Nano-Man of the Moment
Changing the Way We Think About Medicine
In 1950, LIFE Magazine sent famed photographer Alfred Eisenstaedt to Ann Arbor to capture photographic impressions of the everyday academic and personal lives of University of Michigan medical students and residents. Evocative of the era, the photos capture on paper a far different time, but one that still speaks powerfully of the challenges and satisfactions of the world of medicine at Michigan.
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Gilbert S. Omenn, U-M Executive Vice President for Medical Affairs, and CEO, U-M Health System;
Allen S. Lichter, Dean, U-M Medical School;
Larry Warren, Executive Director, U-M Hospitals and Health Centers

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Dear Alumni/ae and Friends,

June in Ann Arbor, with its summer green — not only in the lawns and foliage but in the traditional velvet of our new graduates’ hoods — is a time that brings reminders of the cycles of renewal that grace not only nature but academic institutions as well. Graduation ceremonies represent achievement, but they also represent growth and new opportunities. For the Medical School itself, such new directions are also on the horizon. As you will read in Gil Omenn’s letter in this issue, the Health System recently completed an intensive strategic planning process that will ultimately lead to important changes in the way we teach, conduct research and care for patients.

The rise of managed care and the increased emphasis on outpatient treatment have already brought changes in how we prepare medical students to serve their patients. The Strategic Plan has identified several curricular innovations that we will begin implementing over the next few years. These include an increased emphasis on ambulatory care experiences, new reliance on Web-based educational tools and an enhanced effort to improve the teaching skills of our faculty. Such innovations are necessary to maintain our role as one of America’s leading academic medical institutions, a role of which we have been made especially aware during the celebration of our Sesquicentennial and the many great achievements that are part of the School’s history.

Biomedical research is also being restructured and improved at Michigan. The Life Sciences Initiative is well underway, and will do much to help us coordinate and expand research and teaching in such rapidly advancing fields as genomics, chemical and structural biology, cognitive neuroscience and bioinformatics, as well as in other areas of study that bear on and are influenced by the life sciences.

The Life Sciences Institute, a research complex that will serve as a hub for cross-disciplinary research and teaching in the life sciences, is part of the Initiative. Both the Initiative and the Institute are important elements in the state of Michigan’s Life Sciences Corridor, a billion-dollar project to invest in and promote life sciences research and business development. Organized by the Michigan Economic Development Corporation, the Corridor includes the University of Michigan, Michigan State University, Wayne State University and the Van Andel Institute in Grand Rapids.

We intend to play our part in keeping the University and the state in the forefront of biomedical research and the translation of that research into products and services that enhance life. In conjunction with the Life Sciences Initiative, we are examining ways to improve the research enterprise at the Medical School, including designing a spectacular new research building to house researchers by program and theme, as opposed to department, in order to facilitate collaboration among disciplines. Construction of this new research building will begin next year. The building will be on the north side of Washtenaw Avenue, west of Couzens Hall. Across Washtenaw, on the south side, will be the new Life Sciences Institute. The two buildings, the Medical School’s new building and the Life Sciences Institute, will be linked by a pedestrian bridge over Washtenaw Avenue. Many of our colleagues in the Institute will have primary and joint appointments in the Medical School.

This new Initiative, and the Medical School’s refocused efforts to foster and support faculty research, make this an exciting time to be dean. I am pleased to be able to oversee this important evolution and growth of the Medical School.

By now you should have received an invitation to the Sesquicentennial Celebration/All-Classes Reunion that will take place October 13-14. The event is a wonderful opportunity for all the classes of the Medical School to be together for what promises to be a festive occasion and to celebrate the outstanding work of the many men and women who, over the past 150 years, have helped make the Medical School the strong and proud institution that it is today. I hope you’ll be a part of this historic event and join me in looking forward to the beginning of an even greater future for the Medical School.

Allen S. Lichter, M.D.
Dean
The Howard Hughes Medical Institute has made a gift of $4 million to the U-M Medical School to support a new program in bioinformatics. The interdisciplinary program will include graduate education and research in the emerging field of bioinformatics, which merges recent advances in molecular biology and genetics with advanced computer science technology.

The goal is increased understanding of the complex web of interactions linking the individual components of a living cell to the integrated behavior of the entire organism.

“The Human Genome Project and advances in molecular biology have generated a flood of new data about individual components of cells,” says Allen Lichter, M.D., dean of the Medical School. “Yet we know very little about how all these parts work together to create a living organism. The funding from Howard Hughes will help us obtain the computer technology and expertise we need to develop the next generation of bioinformatics tools and educate tomorrow’s scholars in this important new discipline.”

According to Michael A. Savageau, Ph.D., professor and chair of Microbiology and Immunology and director of the bioinformatics program, the Hughes grant will be used to recruit four new junior faculty members and hire technical support staff for a new Bioinformatics Core Facility under construction in the Medical School.

“The Hughes award also will help fund pilot research projects in which bioinformatics faculty and graduate students will work closely with other U-M investigators to develop a deeper understanding of living systems and new applications for this technology,” Savageau says.

“This major grant from the Howard Hughes Institute complements a substantial investment made by the U-M Health System,” says Gil Omenn, M.D., Ph.D., executive vice president for medical affairs. “As part of our Life Sciences Initiative, we want to help shape the future directions of concepts, modeling and analysis in bioinformatics and biocomplexity.” The U-M Health System has committed $5 million to bioinformatics, matched by $5 million from Parke-Davis, a division of Warner-Lambert.

The Medical School is one of 41 medical schools selected this year to receive a Howard Hughes Medical Institute grant for biomedical research support. More than 320 Hughes investigators, including seven in the U-M Medical School, conduct medical research in Howard Hughes Medical Institute laboratories at 71 medical centers and universities nationwide.

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Medical School Ranks Ninth Nationally in 1999 NIH Research Awards

The National Institutes of Health have nearly doubled funding for medical research at the University of Michigan Medical School over the past eleven years, making the school ninth in the nation and third among public universities in total grants from the NIH.

The NIH awarded a record $156.5 million to Medical School investigators in fiscal year 1999, up from $136.2 million in 1998 and $79.7 million in 1989. In both of those previously historical years, the school ranked tenth among NIH-funded institutions.

Last year, the allocations funded 451 individual research awards — the sixth largest total in the nation. Training grants, fellowships, research and development contracts, and other awards are also included in the total.

“As we celebrate our school’s 150th anniversary, we’re excited by the prospect of the new knowledge and therapies that will surely arise from this unprecedented level of funding for our faculty,” says Allen Lichter, M.D., dean of the Medical School.

Lichter attributes the steady rise in NIH funding to the research faculty’s productivity and responsiveness to national medical needs. Not only are the NIH awards a majority of the Medical School’s external funding, but they also make up a large percentage of the University’s total research funds. Medical School NIH awards make up nearly 68 percent of all NIH funding at the University, helping make Michigan sixth in the nation in NIH award totals at higher education institutions.

When all sources of funding — including other federal and state agencies, corporations, and foundations — are totaled, Medical School researchers were awarded $204.6 million during the University’s fiscal year 1999, comprising more than 40 percent of the University’s $480.1 million in awards for use in 1999.

Juvenile Diabetes Foundation Awards $6.6 Million to U-M Medical School for Research on Complications of Diabetes

The Juvenile Diabetes Foundation International announced the opening at the U-M of a new $6.6 million center for the Study of Complications in Diabetes. Each year, such complications rob millions of Americans of their sight, mobility or their life. Many more of the country’s 16 million people with diabetes suffer heart problems, vision deficits, nerve damage and kidney failure, yet researchers do not fully understand why.

More than 60 percent of people with diabetes suffer from some form of progressive nerve damage, or neuropathy, in one or more of their arms, legs or feet. It affects those diagnosed with type 1 (juvenile) and type 2 (adult onset) diabetes. Another of the most common diabetes complications is retinopathy, or progressive damage of the retina due to the deterioration of small blood vessels that supply the retina with oxygen and nutrients.

“I describe diabetic neuropathy to my patients as Alzheimer’s disease of the peripheral nerves,” says Douglas A. Greene, M.D., until recently director of the Center, professor of internal medicine, and director of the Division of Endocrinology and Metabolism. “It is a degeneration of the nerves, and it’s a dynamic process in which degeneration and regeneration are occurring simultaneously.”

Greene has devoted much of his career to understanding and treating diabetes complications. He coordinated much of the diabetes work at the U-M as director of the Michigan Diabetes Research and Training Center before leaving, in the spring, to become executive vice president of clinical sciences and product development for Merck Pharmaceuticals.

The Juvenile Diabetes Foundation Center for the Study of Complications in Diabetes at the University of Michigan will sponsor several related research projects on the role of blood sugar, or glucose, in the development of diabetes complications. Among the lead researchers is Eva L. Feldman, M.D., Ph.D., who will also serve as the associate director of the Juvenile Diabetes Foundation Center in addition to her appointment as an associate professor of neurology in the U-M Health System.

