

Looking Ahead to the Bicentennial...

When the University of Michigan Medical School's bicentennial is celebrated in 2050, what will be the major developments to appear on the timeline that chronicles those 50 years? As today's new Medical School graduates approach their 80s, what will they have witnessed over the course of their medical careers?

The new language of medical science — nanotechnology, genomics, proteomics, bioinformatics — suggests that we are on the threshold of amazing developments, moving toward more spectacular perspectives on biology than ever dreamed about...a day, for instance, when we may know the three-dimensional structure of every protein created by genes.

...GREAT MINDS
DOING GREAT THINGS
IN PURSUIT OF INTELLECTUAL DISCOVERY
AND THE BETTERMENT OF HUMANKIND.

As Lee Bollinger, president of the University, noted in a recent communique about the life sciences at Michigan, "Advances in the life sciences are raising new questions about what it is to be human, how best to lead a human or humane existence, what it is to be a living organism on this planet, and other crucial questions of human values that will reverberate throughout the social sciences, the humanities, the arts, and medicine. We also can expect transformations in the practice of health care, the nature of scientific research and significant segments of the economy, technology and education."

**"ADVANCES IN THE LIFE SCIENCES ARE RAISING
NEW QUESTIONS ABOUT WHAT IT IS TO BE HUMAN..."**

—U-M PRESIDENT LEE BOLLINGER

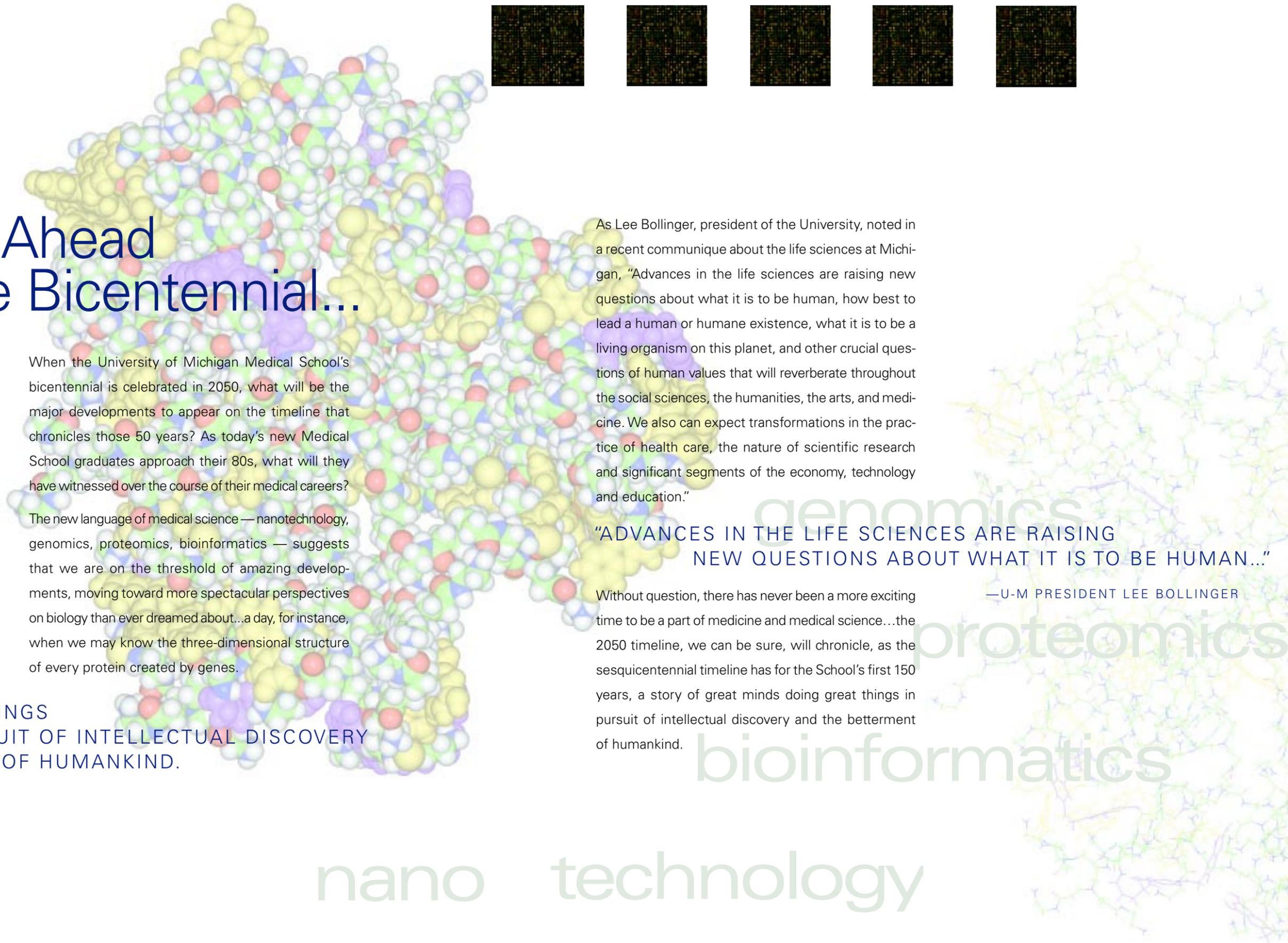
Without question, there has never been a more exciting time to be a part of medicine and medical science... the 2050 timeline, we can be sure, will chronicle, as the sesquicentennial timeline has for the School's first 150 years, a story of great minds doing great things in pursuit of intellectual discovery and the betterment of humankind.

