University of Michigan
Medical School

Dear Alumni and Friends:

The accomplishments of our outstanding program in genetic counseling, the result of a long tradition of leadership in this field, are highlighted in the cover story of this issue of *Medicine at Michigan* (page 20).

In 1941, the University of Michigan established a heredity clinic, the first of its kind in the country, staffed by several faculty members, among them Harold Falls (M.D. 1936, Residency 1939), then a young ophthalmologist who had become interested in hereditary eye disease. At age 94, Harold is still going strong. It was wonderful to see him at Reunion this past October, and to be reminded of the many contributions he and his colleagues have made toward genetics and genetic counseling at U-M and in the world.

The late James Neel, M.D., Ph.D., nationally and internationally recognized as an important pioneer in the field of human genetics, was one of Falls' fellow researchers, joining the Heredity Clinic in 1946. As Neel later wrote in his book *Physician to the Gene Pool*, "Humans were not [viewed] as a favorable object for genetic study. Their generation time was too long, they had too few offspring, genetically interesting matings could not be arranged, and they had so many chromosomes compared to the [fruit fly's] four pairs that establishing gene-linkage groups was bound to be difficult." Nonetheless our pioneering researchers undertook the challenge of human genetic study. As the Heredity Clinic grew, it was followed in 1956 by the formation of the nation's first academic department of human genetics, with Neel as its chair.

The accomplishments of this Michigan group of faculty-physicians are legion. For example, Jim and his colleagues deduced the relationship between sickle cell anemia and sickling trait and, in 1949, published the mode of inheritance of this disease. His "thrifty gene" hypothesis, first articulated in 1962, explained the current huge increase in type 2 diabetes and is referenced in leading scientific publications to this day.

Other Michigan students and faculty also have left lasting imprints on the field of genetics. Marshall Nirenberg (Ph.D. 1957) unlocked the genetic code showing how only four DNA bases, arranged in three-letter triplets, could code for 26 amino acids. Nirenberg was recognized for his accomplishments with the 1968 Nobel Prize in Medicine. Hamilton Smith, M.D., who did his postdoctoral work in the lab of Mike Levine, Ph.D., in our Human Genetics Department from 1962-67 before joining Johns Hopkins, went on to win the Nobel in 1978 for his discovery of restriction enzymes that cut DNA at specific sites. While at Michigan, Francis Collins, M.D., Ph.D., helped pioneer the concept of positional cloning to find disease-causing genes, discovering the genes for Huntington's disease, cystic fibrosis and neurofibromatosis. He then went on to lead the Human Genome Project and direct the National Human Genome Research Institute at the NIH.

Following in this grand tradition, our genetic researchers continue to innovate, discovering important new disease-associated genes and gaining new insights into the workings of the human genome. For example, Friedhelm Hildebrant, M.D., in the departments of Pediatrics and Human Genetics, has identified a series of genes involved in juvenile renal diseases. Marci Lesperance (M.D. 1988, Residency 1994) and colleagues at the Kresge Hearing Research Institute are finding genes associated with inherited hearing loss. Using some of the same families whose data Harold Falls began collecting more than 50 years ago, Anand Swaroop, Ph.D., in the Departments of Ophthalmology and Human Genetics, has discovered genes associated with macular degeneration.

At the University of Michigan, we are the proud stewards of a powerful tradition of innovation in human genetics going back to the 1940s.

Of course, the issues surrounding the use of genetic information for the benefit of our patients are daunting. The complexity will, no doubt, only increase over time as we move from counseling patients and families about single-gene disorders (there are over 1,000 such disorders we can test for today) to counseling for complex disorders such as diabetes or behavioral disorders whose multi-gene origins are yet to be learned.

We will continue our innovative research in genetics in the years ahead. Our top-ranked programs in statistical genetics are unraveling the mysteries of complex genetic disorders. Research in our renowned mouse genetics program is creating accessible and convenient models of human disease. As we find genetic abnormalities that lead to anatomic anomalies, a new program in fetal surgery may soon correct some of these anomalies before birth.

At the University of Michigan, we are the proud stewards of a powerful tradition of innovation in human genetics, and we are likewise proud to present to you in this issue the current state of some of our work in this fascinating and still challenging field.

Sincerely,

Allen S. Lichter (M.D. 1972)
Dean