More than 60 percent of people with diabetes suffer from some form of progressive nerve damage, or neuropathy, in one or more of their arms, legs or feet.
Diabetes Foundation has provided more than $326 million in research grants to diabetes research worldwide. The Foundation's mission is to find a cure for diabetes and its complications through the support of research, and since its inception the Foundation has been the world's leading nonprofit, nongovernmental funder of diabetes research. It was founded in 1970 by parents of children with diabetes. The Foundation's mission is to find a cure for diabetes and its complications through the support of research, and since its inception the Foundation has provided more than $326 million to diabetes research worldwide.

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Depression Can Be Bad for Your Physical Health, New Study of Americans Over 70 Shows

Depression, in older people, can be as dangerous to one’s health as smoking. Older Americans who have symptoms of depression are as likely as those who smoke to develop a new disease within two years, according to a U-M study involving more than 6,000 Americans 70 years of age or older.

The study, presented at the annual meeting of the Gerontological Society of America in November, 1999, was conducted by Caroline S. Blaum, assistant professor of internal medicine. It is based on data from the U-M Health and Retirement Study, funded by the National Institute on Aging.

“The relationship of depression, disease and disability is complex,” says Blaum, who is also an assistant research scientist at the U-M Institute of Gerontology. “Not only do disease and disability lead to depressive symptoms, but depressive symptoms seem to be a precursor of the development of future disease. This effect is seen with relatively mild depressive symptoms such as decreased energy and restless sleeping, not just severe clinical depression.”

To evaluate the link between disease and depressive symptoms, Blaum analyzed data collected from the same group of older people in 1993 and again in 1995. The population-based study contains extensive information on physical, mental, financial, and emotional health, as well as a wide range of demographic and behavioral information for a nationally representative sample of Americans born in 1923 or before.

Controlling for gender, marital status, education, the number of diseases at the start of the study, and the presence of mental or sensory impairments and disabilities, Blaum analyzed how age, race, body mass index, smoking, physical limitations and depressive symptoms were related to the odds of developing a new disease during the two-year period. The types of diseases included the most common chronic conditions of older adults, such as diabetes, stroke, arthritis, and cardiac disease.

Physical limitations, such as limitations in the ability to walk several blocks, climb stairs, or lift a 10-pound object, were the strongest predictors that a person would develop a new disease two years later, increasing the odds of developing at least one new disease by nearly 50 percent. But older people who smoked or had multiple symptoms of depression such as feeling lonely or sad in the past week were 34 percent more likely than those who did not to develop new disease, according to Blaum’s analysis.

“Other recent studies have suggested that depression and its symptoms are risk factors for cognitive decline and cancer,” says Blaum. “This study suggests that depressive symptoms may represent pre-clinical indicators of a wide range of future diagnosed diseases. Along with obesity and smoking, symptoms of depression may be a potentially modifiable risk factor for increased disease burden in older people. Clinical trials are needed to find out whether treatment of mild depression leads to decreased disease burden and improved function in older adults.”

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Other researchers include Christin Carter-Su, Ph.D., professor of physiology and associate director of the Michigan Diabetes Research and Training Center; Martin Stevens, M.D., associate professor of internal medicine; James Russell, M.D., assistant professor of neurology; Arno K. Kumagai, M.D., assistant professor of internal medicine; and Irina Obrosova, Ph.D., research investigator in internal medicine.

The Juvenile Diabetes Foundation is the world’s leading nonprofit, nongovernmental funder of diabetes research. It was founded in 1970 by parents of children with diabetes. The Foundation’s mission is to find a cure for diabetes and its complications through the support of research, and since its inception the Foundation has provided more than $326 million to diabetes research worldwide.

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Blaum can be reached at cblaum@umich.edu.
A new line of transgenic mice, created by researchers at the University of Michigan and the Hospital for Sick Children at the University of Toronto, will help scientists understand genetic and biochemical changes that cause a common form of human skin cancer called basal cell carcinoma.

“More than one million skin cancers are diagnosed in the U.S. each year and the majority are basal cell carcinomas,” says Andrzej A. Dlugosz, M.D., associate professor of dermatology and scientific director of the Cutaneous Oncology Program at the U-M Comprehensive Cancer Center.

Previous studies revealed that a mutation in a gene called “patched” (PTCH) was associated with development of human basal cell carcinomas, but it is not known how this genetic change causes a normal skin cell to become a tumor cell.

An initial study describing the new mouse model, published in the March 1, 2000, issue of *Nature Genetics* by Dlugosz and his co-investigators, strongly suggests that the protein Gli2 plays a key role in this process.

PTCH is an important component of a biochemical pathway, called the hedgehog pathway, which regulates embryonic development in organisms ranging from flies to humans. The hedgehog pathway is normally regulated in a very precise manner and is active only at certain times during development of different organs. Dlugosz explains that “when the PTCH gene is mutated, as in basal cell carcinomas, the hedgehog pathway is activated permanently.”

In earlier studies, Dlugosz and coworkers studied the hedgehog pathway in normal skin as a foundation for understanding how basal cell carcinomas arise. They found that the hedgehog pathway controls hair follicle development through a protein called Gli2, suggesting that this molecule may also play an important role in basal cell carcinoma development when the hedgehog pathway is deregulated. To test this hypothesis, the research team created mice which produce abnormally large amounts of Gli2 in their skin. By three months of age, these animals spontaneously developed multiple skin tumors that appeared strikingly similar to human basal cell carcinomas. Mouse tumors also expressed the same protein and RNA markers found in human tumors.

“These mice will help us learn more about the biology of these common skin tumors,” Dlugosz says. Basal cell carcinomas rarely metastasize and can be treated effectively with surgery, but the tumors can be disfiguring since they frequently occur on the face. New forms of non-invasive therapy would be beneficial, especially for high-risk patients who develop multiple tumors.

While other mouse models for basal cell carcinoma exist, Dlugosz says the U-M/Toronto model has advantages for use in scientific research. Other mice either cannot reproduce or the offspring die at birth. U-M/Toronto mice are viable and produce offspring. Plus, they produce tumors spontaneously without radiation exposure, which is commonly used to generate skin tumors in other mouse models.

First author of the *Nature Genetics* paper is Marina Grachtchouk, Ph.D., a research fellow in the U-M Medical School. Co-authors from the Hospital for Sick Children at the University of Toronto are Rong Mo, Sandy Yu, Xiaoyun Zhang and Chi-Chung Hui. Hiroshi Sasaki of Osaka University also is a co-author.

The investigators have applied for a joint patent on the new mouse model. The study was funded by the U-M Comprehensive Cancer Center, the U-M Center for Organogenesis and the National Cancer Institute of Canada.

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By depriving cancer tumors of the copper supply they need to form new blood vessels, researchers in the U-M Medical School have stopped the growth of the disease in a small group of patients with advanced cancer. Five of six patients whose copper levels were kept at one-fifth of normal for more than 90 days had no growth of existing tumors or formation of new ones, according to a paper published in the January, 2000, issue of Clinical Cancer Research. The sixth patient had progression of only one tumor; all other tumors within her body remained stable. Twelve other patients did not achieve the target copper level, or could not stay at the target level for 90 days, because of disease progression.

The finding is the first evidence in humans that physicians might fight multiple types of cancer by targeting copper as a ‘common denominator’ of angiogenesis — the process by which tumors grow the blood vessels that allow them to expand beyond a tiny cluster of cells. The copper strategy is not limited to a single type of cancer, as are other anti-angiogenesis agents now being studied.

Patients in the phase I trial at the U-M had metastatic cancer of the breast, kidney, colon, lung, skin, pancreas, prostate, throat, cartilage, blood vessels or endothelium. All had exhausted other conventional treatment options.

The U-M trial used oral doses of an inexpensive compound called tetrathiomolybdate, or TM, to lower patients’ copper levels. TM was originally developed for clinical use by George J. Brewer, M.D., Morton and Henrietta Sellner Professor of Human Genetics, to treat people with Wilson’s disease, a rare genetic disorder associated with excess copper. His work has shown TM to be the world’s most potent anti-copper agent, and safe to use.

Aware of earlier research indicating that copper is important for angiogenesis, Brewer did work in the early 1990s on animal cancer models treated with TM, with encouraging results. Then he teamed up with Sofia Merajver, M.D., Ph.D., associate professor of internal medicine, molecular genetics researcher, and oncologist in the Comprehensive Cancer Center.