nano technology

bioinformatics

proteomics

genomics



James V. Neel, M.D., Ph.D.

MARCH 22, 1915 – FEBRUARY 1, 2000

A Remembrance by His Colleagues



The world of medicine has changed in dramatic ways over the past quarter-century, but the qualities that make for a fine physician and an outstanding medical scientist have changed very little, if at all. The profound ethical and moral issues raised by our technological advances have, in fact, made the ancient virtues of honesty, humility, hard work, intellectual rigor and respect for one's fellow man more important than ever.

Perhaps no man in the U-M Medical School's history better exemplified those qualities than James V. Neel, M.D., Ph.D., who died earlier this year. Both scientist and physician, Neel joined the Medical School faculty in 1946, chaired its Department of Human Genetics, which he founded, for 25 years beginning in 1956, and continued to apply himself to his research, which centered on genetic mutations and their effects on human populations, until shortly before his death from prostate cancer earlier this year at the age of 84.

In a May 22 memorial service held in the Rackham Building on the Michigan campus, Neel's colleagues remembered fondly the many qualities he brought to his work and the powerful influences he had on those who had the good fortune to know and work with him.

At the time the young Neel discovered his fascination with genetics as an undergraduate at the College of Wooster in Ohio in the early 1930s, studies in genetics were largely confined to organisms such as the fruit fly. Sixty-plus years later, as we celebrate the mapping of the human genome, it is difficult to imagine that when Neel was earning his doctorate (1939) and his medical degree (1944), in the turbulent years before and during the Second World War, genetics was, as **Thomas Gelehrter** noted in his opening remarks, "a field in disrepute, sullied by the sloppy and irresponsible work of the eugenicists." It was only Neel's extraordinary vision, Gelehrter noted, that allowed him to foresee what "solid, honest and responsible science" could accomplish in the area.

When Neel came to Michigan in 1946, it was, Gelehrter noted, because he recognized he would have "room to run" with his ideas, something he also provided to so many others over the years he chaired the department.

William J. Schull, who first met Neel in 1947 and was persuaded by him to join the Michigan faculty in 1951, remembered how much Neel accomplished so early with so little: "Jim's office was small, and I shared mine with an old piano whose purpose I did not know then nor now.

Nonetheless, out of these limited quarters and with a small staff, Jim had already fashioned a substantial scientific program, and his own research was defining the future of human genetics. Three seminal publications in these early years document this fact — his recognition of the mode of inheritance of thalassemia or Cooley's anemia (1944), the delineation of the importance of the carrier state in the manifestation of hereditary diseases (1947), and, finally, the definition of the mode of inheritance of sickle cell anemia (1949)."

Being the pioneer that he was, Neel might eventually have been expected to display at least some of the self-importance to which he would have been fairly entitled. But his modesty and his deep devotion to the science itself kept him open always to the ideas of others, and that openness he considered a high value in his life and work. As **Allen Lichter** noted, Neel himself had said that his most important objective as a teacher was to imbue every student with "complete intellectual honesty and a willingness from time to time to reconsider one's position."

Neel's genius for inspiring others with his scientific passion was not limited to his students. Even in his late 70s, he was able to pull a fellow scientist he had never met into his web of enthusiasms, as **Eugene O. Major** gave personal testimony to:

Nearly eight years ago an unusual journey began for me, a trained molecular virologist interested in how viral infections affect the human nervous system, when I received a telephone call in my office at NIH from James V. Neel, world renowned scientist, pioneering geneticist, peripatetic questioner of nature's secrets.... Dr. Neel introduced himself, in very humble terms by the way, and began to narrate a story about his decades of observations of chromosomal aberrations in numerous populations.... I listened... but mostly I waited for the punch line, since I could tell by the slight gleeful tone in his voice that there was a question for me coming up, a mega-question as we say in the lab, and so finally after his prologue, Dr. Neel summarized his thesis and declared his hypothesis that not all chromosomal damage is due to conventional mutations, to environmental toxins... that some can be ascribed to infections, chronic infectious episodes in populations that come in waves... he tells me that he searched the literature and determined that viruses can be mutagenic, cause sustainable chromosomal damage... now I'm really listening... and that he scoured the journals and found the human polyomaviruses are a prime candidate for such an agent, ▶

and that in his searches I was the investigator whose named popped up as the likely expert in the field who could help develop this hypothesis... it was the way he put it... a little flattery, a little challenge, a little request... the quintessential offer... you couldn't refuse... what we were about to venture ahead on was to define the etiology of the 'rogue cell,' a name given to severely damaged cells...

