red brick factory buildings that together had made the Kendall Square area second only to Boston as the state's largest manufacturing center. Early during our undergraduate years it was still possible, on an almost-daily basis, to breathe in the stench from Lever Brothers major fat rendering soap factory as well as well as the aroma from factories manufacturing various types of rubber substitutes just north of Main Street, the Institute's northern border. Early during our time at Tech all of this industry was gone, leveled to the ground and leaving behind a vast wasteland that would, at least on the plans, make way for the future NASA center.

All this changed after November 22, 1963. Lyndon Johnson was sworn in as President, and the bulk of NASA's planned Kendall Square functions were mysteriously relocated to Houston, Texas. Many in Cambridge viewed this loss as a major tragedy, in that MIT would no longer be juxtaposed, cheek-by-jowl, with the burgeoning electronics field that was being fueled by federal money at its NASA Electronics Research facility. In the end, things turned out much better for eastern Cambridge and for the Institute. When the recombinant DNA revolution (which led directly to the biotechnology industry) began in the mid-1970s, there were two academic centers of the nascent molecular biology research in Cambridge, one at Harvard and the other at MIT. The Harvard Square area had, at most, several square feet of land that were not spoken for, while MIT sat next to the 30 acre parking lot to its north, which had remained largely undeveloped after the early 1960s clearing of the land.

Figure 2 – Kendall Square circa 1980.

In the decades that followed, the dozens of biotech and big pharma firms that located or relocated immediately north of the Institute's campus said that they were attracted because Kendall Square offered them the opportunity to be part of MIT's vibrant community of molecular biologists; they would be, so they maintained, active participants in the community's intellectual life.

Nothing was further from the truth. In fact, these companies craved the vacant land on which they could build their research and development facilities. In addition, it was vastly easier to recruit top-notch personnel to Cambridge, MA than to rural New Jersey or Basel, Switzerland, where the pharmaceutical firms had previously built their R&D facilities. These dynamics led the eastern part of Cambridge to grow into one of the country's two major centers of the biotech industry, the other being in the Bay Area south of San Francisco. The developments in Cambridge accrued to MIT's luster, which was, once again, credited with spawning yet another major technology shift in the US. So, as it turned out, NASA's flight from Cambridge was not as tragic as many depicted in the months before our graduation.

While this explosion of development was going on, there was much change within the Institute itself: In 1990 MIT made one semester of biology a part of the General Institute Requirements for graduation, having recognized – a bit belatedly – that an understanding of the elements of modern biology had become an essential part of educating scientifically literate graduates and that the science of biology had developed an intellectual rigor and conceptual coherence that rivaled the fields of chemistry and physics.

Figure 3 – Whitehead Institute Today.

I myself taught the much-visited, required introductory 7.012 lecture course for two decades, which was full of restless engineers and physicists who clearly chafed under this requirement. Much to the amusement of the many hundreds in attendance, I began the first lecture of each Fall semester as follows. "Class! I have a confession to make." (They all looked up from their laptops and cell phones.) "When I took this course in 1961, I got a D." which elicited much applause and laughter. I announced this not to make the students more relaxed in taking 7.01; instead, I only spoke the truth, which came to haunt me years later when I undertook to apply to grad school PhD programs in biology. None of the graduate programs would even look at me except our own Biology Department, which knew, somehow, that my potential in biomedical research exceeded what my deplorable academic record indicated.

This pattern of almost-accidental incest and inbreeding in my career was extended when Luria passed by my post-doctoral research laboratory in La Jolla, CA and told me that I would be part of the new MIT Cancer Center that he was putting together. He did not seem interested in my response, taking for granted that I would surely accept his offer. I pretended indifference for two or three days before I reluctantly accepted his wonderful offer. This ancient history explains my longevity of my association with our Biology Department, which by now exceeds six decades.

I actually ended up as an MIT freshman because friends of my parents had sent their sons to the Institute. My parents, as refugees from Germany, knew relatively little about American higher education, and I even less. I entered convinced that I should pursue a premedical academic career as an undergraduate...after all, what else could I, as a young Jewish man, reasonably entertain in 1960? Once at the Institute, I learned that physicians often needed to stay up all night to care for patients. I, for my part, needed my sleep, and for that reason alone switched from pre-med to biology as my educational focus.

Once on the faculty, my own cancer research at the Institute thrived not because of my talents but because of the quality of the PhD students and post-docs whom I could recruit to work in my lab. In the end, many of the truly original scientific ideas in our research came from their brains, not mine. Their quality reflected an oft-cited difference between the two coasts and the remaining "fly-over" states in the middle of our country: The young people, especially those from overseas, wanted to study and learn in higher institutions on one of the coasts or the other, representing a trend that, to my mind, did not serve the best interests of our country, since there was clearly as much brainpower (if not much more) in the middle of the country than on its east and west boundaries. For whatever reason, these disproportionate realities benefited me and others at the Institute enormously and continue to do so to this day.