Independently, Merajver was interested in exploring the inhibition of angiogenesis at very early stages in cancer development. Together with Brewer, she designed specific animal studies that allowed the team to test whether TM had the ability to prevent tumors from arising in animals at high risk for cancer. Her laboratory has also begun to uncover the molecular and cellular events involved in the inhibition of blood vessel growth by copper deficiency.

Their first results with humans actually came from a trial that was designed only to see how well TM could reduce copper levels in cancer patients, not to test its effect on the cancer itself. At all three daily dose levels given in the trial, copper levels were reduced to 20 percent of normal in four to six weeks. Neither the drug, nor the long-term copper deficiency, produced side effects.

“What began as a scientific hunch now appears to have potential as a simple but effective general anti-angiogenesis strategy,” says Brewer. “We are proceeding with a clinical trial aimed at accelerating TM-induced copper reduction and assessing its effect on advanced-stage cancer. Later this year, we hope to test this approach in 100 patients with five types of less advanced cancer.” Neither trial is currently accepting patients.

Adds Merajver, “These initial results suggest that the tactic of preventing angiogenesis through copper deficiency holds significant promise. Through this and other therapies, we may one day be able to turn cancer into a chronic or controllable disease or to contribute to its eradication. Still, much more research is needed before we can know the full potential of anti-angiogenesis.”

Angiogenesis happens in the body all the time, whether to repair a wound or help with the normal growth of children’s bodies. It occurs through a so-called angiogenesis “cascade” — a series of biochemical steps by which cells make and secrete molecules that initiate the growth of capillaries. After the job is done, other molecular “factors” turn off the angiogenesis process. But...
cancer cells use this normal process for a nefarious purpose — creating an imbalance of angiogenesis activators that overrides the inhibitors and gives the nearby tumor ready access to a blood supply. This creates a vicious cycle of growth that allows tumors to grow faster than the body can respond.

In recent years, researchers have found that copper is a common denominator to several of the key factors that activate the angiogenesis process. Specifically, it acts as a co-factor, or helper, to molecules known as basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF), and angiogenin. Without copper, the molecules can’t function and construction of blood vessels stops.

That’s why TM makes such a good choice, Brewer explains. It binds with copper and protein, making a stable compound that can’t be used by tumor cells or any other part of the body. Taken at mealtime, TM prevents the body from processing and absorbing the copper in food as well as the copper normally found in saliva and gastric secretions. Taken between meals, TM is absorbed into the blood and binds copper to blood protein. In either case, the TM-protein-copper complex does not interact with other biological molecules and is excreted.

The discovery of TM’s potential effect on cancer grew directly out of Brewer’s decades-long research on trace metals’ importance to the body. He began by examining the role of zinc in sickle-cell anemia, a disorder of the red blood cells, and unexpectedly found that zinc acetate reduced the level of copper in the blood of some patients. This gave him the idea to test the compound’s effect on the dangerously high copper levels in the systems of patients with Wilson’s disease, a potentially fatal recessive genetic condition that strikes 5,000 teen-agers and young adults each year. Finding that zinc acetate brought the patients’ dementia, drooling, slurred speech, temper outbursts and tremors under control if taken regularly, without side effects, he sought and received FDA approval for the compound.

But he needed a faster-acting compound to bring copper levels under control quickly. That compound turned out to be TM, now in clinical trials at the U-M General Clinical Research Center. To date, 63 Wilson’s disease patients have come to the U-M for eight weeks of treatment with TM to lower their copper levels, then returned home to take zinc acetate and follow a copper-restricted diet to maintain their copper levels.

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M-CARE: It’s Award-Winning

M-CARE, the University of Michigan Health System’s managed care organization, one of a few in the nation owned by an academic institution, recently has received several awards for its excellence in the delivery of health care. M-CARE’s high praise came from:

- The National Committee for Quality Assurance
- HealthGrades.com
- Greater Detroit Area Health Council’s 1999-2000 Consumer Guide to HMOs

M-CARE received a “commendable” accreditation rating from the Committee, an independent organization which evaluates how a health plan manages all parts of its delivery system in order to continuously improve health care for its members. M-CARE was one of five commercial, Medicare or Medicaid HMOs in Michigan to receive a “commendable” rating. “The accreditation demonstrates in a measurable way M-CARE's commitment to clinical and service quality,” says Robert Church, D.O., M-CARE’s medical director. “Coupled with our very positive HEDIS scores, the accreditation shows that M-CARE is providing the health care people need with the quality and service they expect.” (HEDIS, which stands for Health Employer Data and Information Set, is the nation’s premier measurement tool for managed care.)

The National Committee for Quality Assurance also selected M-CARE for inclusion in a new book the Committee produced with support from Pfizer, Inc. Entitled Quality Profiles: In Pursuit of Excellence in Managed Care, the publication is a compendium of case studies to showcase outstanding quality improvement efforts. M-CARE was one of 38 health plans chosen from NCQA-accredited plans nationwide and the only plan in Michigan to be highlighted. “M-CARE’s inclusion in Quality Profiles is a true mark of distinction,” says Zelda Geyer-Sylvia, executive director of M-CARE. “Everyone in the M-CARE organization is committed to providing the highest quality care that we can, and being chosen for Quality Profiles is recognition of our ongoing efforts.”

M-CARE received 76 points out of 100, the highest score in Michigan, from HealthGrades.com, an Internet-based firm providing information to consumers to help them select providers of health care. The firm used HEDIS data to grade nearly 250 HMOs from 39 major metropolitan areas in the U.S. M-CARE met or exceeded the national average in all categories evaluated by HealthGrades.com.

M-CARE has more than 180,000 members and contracts with more than 2,000 employer groups. With field offices in Flint and Southfield, M-CARE has more than 5,000 physicians and over 40 hospitals in its 19-county commercial provider network, and over 3,000 physicians and 42 hospitals and health centers in its six-county Medicare network. M-CARE offers HMO and Point of Service as well as Medicaid and Medicare plans.

For more information about M-CARE, visit their Web site at www.mcare.org.
Anatomy and Cell Biology Becomes Cell and Developmental Biology

When the U-M Medical School opened its doors in 1850, a professorship in anatomy was one of the six established professorships comprising the medical faculty. For the next hundred years, the Department of Anatomy at Michigan developed along the traditional lines of teaching and research in gross anatomy, microscopic anatomy, embryology and neuroanatomy. In the process, the department produced some major scholars in the field, including James McMurrich (gross anatomy), George Streeter (embryology), Carl Huber (neuroanatomy), Bradley Patten (embryology), and Elizabeth Crosby (neuroanatomy).

The Department retained its traditional orientation and areas of teaching and research emphasis until the 1970s, when sweeping changes in the biomedical research arena began to pull apart the monolithic bases of traditional preclinical disciplines. One reason for this change was the proliferation of many research-oriented professional societies, such as those of cell biology and the neurosciences, and the increasingly interdisciplinary nature of research in the field. The change in name to the Department of Anatomy and Cell Biology more than 10 years ago was a reflection of those trends.

Although the related disciplines of cell and developmental biology have historical scientific roots in the discipline of anatomy, both have incorporated and come to rely upon techniques of modern molecular biology. This has required a substantial movement away from classical anatomical methods of research. Thus at the end of 1999, the Department of Anatomy and Cell Biology became the Department of Cell and Developmental Biology, its evolution in many respects mirroring the historical changes in the discipline of anatomy throughout the century.

Bruce Carlson, Ph.D., chairs the Department of Cell and Developmental Biology. While Carlson is on sabbatical this year, Michael Welsh, Ph.D., professor of cell and developmental biology, is acting chair. Even as the academic discipline of anatomy has evolved into the interrelated disciplines of cell and developmental biology, the teaching of anatomy remains an integral and essential element of the Medical School curriculum.

To learn more about the Department of Cell and Developmental Biology, visit the department Web site at: www.med.umich.edu/cdb/index.html.

New Peptide Blocks

Medical School scientists have developed a new cancer-inhibiting peptide, or chain of amino acids, that has proven to be effective at preventing metastatic prostate cancer in laboratory rats from spreading to other organs.

Rats treated systemically with the new peptide developed smaller primary tumors and fewer lung metastases than untreated rats and showed no toxic side effects from the treatment. The peptide was effective even if primary tumors were allowed to grow to a large size before surgery and beginning peptide treatment. If future studies show the peptide works as well in humans, it could be the basis for a new approach to cancer therapy.

In an article published in the January 15, 2000, issue of Cancer Research, U-M scientists presented results from an extensive series of experiments which document the peptide’s ability to block cancer cells’ invasive activity and limit the growth and spread of tumors in laboratory rats. Donna L. Livant, Ph.D., assistant professor of cell and developmental biology, created the peptide by changing just one amino acid in a short sequence of a common blood protein called fibronectin, which circulates freely through the body in blood plasma, lymph, serum and interstitial fluid around cells.

