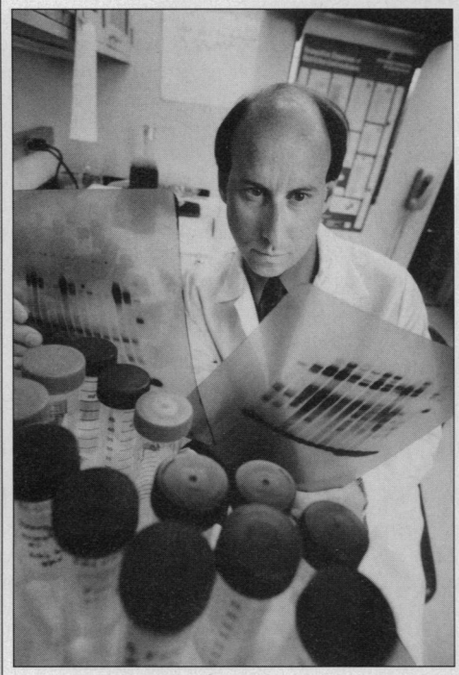
Molecular Medicine: A Calling for the Dual-Degreed

Science often makes a leap when one of several competing teams achieves a breakthrough that is then confirmed by one or more of the "losers." So it was a bit out of the ordinary when a collaboration between Harvard and University of Chicago medical researchers made a startling discovery only to find that very few were prepared to prove them right by repeating their work. Molecular medicine, a new discipline that relies on expertise in both clinical medicine and molecular biology, was only beginning to recruit talent.

The year was 1989 and the discovery was made by a team headed by Ralph R. Weichselbaum, a University of Chicago radiation oncologist. What they observed was a remarkable—and counterintuitive—phenomenon: Radiation has long been known to cause DNA damage or cell death. But Weichselbaum's group noticed that they could use ionizing radiation of the sort used in cancer treatment to activate human genes that, in turn, stimulate the production of one of our most powerful immune proteins, tumor necrosis factor (TNF). And that, in turn, raised a tantilizing notion: that such a technique could be used to improve the outcome of radiation therapy for cancer patients. This idea stirred up the cancer research community when Weichselbaum's team published their results the same year in the *Proceedings of the National Academy of Sciences*. But was it real? The situation cried out for a confirming study, but no one immediately took on the job. "Most radiation oncologists were [only] just starting to get experience in molecular biology," recalls Weichselbaum. So for a couple of years, no one knew enough to take on the task of confirming this exciting work.



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From bench to bed. Jeff Leiden reads gene sequences used in gene therapy experiments.

The time lag between initial result and confirmation underlines the fact that until very recently, many medical scientists were unfamiliar with the tools of molecular biology, and therefore much promising research was stymied. "There was initially a delay in the widespread application of these powerful techniques to problems of medicine," says Francis Collins, director of the National Center for Human Genome Research at the National Institutes of Health. But, he adds, the situation is changing rapidly. "There's a growing realization, especially among physicians in research, that molecular biology answers questions that can't be answered any other way." Now most medical schools are gearing up to better equip medical scientists with the tools of molecular biology.

As a rule, medical researchers have probed organs, tissues, and finally, cells in the hope that they could determine disease etiology. In contrast, molecular medicine has opened entirely new doors by looking first at genes and gene products to understand how their normal expression guides healthy physiology while abnormal expression leads to pathological changes. "It's at that level that we'll find new cures for disease," says Nobel laureate Paul Berg, director of the Beckman Center for Molecular and Genetic Medicine at Stanford University. "That's the future of medicine."

Indeed, it was at Stanford, in 1989, that a medical school first made a major commitment to molecular medicine. "We at Stanford raised a flag with a major investment," says Berg. Since then at least three other schools, the University of Chicago, the University of Southern California, and Yale, have started programs. And all have obtained much of the additional cash needed from private sources, such as the Howard Hughes Medical Institute, the Lucille Markey Charitable Trust, and Genentech cofounder Herbert Boyer and his wife, Marigrace. Dozens of other medical schools are now following suit, patching together support with a combination of discretionary funds, federal research money, and private donations, for more modest programs featuring new research and courses in, for example, gene therapy and molecular diagnostics.

Molecular medicine practitioners are roughly split among the holders of Ph.D., M.D., and M.D.-Ph.D. degrees. The last are most numerous and are being heavily recruited by industry and academic medicine. For people with Ph.D.s only, the greatest challenge is learning to translate a laboratory finding into clinical use. But as increasing numbers of medical schools develop programs in molecular medicine, more Ph.D.s are getting the chance to use their skills in collaboration with practicing physicians. "Pure Ph.D.s who once might have eschewed medicine are now finding satisfaction in seeing an application for their work," says Berg.

Perhaps the most pleasant surprise is that increasing numbers of M.D.s, many of whom took the Hippocratic oath long before molecular biology became fashionable, are eagerly seeking additional training so they can share the excitement of molecular medicine and use it in their work. Berg, who has a neurosurgeon on a 2-year break working in his lab, says: "M.D.s who are dissatisfied with ordinary explanations are coming back to learn more." And this positive attitude extends beyond medical school. While only a few years ago the American Medical Association (AMA) dropped a continuing education course for physicians on "biotechnology and medicine" because of poor enrollment, the AMA is now developing instructional programs on molecular medicine that practicing physicians can load onto their PCs. "Within the last 3 years interest has expanded significantly," says the AMA's Jerod Loeb. "The technology is making its way into community hospitals."

Jeffrey Leiden, a University of Chicago chief of cardiology with a Ph.D. in virology, is developing novel gene therapy approaches to treat certain types of cardiovascular disease. Says he: "I sense a real receptiveness" at the grassroots. "I'm even getting invitations to deliver grand rounds [seminars] at small hospitals." Loeb adds: "What was unthinkable a decade ago, such as human gene therapy, is making its way into mainstream medicine."

–Anne Simon Moffat