My work focused on how normal cells in our tissues became cancer cells – uncovering the origins of cancer rather than figuring out how to treat already-diagnosed cancers. The prevailing concept in the 1960s and 70s was that cancer cells were, with great likelihood, mutant cells, that is, cells that carried damaged genes encoding abnormal cellular behavior. As attractive as this notion was, there was no proof of its correctness until, in 1979, my lab reported that the DNA of cancer cells indeed carried mutant genes that could orchestrate the abnormal behavior of previously normal cells.

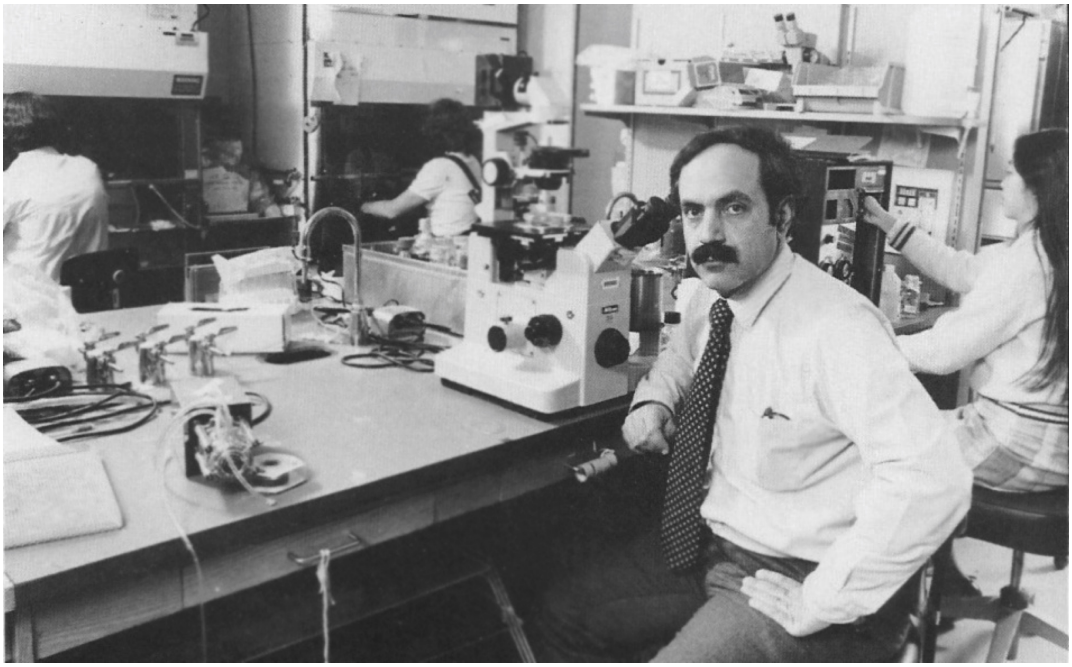
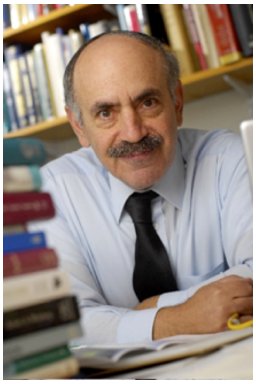


Figure 4 - Weinberg in his lab circa 1980.

Moreover, we proceeded to isolate the responsible damaged gene and reported, using the then-recently developed technique of DNA sequencing, that a normal human gene composed of six thousand DNA base had suffered damage, in that a single change (i.e., a mutation) in a single base of this gene sufficed to convert a normal cellular growth-regulating gene into a potent genetic agent that drove the cell into endless rounds of proliferation and thereby created the large cluster of cells that we considered to be a tumor. Such mutant, cancer-causing genes came to be called "oncogenes". Some years later we isolated the representative of a large class of genes that operate in a fashion opposite to that of oncogenes; this other gene, which caused a rare eye tumor, was classified as a "tumor suppressor gene". My work since that period in the late 1970s and early 1980s has been interesting but has never approached in its fundamental importance and impact our discoveries made during that brief window of time.

I have never regretted my stick-in-the-mud career and my deep roots in Cambridge, working with extraordinary colleagues and never-ending intellectual excitement. Now that it's soon coming to an end, I can say, most sincerely, that it's been a good run. How lucky I've been !



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