When tissue is damaged, fibronectin at the injury site fragments and diffuses outward. Unlike intact fibronectin, which is present everywhere in the body, these fragments bind to fibronectin receptors on cells surrounding damaged tissue, which stimulates them to invade and repair the injury. The downside to this process, according to Livant, is that cancer cells can mutate so that intact fibronectin stimulates them to invade surrounding tissue also. “Cancer is the price we pay for our ability to heal from wounds,” Livant says.

“While intact fibronectin stimulates cancer cells to invade, they can easily reach the blood or lymphatic system and metastasize or spread to other parts of the body.”

In early cell culture studies, Livant discovered that metastatic tumor cells are not invasive unless serum — the fluid component of blood that remains after clotting — is present. “No one realized serum was required, because no one had studied cancer cell invasion in the absence of serum before,” Livant explains. Additional studies showed that plasma fibronectin was the only part of serum required for invasion. Finally, Livant isolated one specific peptide in fibronectin called PHSRN that triggered the invasion process.

Key Component of Bio-Artificial Kidney Moves Concept Closer to Reality: Clinical Trials May Begin Soon

Researchers at the University of Michigan are developing a bio-artificial kidney that uses living kidney cells to duplicate nearly all the functions of a healthy organ. While still in the experimental stage, the bio-artificial kidney could one day provide life-saving treatment for thousands of people with serious kidney disease.

“The kidney is the first human organ for which a mechanical substitute — the kidney dialysis machine — was designed,” says H. David Humes, M.D., professor of internal medicine. “We believe it also will be the first organ to have a fully functioning, implantable substitute created with the new science of tissue engineering.”

Humes and his U-M research team recently completed animal testing of a key component of the bio-artificial kidney, called a Renal Tubule Assist Device. This device is designed for use outside the body to treat acute kidney failure. Each year in the United States, about 190,000 people face this life-threatening condition, in which the kidneys suddenly shut down as a result of infection or injury. Individuals with acute renal failure typically spend at least 10
Spread of Prostate Cancer in Rats

“This PHSRN sequence on fibronectin fragments binds to the fibronectin receptor on many types of epithelial cells and stimulates them to migrate into damaged tissue,” Livant explains. “Metastatic prostate cancer cells also express the fibronectin receptor, but unlike normal cells, invasion is stimulated when their fibronectin receptor encounters the PHSRN sequence of intact fibronectin. This interaction triggers a process that stimulates malignant cells to invade surrounding tissue, as well as blood and lymphatic vessels. Once tumor cells have entered blood and lymphatic vessels, the process also stimulates them to leave the vessels to colonize distant sites.”

Using knowledge of the biochemistry of the fibronectin receptor site, Livant substituted the amino acid cysteine for arginine in the PHSRN sequence. “We speculated that cysteine might interact with the PHSRN-binding pocket of the fibronectin receptor in such a way as to block binding and prevent triggering cancer cell invasion,” she says.

Livant tested this new peptide derivative, which she calls PHSCN, on human and rat prostate cancer cell lines in culture and found it to be a powerful cell invasion inhibitor. She then tested it on laboratory rats injected with 100,000 cells from a naturally occurring, metastatic rat prostate cancer cell line called MAT-LyLu, which can kill a rat in just 25 days. Experimental rats in the study received intravenous injections of the new peptide three times each week; control rats received no treatment.

After 16 days of tumor growth and five PHSCN injections, the mean diameter of tumors in treated rats was less than 0.5 millimeters. The mean diameter of tumors in untreated rats was 1.8 centimeters, a 2,000-times larger volume. Untreated tumors had more than 10 times the blood vessel density found in tumors from treated rats. This is significant, because tumors must have a blood supply to grow.

To more accurately model clinical situations, Livant did not begin intravenous therapy in another group of rats until after surgically removing their large, primary tumors. Rats in this group which first received PHSCN 24 hours after surgery developed 99 percent fewer visible lung metastases and 95 percent fewer microscopic lung micrometastases than rats treated with surgery alone.

The exact mechanism of PHSCN’s anti-cancer activity remains unknown, although Livant has several possible explanations to test in future research. Her goal is to discover why this new peptide is so effective at preventing malignant cells from spreading and how it blocks the growth of blood vessels into the primary tumor.

“Most scientists think cell adhesion is the most important factor in metastasis,” Livant says. “But we believe aberrantly regulated or uncontrolled cell migration will prove to be equally important. There appears to be a biochemical ‘switch’ controlling tumor cell movement, which may be activated by the defective receptor pattern of key receptors on cancer cells. Our goal is to learn how to use this new peptide to turn that switch off.”

Co-authors from the Medical School include R. Kaye Brabec, research associate; Kenneth J. Pienta, M.D., professor of internal medicine and professor of surgery; David L. Allen, Ph.D., post-doctoral research associate; Kotoku Kurachi, Ph.D., professor of human genetics; Sonja Markwart, research associate; and Ameet Upadhyaya, research associate. The U-M holds several patents on the PHSCN peptide related to the diagnosis and treatment of cancer. The study was funded by the March of Dimes, the National Institutes of Health and the U-M Office of the Vice President for Research.

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days in intensive care attached to a hemofiltration unit, which removes toxic waste products from their blood. Even with advanced medical care, more than 50 percent of these patients die before their kidneys can recover.

In a study published in the May, 1999, issue of Nature - Biotechnology, Humes described how the Renal Tubule Assist Device, connected to a standard hemofiltration unit, helped improve kidney function in laboratory animals with acute renal failure.

According to Humes, kidney cells lining hollow fibers in the device reabsorb vital electrolytes, water and glucose filtered out of blood during hemofiltration, in addition to producing other important molecules. Without these substances, the patient cannot fight off infections and maintain a normal fluid balance. In Humes’ study, the device reabsorbed about 50 percent of water and other important molecules, an amount similar to the reabsorption capacity of a normal kidney.

Pending FDA approval, human clinical trials for the Renal Tubule Assist Device in patients with acute kidney failure could begin as early as this fall. Within five years, Humes hopes to develop additional components of the bio-artificial kidney for patients with chronic renal failure — a gradual deterioration of kidney function that currently affects over 300,000 people in the United States, a number growing by about six percent each year.

“Our goal is to bring all the components for a bio-artificial kidney together in one implantable device that will carry out all the functions of a natural kidney,” Humes says. “We hope that one day it will be available as a universal-donor organ. This could eliminate the shortage of kidneys for transplant, end long waiting times for transplant organs, and replace dialysis as a treatment for chronic renal failure.”

Research on the bio-artificial kidney is being conducted at the Department of Veterans Affairs Ann Arbor Healthcare System. Funding to support the research is provided by the National Institutes of Health, the VA Research Service and Nephros.
New Surgical Technique Will Give Baby Jacob Prosthetic Eyes

Toddler Jacob Johnson of Grand Rapids, born with a rare condition called anophthalmia, has no eyes. He suffers from a total absence of ocular soft tissue and has no optic nerves. His eye sockets are also smaller than in a normal infant.

While Jacob’s blindness cannot be overcome, it will be possible to provide him with a normal appearance thanks to a new surgical technique developed by Christine C. Nelson, an ophthalmic plastic surgeon and associate professor in the Department of Ophthalmology and Visual Sciences in the U-M Medical School. Nelson’s surgery will make it possible for Jacob to eventually be fitted with prosthetic eyes. Jacob was referred to Nelson by his Grand Rapids ophthalmologist, Patrick Droste, M.D.

In order to prepare his eye sockets for the eventual prostheses, Nelson transplanted amniotic membrane within the bony structure of Jacob’s two orbits. She then placed two conformers, synthetic “shells,” inside the orbit that will help his sockets to open and expand.

Parents of children who are born with bilateral anophthalmia must deal with the realization that their children will be blind and disfigured. “Dealing with anophthalmia is like a roller coaster,” says Jacob’s mother, Michelle. “Sometimes it just hits you like a ton of bricks. But as time passes and we see how happy Jacob is, the pain lessens.” While blindness cannot be helped, disfigurement can be essentially eliminated by the use of carefully created prosthetic eyes that are produced by an ocularist, a person who combines artistry and engineering. The ocularist works closely with the ophthalmologist and the patient to create life-like artificial eyes that fit and move comfortably within the sockets. They are made of polymethylmethacrylate, the same material that is used to make hard contact lenses.

At two years of age, Jacob is the perfect candidate for a surgical technique developed by Christine C. Nelson, an ophthalmic plastic surgeon and associate professor in the Department of Ophthalmology and Visual Sciences in the U-M Medical School. Nelson’s surgery will make it possible for Jacob to eventually be fitted with prosthetic eyes.

“Dealing with anophthalmia is like a roller coaster,” says Jacob’s mother, Michelle. “Sometimes it just hits you like a ton of bricks. But as time passes and we see how happy Jacob is, the pain lessens.”