There was a series of telephone calls... I began to look forward to those conversations, mostly the science side of the story but always embellished with that sense of a jackpot at the end of the experiment, the rainbow effect, the big lottery ticket, the 'what ifs?'... just when it seemed there were few leads to follow, a new finding would pop up and Jim knew how to nurture it... he could grow information out of a barren rock...

Jim had an extraordinary vision, to know what, how and why to ask questions, and then an enthusiasm and focused passion to simply get there... and to know where it is you are when you arrive...

I regret only one thing in the time I had with Jim and that is that the first telephone call hadn't come much longer ago... (he had) an inner confidence of incredible proportion... but could still write, as he did in his book, Physician to the Gene Pool, "Sometimes flushed with new knowledge, I stop to ponder the unnecessary delicacy of butterfly wings and orchids."

Schull, too had vivid remembrances of Neel's persuasiveness: "He could and would further his argument with his sense of drama, an appreciation of the worth of a pithy remark, a grimace (usually a raised eyebrow, suggesting you surely did not mean to say that) and a... well-timed pause..."

Neel's great enthusiasm for his work extended almost to the end of his life, even after he had become ill. As **Gil Omenn** noted in his remarks, even in his last few years Neel was a distinctive physical presence on campus. "When I came here in 1997," he said, "Jim Neel was still a really remarkable figure, with his backpack, trudging almost every morning like clockwork across the streets in front of the Medical Center, over to the Kresge Building." As with everyone else, however, it was Neel's mind that most intrigued his newly arrived colleague: "When I sent him comments about a couple of his papers and asked him for comments on some manuscripts I had recently drafted, we struck up some very, very good conversations, the kind of experience that all of you have had over the decades with him... so I share with you a sense of loss but, even more, a sense of great pleasure at having known the man..."

For **Francisco M. Salzano**, whose relationship with Neel extended over 44 years, his example as a scientist and the many fine qualities he brought to his work stood always, Salzano said, "as a paradigm" for him and many others. "The

elegance of his attitude when fiercely attacked by other professionals will always be admired," Salzano said. "He was strong, physically and intellectually. The last time I saw him, in October 1997, he was 82 and in ill health, but he was still most willing to use the stairs instead of the elevator in moving from one floor to another at the convention center where we were."

Neel's colleague and fellow pioneer **Arno G. Motulsky**, M.D., pointed out that Neel's long string of impressive discoveries will remain an extraordinary scientific legacy: "Jim was among the first in this country to concentrate on clinical applications of genetics," he noted. "Many other scientific accomplishments followed... his demonstration of sickle cell anemia as the first molecular disease... His thrifty gene hypothesis was influential in pointing to the role of selection in increasing gene frequencies of deleterious genes involved in diabetes and arteriosclerosis, demonstrating that the possession of such a gene may have been life-saving for our distant ancestors under conditions of semi-starvation... His work with William Schull on survivors of the atomic bombing in Japan were models of design, organization, diplomacy, persistence and plain hard work over many years..."

The celebration of the Medical School's sesquicentennial has given students, faculty, alumni/ae and friends the opportunity to contemplate its remarkable 150-year history, a good portion of which included the scholarly contributions of James V. Neel. But Neel himself, geneticist that he was, tended to think on a much grander scale. He ended his book, *Physician to the Gene Pool* (John Wiley & Sons, Inc., 1994), on a cautionary note, hoping that the important issues of population growth and the attendant depletion of the world's resources would be resolved so that "the genetic legacy from the past five million years of human evolution" would not be squandered. □

Remembrances by:

Allen S. Lichter, M.D., Dean, University of Michigan Medical School
Gilbert S. Omenn, M.D., Ph.D., U-M Executive Vice President for Medical Affairs and CEO, U-M Health System

Thomas D. Gelehrter, M.D., Chair, Department of Human Genetics
William J. Schull, Ph.D., Professor Emeritus, University of Texas School of Public Health

Eugene O. Major, Ph.D., Chief, Section on Molecular Virology and Genetics, National Institute of Neurological Disorders and Stroke, NIH

Francisco M. Salzano, Ph.D., Emeritus Professor, Departamento de Genética, Instituto de Biociências, Brazil

Arno G. Motulsky, M.D., Professor Emeritus of Internal Medicine and Genetics, University of Washington

The Department of Human Genetics has established an annual lectureship and fellowship to honor James Neel. Contributions may be sent to the U-M Medical School, Department of Human Genetics, Box 0618, Ann Arbor, Michigan 48109-0618.