Within the past year, a different procedure has been developed that avoids having to take tissue from a patient’s mouth — amniotic membrane transplantation. It was first introduced into the medical literature in the 1940s, but because it was difficult to store and transplant the tissue, it was not very successful until recently.

Amniotic membranes are donated by women who have undergone deliveries by Cesarean section. There are many advantages to using amniotic tissue rather than autologous tissue. Amniotic membrane forms the innermost layer of the fetal membrane. Because fetal membrane has antimicrobial properties, these transplanted membranes have fewer risks of developing postoperative infections. In addition, because there are no “live” cells, there is no risk of rejection or the graft-versus-host-disease that so commonly sabotages allograft transplants. There are, also, large pieces of this tissue available for use. Finally, some physicians believe that amniotic membrane transplants have a cosmetic result that is superior to an autologous graft. “That’s even better,” says Nelson, “is that the wound seems not to hurt quite as much as when mucosal tissue was used. Any doctor who deals with kids knows that the number one priority is to minimize their pain if it’s at all possible.”

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Cochlear Implants: A Modern Hearing Miracle

For little Alivia Anderson, being able to hear the simple songs that toddlers love is a miracle of modern technology. Alivia, now almost two, was born with a malformation of the cochlea—the snail-shaped part of the inner ear that channels vibrations to the auditory nerve and the brain. Instead of a hollow spiral for sound to travel through, her cochleae are incomplete, preventing or limiting the ear-to-brain communication that makes hearing possible. But a cochlear implant, which Alivia received at 13 months of age as a patient in the U-M Cochlear Implant Program, has given her the gift of hearing. She is among the youngest ever to receive a cochlear implant.

The University of Michigan has been a leader in cochlear implants since the program, one of the nation’s first, was established 16 years ago. Since then, 200 adults and 300 children with hearing impairments have received cochlear implants at Michigan. Receiving a cochlear implant at Alivia’s age can be a distinct advantage, says Terry Zwolan, Ph.D., clinical associate professor and assistant research scientist in the department of otolaryngology and director of the U-M Cochlear Implant Program.

“We’re seeing that the sooner a child gets an implant, the sooner we can tap into speech and language development,” she notes. Zwolan and Paul Kileny, Ph.D., professor of otolaryngology, recently completed a study of 102 children with cochlear implants showing that children who received their implants at a younger age did better on word and sentence recognition tests.

Whether children like Alivia will lead normal hearing lives remains to be seen, however. “We have great hopes that these children will lead a normal hearing life,” Zwolan says. “But it’s so recently that we’ve started to do these really young children that only time will tell if we’re able to fully mainstream them into normal hearing classrooms.”

Cochlear implants transform speech and sound into electrical signals that the brain can interpret. They bypass the normal function of the outer ear, hair cells and cochlea, using surgically implanted electrodes and digital signal processors worn on the ear or body to do the work that the damaged or malformed ear structures can’t do.

The first step is capturing sound: A small magnetic microphone on the outside of the head, held in place by an implanted magnet, picks up sounds and sends them to a processor. After the processor’s programming translates the signals, the impulses travel through a coil to a receiver inside the ear. The implant transmits these signals through dozens of electrodes to the auditory nerve and brain, allowing the wearer to detect and understand speech and noise.

The technology of cochlear implants has improved greatly over the past decade. “In the early years, cochlear implants were suitable only for people who had some residual hearing,” says Zwolan. “Now we’re getting such nice results that criteria have expanded to include adults and children with severe to profound hearing loss.”

“Hearing aids and cochlear implants are very different instruments,” says Zwolan. “A hearing aid amplifies normal sound and uses the hearing that a person has to let them process that sound. It’s simply making sounds louder. A cochlear implant replaces the hearing inside the cochlea — that’s why it’s reserved for people who can’t benefit from hearing aids.”

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“NANO” IS “NOW” AT MICHIGAN——

AND JAMES BAKER IS LEADING THE WAY

James Baker and His Colleagues at the Center for Biologic Nanotechnology Are Using Nanoengineering to Fight Infections, Deliver Genes, Destroy Cancer Cells and Completely Alter the Way We Define Medicine.
Imagine tiny plastic balls a zillion times smaller than anything you can think of. Imagine drops of ordinary soybean oil a zillion times smaller than anything you can think of. Imagine the tinier-than-tiny plastic balls and the super-small drops of soybean oil saving your life.

Welcome to the fantastic new world of nanomedicine — a world where doctors, biological scientists, chemical engineers and microchip builders are all speaking the same language, working together in a new and very tiny world of truly cross-disciplinary miracles.

“This is the start of the post-genomics therapeutic revolution,” says James R. Baker Jr., M.D., an allergist and immunologist by training and now director of the new Center for Biologic Nanotechnology he founded at the University of Michigan Medical School in 1998. One of the early believers in nanomedicine, Baker is a convincing proponent of this nascent field. “What we are doing is developing synthetic materials — not biologic molecules — to form tiny structures, or nanodevices, that perform medically important tasks,” he explains. The Center has pioneered research in nanodevices that perform these tiny miracles. These devices are so small that they can slip inside cells without being recognized, but at the same time alter the function of entire organs “where we specifically address problems identified by genetic analysis using tailored therapies that restore normal molecular function.” A number of extremely promising avenues of research are underway in the Center, including several that are advancing into clinical trials.

The whole concept of nanomaterials is difficult for the layperson to understand. By definition, nanomaterials are thousands to millions of times smaller than the cells that make up our bodies, and the ability to make materials this small is a recent accomplishment. (The prefix “nano” actually means “billionth.”) Much of the basic research in these materials came from the semiconductor industry, where the need for smaller circuits and storage devices drove the miniaturization of engineered parts. These studies have led to the assembly of materials, literally atom by atom, into devices like motors and disk drives. Many of the materials Baker works with actually self-assemble into more complex arrays and devices. However, as difficult as it might be to produce these materials, it is even harder to visualize them and assure that the structure is correct. This has spawned a new industry to develop machines that can analyze and image nanodevices. “These materials are so small they cannot be viewed with traditional tools, even electron microscopes,” Baker explains. “We often have to examine them indirectly, as if we are observing a shadow. It makes the whole process very difficult.”

Despite the complexity of the manufacture and analysis of nanostructures, the potential benefits are truly remarkable. “We believe that most human afflictions can be addressed by nanotherapeutics,” Baker says with the confidence of the laboratory-rooted dreamer that he is, and he goes on to illustrate his point. “For example, we have developed non-toxic nanoemulsions that penetrate and kill infectious microbes from the flu virus to anthrax spores. We are using synthetic molecules called dendrimers as machines to detect and characterize cancer cells, then destroy them by selecting and delivering a specific drug or gene therapy. Other work is focused on developing polymers that replace defective cellular proteins to treat genetic disorders, such as cystic fibrosis. The possibilities are truly limitless.” Not that it will be easy. Scientists in nanomedicine are faced with the challenge of not only developing materials, but also adapting and inventing new tools. They have to bring a totally fresh mindset to the treatment of disease. At Michigan they’re doing it with a uniquely integrated multidisciplinary approach, with ongoing collaboration between scientists from materials science, chemistry, pharmacology and medicine. “It is really more of a think tank than a traditional medical research program,” says Baker with a pride he finds hard to conceal.
**Fighting flu with vegetable oil**

The project that has moved the furthest towards practical application — using nanoemulsions of vegetable oil to kill microbes — is perhaps the most dramatic demonstration of the power of nanotechnology. Soybean oil in its standard form does not kill any microbes — in fact quite a few use it for food. But Baker and colleagues Tarek Hamouda, Andrzej Myc, Peter Cao, Amy Shih and Brian Donovan found that if the oil is emulsified with detergents to form nanodrops 400-600 nanometers (nm) across, they act with devastating effect on nearly all pathogens. It is not a chemical action, but a physical one similar to what causes the oil and water in salad dressing to separate. The droplets’ surface tension makes them want to coalesce with other lipid droplets, even though they are stabilized so they cannot coalesce with themselves. The smaller the droplets, the greater the surface tension and the stronger the urge to merge. When the oil droplets contact the membranes of bacteria or enveloped viruses, the surface tension forces a merger with the membrane, blowing it apart and killing the pathogen. “Basically what we have created are nanometer-sized bombs,” says Baker. “But the tissue structure of the cells of humans and other higher organisms prevents them from being disrupted by the droplets.” As a result, the emulsion is entirely safe when applied externally, but a physical one similar to what causes the oil and water in salad dressing to separate. The droplets’ surface tension makes them want to coalesce with other lipid droplets, even though they are stabilized so they cannot coalesce with themselves. The smaller the droplets, the greater the surface tension and the stronger the urge to merge. When the oil droplets contact the membranes of bacteria or enveloped viruses, the surface tension forces a merger with the membrane, blowing it apart and killing the pathogen. “Basically what we have created are nanometer-sized bombs,” says Baker. “But the tissue structure of the cells of humans and other higher organisms prevents them from being disrupted by the droplets.” As a result, the emulsion is entirely safe when applied externally.

Tests in mice have been promising. When mice were given nose drops of the oil nanoemulsions and then exposed to a lethal dose of influenza virus, 75 percent were protected against the disease, while 80 percent of the control mice died. “We think the results in humans will be much better,” explains Hamouda, “because the virus dosages in the experimental animals were far higher than people would be normally exposed to.”

In other experiments, mice were given wounds and then infected with anthrax-like spores. Without treatment, the mice developed large infected sores, similar to cutaneous anthrax. However, mice whose wounds were washed with dilute nanoemulsion solution hours after infection developed essentially no lesion at all.

It was particularly surprising in the nanoemulsion research that bacteria spores, as well as active bacteria, were killed. Spores are especially hard to kill because they have a hard exterior coating rather than a membrane. “The oil emulsion seems to trick the spores, because it looks like food to them,” says Baker. “Once the spores become active and generate a membrane, the emulsion kills them.” This action has been of particular interest to the Defense Advanced Research Projects Agency that has funded some of this work, as it is a promising way to fight the use of anthrax spores in biological warfare.

**Molecular toolboxes**

While the nanoemulsion works as tiny bombs, for most uses more subtle interventions are needed, using a variety of molecular tools. To deliver these tools, the Center’s researchers have been developing a kind of all-purpose molecular toolbox called a dendrimer. Dendrimers are spherical, branching molecules whose structure looks like a very regular bush. They can be made in various diameters, depending on how many shells or branchings they have, and are covered with dozens of molecular “handles” (simple amino groups) that researchers can use to attach a variety of biochemically active molecules. The more shells, the larger number of amino groups — two shells have eight groups, four shells have 16, and so on. Dendrimers can act as nano-sized tool kits, able to deliver the modular tools to the right place, and even as nanomachines, able to use the tools in the right sequence at the right time.

Dendrimers were invented in the late 1970s by Donald Tomalia, now scientific director of the Biologic Nanotechnology Center. “I was looking for a way to make branching molecular structures that imitated the branching of trees,” Tomalia recalls. Initially the molecules were applied for non-biological uses, but in the mid-1990s Tomalia and Baker started to look at possible medical applications, especially for gene therapy. “The great advantage of dendrimers is that they don’t trigger the immune system,” says Lars Pielhier, a biochemist at the Center. The amino groups that cover the molecule are not recognized as foreign by the immune system, unlike the proteins of other vectors such as adenovirus or adeno-associated virus (AAV).

Perhaps the most far-reaching potential application of dendrimers in medicine is for gene and drug delivery. Despite its immense promise, gene therapy has been stymied because of the problem of getting genes into enough cells to make a therapeutic difference. Carrying the gene into the cells as part of a virus, one widely used approach, has the serious disadvantage that the virus, even if benign, triggers an immune...
reaction by the body. If fewer virus particles are used to minimize the immune reaction, not enough cells are altered. Unfortunately, the larger virus dosages required for most applications risk an overwhelming immune response. This can have serious consequences, including fatal reactions, as happened with the highly publicized case of Jesse Gelsinger, a teenager who died following adenovirus gene therapy.

Dendrimers can carry genes into cells without setting off the body’s immune response. “In effect, they are stealth proteins,” says Tomalia. Although they are big enough to carry genetic material, as a virus would, their bushy surfaces lack the complex folds that allow antibodies to bind and alert the body’s immune defense. Instead, they appear as blobs of amino acids. This allows them to carry large amounts of genetic material into the body without undue stress. In addition, the size of a dendrimer, which is adjustable depending on how many shells they have, is in the right range to wrap genetic material around them.

So far, the dendrimer-based delivery or transfection of genes has been demonstrated successfully in vitro and is now being tested intensively in animals. “We’ve found that the efficiency of transfer — the percentage of cells that get working genes — is almost as high as with viruses,” says Baker. But substantial challenges remain. Dendrimers may interfere with genetic transcription, which could prevent the transferred genetic material from functioning within cells. In addition, despite the fact that dendrimer-carried genes did not produce pneumonia when inhaled into animals’ lungs, some of the animals died. This appeared to be the result of the dendrimers pulling fluid into the lungs of the animals. “All new materials will have some toxicity, often unexpected, and require extensive toxicity testing. The important thing is not to take anything for granted,” remarks Baker. So several hurdles will have to be overcome to reach the goal of a general-purpose gene-delivery system using dendrimers.

A cancer-fighting nanomachine

The most ambitious avenue of research in the Center is to adapt the dendrimers’ toolbox capabilities to produce a multi-functional anti-cancer nanodevice. In cancer therapy, the long-sought goal has been a treatment that attacks only the cancer cells and not the healthy cells. Piehler and colleagues are working on ways to do just that — with a dendrimer that locates cancer cells, shows where they are, enters them, confirms they are cancerous, and then kills them.

“Because the dendrimer has so many attachment sites, we can put different chemicals on different sites for a variety of functions,” Piehler points out. In the approach now under development, targeting groups on the...

Lars Piehler, Ph.D., research associate, makes surface-modified dendrimers and biomolecule-dendrimer bioconjugates in order to tailor their biological activity and chemical properties.

Tarek Hamouda, Ph.D., research associate, oversees the development of new anti-microbial nanoemulsions with a broad spectrum of activity against bacteria, bacterial spores, enveloped viruses and fungi. These nanoemulsions will be used against biological warfare agents or for decontamination of food to avoid food-borne pathogens.

Amy Shih develops and manufactures anti-microbial nanoemulsions and tests their activity against spores and vegetative bacteria.

Research Assistant

Amy Shih
One of the great advantages of dendrimers is that you can bind chemicals at precise locations, including in the interior of the molecule, because of the way they are built up from the inside out.

—Donald Tomalia

Dendrimer would attach preferentially to cancer cells rather than healthy ones. A second attached group would be fluorescent, so that the cancer cells can be viewed by surgeons using a weak laser light, or labeled for use with MRI imaging techniques. Once inside the cells, another dendrimer will confirm the “signature” of cancer within the cell, to assure normal cells have not been targeted. Inside another part of the polymer structure, the dendrimers will carry a cytotoxin, such as cisplatin. The poison will be bound up with the dendrimer and be inert until release. Then, release of the poison, which can be triggered by several methods including laser light, kills the cancer cells and gives a readout that the tumor has been killed. In this plan, laser light could be introduced to an internal tumor through a narrow fiber, minimizing surgical damage to healthy tissue.

“One of the great advantages of dendrimers is that you can bind chemicals at precise locations, including in the interior of the molecule, because of the way they are built up from the inside out,” explains Tomalia. Each time a new shell is added to the dendrimer, new functional groups can be attached and then incorporated within the molecule as an additional shell is added. With multiple attachment points, several copies of each functional chemical can be used, increasing the effectiveness of the group.

Tomalia, Piehler and others are pursuing a number of possible strategies for anti-cancer nanomachines. In another version the dendrimers carry boron clusters into the cancer cells. Boron is a heavy absorber of neutrons, so when the tumor is irradiated with a neutron beam, the boron nuclei absorb energy, releasing it as short-range, but deadly, X-rays, killing the cells they are in. But the neutrons pass relatively harmlessly through the healthy cells, producing little damage.

Wrapping up a virus

The Center is also investigating the possibility that dendrimers might be used in novel ways to fight viral infections. A first step in many viral infections occurs when a virus attaches itself to the sialic acid molecules found in the human cell membrane. (Sialic acid is a sugar-coated lipid known as a glycolipid that is a component of human cell membranes.) By coating dendrimers with low concentrations of sialic acid, it is reasoned, one could “fool” the virus into attaching itself to the dendrimers instead of to the cell itself. “We can grow dendrimers to be long and rod-like instead of spherical,” explains Tomalia. “If we cover them with sialic acid, they can wrap themselves around the virus in such a way as to prevent the virus from binding to the cell.” Tomalia and his collaborators have found in laboratory experiments that these multiple-branched, linear dendrimers, which vaguely resemble ivy vines, have been most effective in preventing various strains of flu viruses from binding to cells.

While much work remains to be done in this area, Tomalia and his colleagues at the Center share the heightened enthusiasm that comes from exploring a true frontier, both medical and scientific. They feel confident that the incredibly small world of nanotechnology is opening up a giant new world of medicine, one with possibilities never even dreamed of before now.

Baker, the nano-man of the moment, finds inspiration in a quote from Sir Arthur Conan Doyle: “I think that little things are infinitely more interesting.”
Since then, those first 12 years with the Army in the Washington, D.C., area have evolved into a rather extraordinary saga — one that even the highly inventive Ian Fleming would find in many ways astounding. The plot twists are not minor — and they are not fiction. They involve the real stuff of life and death, but life and death on a dramatic scale that the young Jim Baker could never have envisioned as he contemplated his future career as a doctor. It was his lot to watch hundreds of young men (and older Army generals), and then eventually women, die in the prime of their lives of a disease no one had ever heard of — AIDS. “All my patients died,” he says, and then finds the positive filter he seems to use to help maintain his steady focus on the work ahead: “It was a good experience to go through as a doctor; it defines you as a physician and gives you a healthy respect for nature and how tenuous life can be.”

One of the men he watched die had helped save Baker’s own life when they were part of a group of soldiers on a misguided training exercise in Virginia. Due to a commander’s error, Baker and his fellow trainees had been put in a life-threatening situation in a swamp, and this man had gotten them out. “He was a gutsy guy and the commander’s aide,” Baker says. “He was also exactly my age. Four years later he came down with Kaposi’s sarcoma.”

It was also Baker’s lot, since he was still in the Army Reserves, to be called back to duty for the Gulf War and to then find himself contemplating the possible deaths of thousands of the young men and women sent off to fight a war there. Here the issue was not gunfire but the more silent and invisible killers made from deadly germs and chemicals. “I’d go into a meeting and they’d be talking about 100,000 burn victims or 10,000 inhalation injuries,” he remembers vividly. “It forces you to want to make a difference.”

It’s not that Baker has always sought the monumental personal or professional challenges that have come his way. In the early 1980s he changed his specialty from oncology to immunology just because he couldn’t stand to administer any more of the extreme doses of anti-cancer drugs that were being used in clinical trials at the time. “I watched exceedingly toxic reactions from one particular drug, adriamycin, ➤

“YOUR NUMBER IS 003,” HIS MOTHER TOLD HIM. “YOU’RE GOING TO BE KILLED.”

From AIDS to Desert Storm, Jim Baker’s Life in Medicine Has Not Been an Indifferent One. Perhaps That’s Why Nanomedicine, with its Bold New Death-Defying Promises, Holds So Much Fascination for Him.

by Jane Myers
which was administered into almost every imaginable portal. It was so disturbing I still can’t make red Kool-Aid (the color of the drug) for my daughter,” he says. But such have been the powerful twists of fate to which he has been subjected that a member of his own family was administered the very same drug, in more limited dosages, for breast cancer less than two years ago.

These world events, unpredictable and jolting, on both a professional and a personal scale, have shaped Jim Baker. Part of him is still the teen-ager dazzled by laboratory work, the young man with a mind open to every possibility, always scanning the data (“I like data much better than hypotheses.”) for the new ways of thinking that might be suggested.

Part of him is ancient bearded philosopher. He uses the words “tenuous” and “ephemeral” to describe the precariously delicate nature of our lives with an authority that few people can muster. He does not understand those who worry about not having tenure, those who think that a secure life can be imposed by formal structures. But his ability to distance himself in a thoughtful way from the world of medicine still has its limits. Supporting his immune-deficient patients who have what he calls the “real” problems keeps him firmly grounded in the here and now, and he remains troubled by the death last year of his mother from Graves’ disease, finding it hard to let go of the notion that small corrections in how she was treated could have changed her course.

Part of him is hardened soldier, although Baker suggests with a wry smile that “hard-headed bureaucrat” would be a more apt description. Still, he admits to understanding clearly that victory will go to the side that is best prepared, to the side that has the best resources, to the side that is least naive and most importantly to the side that has the greatest resolve. “I’m not the smartest person in the University of Michigan Health System,” he says, “but I am among the most determined.” These qualities have helped him become a savvy grantsman since arriving at the University in 1989. “I sort of knew where I needed to go” is how he modestly describes his ability to find the funding he needs — now totaling an astounding $20 million in projects currently underway at Michigan.

Baker had been at Michigan only for a year and a half when he was called away from his faculty position to go off to Desert Storm, a wrenching change of venue for someone just getting settled into the academic world. Everything since that time, he says, has felt “like a second chance, an opportunity that I am very lucky to have.”

He is not letting the opportunity go to waste. A serendipitous twist, one not in the harrowing category of so many of Baker’s life turns, happened when he was called in to consult about a patient who, as it turned out, was suffering from a severe drug allergy. The patient, who survived, and the doctor who helped keep him alive established a bond. He was, by chance, a retired Dow Chemical executive. Hearing about Baker’s new work with tiny virus-like lipids and their ability to kill bacteria, he told him about the work of Dow chemist Donald Tomalia, who was just then making something he described as “a new form of matter”—extremely small nanoballs of nylon. The meshing of Baker’s and Tomalia’s ideas was so complementary that the two men were soon working together, and Tomalia joined Baker’s team in the Center for Biologic Nanotechnology at Michigan last year. The nano-scale work being conducted there, where the organic and the synthetic meet on a level not even imaginable a short time ago, is opening up a new world of medicine.

While the work is smaller than small, the extraordinary possibilities for the future are allowing Baker’s visions for the future to grow larger and larger. For “003,” life in the fabulously adventurous world of nanomedicine promises more excitement than Ian Fleming imagined in his most inventive moments.
Total R&D Expenditures for Fiscal Year 1998
University of Michigan: $497 M
UCLA: $447 M
University of Wisconsin: $444 M
University of Washington: $432 M
University of California, Berkeley: $420 M
University of California, San Diego: $419 M
Massachusetts Institute of Technology: $413 M
Johns Hopkins University: $411 M
Stanford University: $410 M
Texas A&M: $394 M
(Source: National Science Foundation; total excludes R&D expenditures for the federal Applied Physics Laboratory at Johns Hopkins University)

Top Ten Academic Institutions Ranked by Article Citations
1. Harvard University
2. Stanford University
3. California Institute of Technology
4. Yale University
5. University of Michigan
6. Massachusetts Institute of Technology
7. University of California, Berkeley
8. University of Washington
9. University of California, Santa Barbara
10. Cornell University

Top-Cited Fields of Study at the U-M in order of frequency of appearances, with Medical School fields noted in boldfaced type: education, psychology, psychiatry, astrophysics, immunology, computer science, pharmacology, economics/business, law, materials science
(Source: Institute for Scientific Information; based on frequency of appearances in 21 scientific fields, 1993-97)

Faculty Serving on National Boards and Commissions:
Harvard University: 95
Massachusetts Institute of Technology: 69
Stanford University: 68
University of California, Berkeley: 57
University of Michigan: 51
University of Washington: 49
Cornell University: 40
University of Wisconsin: 39
University of Colorado, Boulder: 37
UCLA: 36
(Source: Survey conducted by U-M Office of the Vice President for Research)

The National Institutes of Health have nearly doubled funding awards for medical research at the University of Michigan Medical School in the past 11 years. The Medical School now ranks 9th in the nation among all academic research institutions, public and private, and 3rd among public universities in total grants from the NIH.

All information courtesy of the University of Michigan Office of the Vice President for Research.
Muskegon cardiologist Gregory Bernath (M.D. 1980) has been attending the U-M Medical School’s Summer Cardiology Update at the Grand Hotel on Mackinac Island every year for the past nine years. Like most physicians, Bernath receives hundreds of invitations to programs in continuing medical education every year, but most of them don’t hold a lot of appeal, he says. It’s the Summer Cardiology Update that has his loyalty. “I enjoy seeing what’s at the forefront at a major institution like the University of Michigan Medical School,” he says. Michael J. Shea (M.D. 1975, Residency 1982), professor of internal medicine, has directed the CME courses in cardiology for the past 10 years. He estimates that 30 percent of the attendees, like Gregory Bernath, return to the Summer Cardiology Update every year and another 40 percent return every other year.

Keeping physicians up-to-date with what’s happening in their field is the major goal of the Medical School’s programs in continuing medical education, as it has been since the Department of Postgraduate Medicine (now the Department of Medical Education) was founded in 1927 to direct such activities. The success of Michigan’s CME courses is indicated by their sheer number, nearly 100 a year. Last year, 43 of the courses were presented in Ann Arbor at the Towsley Center for Continuing Medical Education (the first building in the nation constructed primarily for continuing medical education), 11 were presented in the Detroit metropolitan area, 18 were presented in conjunction with national meetings in major cities across the U.S., and 20 were presented at resorts like the Grand Hotel.

by Jane Myers with Steve Rosoff
Over the decades a number of factors have expanded the need for continuing medical education at the Medical School. New clinical knowledge has been generated at an increasingly rapid rate for over a century. A trend toward specialization of physicians began during the World War II years with a subsequent enormous push to establish community-based residency programs all over the state of Michigan during the tenure of Dean Furstenberg. A major impetus occurred in 1976, when Michigan became the first state in the nation to require doctors to attend an average of 50 hours of CME instruction per year as a condition for relicensure. (While it benefited his field, Roland “Red” Hiss [M.D. 1957, Residency 1966], chair of the Department of Medical Education since 1982, considers the legislation, which was aimed at reducing malpractice, to have been misguided. “It was a silly idea,” he says, “since most malpractice is not a result of lack of education.”)

Besides keeping physicians current with developments in their fields, CME programs serve an additional function: they provide the U-M Health System with a means of showcasing its physicians and their work and reinforcing the ongoing relationships they have with physicians around the state. Van Harrison, Ph.D., director of the CME program in the Medical School for the past 17 years, indicates a measurable link between physicians’ attendance at CME programs and subsequent referrals to the U-M Health system. “Physicians who have taken our CME courses refer perhaps 50 percent more patients to us than those who haven’t,” he says. “And it works the other way as well: we find that referring physicians who are happy with the care their patients receive at U-M tend to become attendees at our CME courses.”

Michigan’s CME program recently was reaccredited by the Accreditation Council for Continuing Medical Education for a six-year period, putting it in the top seven percent of CME programs nationally.

Thomas Schwenk, M.D., chair of the Department of Family Medicine, has been overseeing CME courses in family medicine for 20 years. “As an academic physician, I feel I have a duty to be a resource to practicing family physicians,” he says. “And I find the one-on-one interaction with them to be enormously rewarding, especially when I can help somebody solve a problem.”

The success of any CME course rests largely on the same factors that always make for great teaching: lively, informed teachers, and material that speaks to the interests and needs of the participants. Harrison describes the most successful CME presenters as “translators,” people who are good at taking the latest in scientific and medical information and putting it into a practical context that relates to the immediate concerns of those in the audience.

Eighteen Years Running and Still Hot:

Pathologists Can’t Seem to Get Enough of Bruce Friedman’s Automated Information Management in the Clinical Laboratory

One of the most popular and longest-running CME courses at Michigan has never attracted interest based on its catchy name, but it doesn’t have to: the Automated Information Management in the Clinical Laboratory course in pathology has been running for 18 years and attracts about 250 registrants every year from all over the world. Run since its inception by Bruce Friedman, M.D., professor of pathology and director of pathology data systems, the course brings together professionals in pathology — physicians, laboratory managers, pathology administrators, technical people — and vendors who pay a fee as exhibitors. Such is the stature of the course, and Friedman’s interest in making it a great resource for professionals in his field, that a number of outside organizations are also invited to take part. This year they included the Clinical Laboratory Management Association, the College of American Pathology, and the American Association of Clinical Chemistry.
There will always be one constant in the continuing education of physicians — the need, first noted by the regents of the University more than a century ago, for doctors “to keep abreast of modern advances in practice.”

Will CME’s traditional person-to-person classroom mode survive the information revolution? Van Harrison thinks it will, at least for a long time. “Most doctors don’t like sitting in front of a computer screen for extended periods of time,” he says. “And a computer can’t substitute for the complex human interaction among physicians that takes place during a class.”

Bernath, the Muskegon cardiologist, agrees. “It’s the one-on-one I especially like,” he says. “Teleconferencing is not the same, and a CD or Web site is not as enjoyable either.”

Hiss thinks it may be time, though, for a new model of continuing medical education, one that might be described as more succinct, more targeted, more specifically aimed at a physician’s specific needs. Hiss has had a lot of time to think about the best way to educate physicians: he’s been involved with education in the Medical School for more than 30 years. “The primary care physician seeing adults probably has between 15 and 20 diagnoses that he or she makes frequently,” Hiss says. He envisions somehow packaging what’s important and new in managing those 15-20 conditions so that the physician can access the information when it is needed. Hiss’s logic is simple: nobody really learns anything, really absorbs anything, until they desperately need to know it.

But how will the physician access the information? Will it be on the Web? And how will it be paid for? Hiss doesn’t have the answers yet, but he and Harrison are both acutely aware of the competition they face from drug companies with their own reasons for wanting to provide physicians with clinical information related to the specific drugs they are producing. As new drugs have been developed at an increased rate, Hiss and Harrison have seen a worrisome increase in the flow of money from drug companies to CME programs.
Reaching Out: The Medical School Has Been Doing It Since the Very Beginning

In his dedication address on March 27, 1969, when the Towsley Center for Continuing Medical Education opened, the late Harry Towsley (M.D. 1931, Residency 1934) noted that the history of continuing medical education at Michigan was a long one, going all the way back to the School's beginnings. Towsley, chair of what was then called the Department of Postgraduate Medicine, referred to what he called “a monumental historical document” by Victor Vaughan, A Doctor’s Memories. In A Doctor’s Memories, Vaughan had written that Moses Gunn, professor of anatomy and surgery, announced to the physicians of the state in the 1850s that “…the forenoons of Wednesday and Saturday would be devoted to consultations with them over their difficult cases. Emergency cases would be seen at any time,” and that “there would be no charge to either the doctors or their patients so far as these consultations were conducted in the presence of the students.” A resolution by the regents in 1878 stated in a more formal way the School’s responsibility to reach out to physicians in the state, stating that “any graduate of any respectable and recognized medical college who may desire to attend the medical courses in this University be permitted such attendance on the payment of the usual matriculation fee only.”

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James D. Bruce, a Saginaw physician who became a member of the Medical School faculty in the 1920s and was chair of the Department of Postgraduate Medicine from its founding in 1927 until his retirement in 1942, contributed a chapter on postgraduate medical education to Wilfred B. Shaw’s The University of Michigan, an Encyclopedic Survey (U-M Press, 1951). He noted that the regents in 1892 again authorized the faculty of the Department of Medicine and Surgery to admit physicians and “in a forward-looking policy, provided an opportunity in this country for the medical graduate to keep abreast of modern advances in practice,” offering to them not only “already established courses, the subject matter of which has been greatly increased since their graduation,” but also special courses in “hygiene, bacteriology, electrotherapeutics, microscopic and gross pathology, physiology, histology, chemistry, and therapeutics.” The courses, Bruce noted, were given “once a year, in the summer, and were usually six weeks in length.”

Van Harrison, the head of continuing medical education in the Medical School for the past 17 years, attributes Michigan’s leadership in this area to three factors, including the School’s longstanding mandate to reach out to the state’s physicians. He also credits the program’s success to the presence of a large number of physicians in a single institution unified by their teaching mission, and a series of directors who, by virtue of their mostly lengthy tenures, have been able to build extensive relationships with physicians throughout the state of Michigan.

Harrison was involved in the early 1990s in helping to develop national guidelines for commercial involvement in CME activities, but both he and Hiss remain highly concerned about commercial influences on physician learning. But they also see the advantage: reduced costs for those attending. Harrison estimates that an average day of CME, because of various subsidies, costs the physician attendee about $130, compared to an average $980 per day for attendance in the U-M Business School’s executive education programs. CME at Michigan has its high-priced programs, too, however: the vascular intervention course, with attendance limited to six physicians, costs $2,000 for four days of training.

The larger questions that have challenged people like Red Hiss and Van Harrison for years remain: How does a physician keep on learning? What separates those who do from those who don’t? What works best? What works at all? And how do you know when learning has taken place? After all these years, Hiss remains modestly insecure about the effects of his work. “Measuring physician behavior is difficult if you don’t have access to their records to see what they did,” he says. “There’s no way to know if something they learned here subsequently changed their behavior.” Harrison, though, is optimistic that research on the effects of various kinds of physician education may become easier as clinical and administrative databases are linked with one another and with third-party payers.

Whatever answers may present themselves, there will always be one constant in the continuing education of physicians — the need, first noted by the regents of the University more than a century ago, for doctors “to keep abreast of modern advances in practice.”

For more information, visit the Web site of the Department of Medical Education at http://www.med.umich.edu/meded/.
In the past two issues of Medicine at Michigan, this series on the history of the deans of the University of Michigan Medical School has commemorated the lives and medical careers of deans from the earliest days of the Medical School through the tenure of Albert C. Furstenberg. In the conclusion of this three-part series, the leadership of the deans over the past four decades is highlighted. Although their legacies are fresher in the minds of the University community, it is hoped that acknowledgment of their contributions within the long-term perspective of the Medical School’s development will help us not only understand the past, but also shed light on the present and the future.

When Albert C. Furstenberg retired in 1959 after 24 years as dean, William N. Hubbard Jr. was appointed to succeed him. Hubbard graduated from Columbia University in 1942 and earned his M.D. at New York University in 1944. He planned to return to his home state of North Carolina and start a general practice, but the opportunities he found in New York changed his plans. He assumed the chief residency at Bellevue Hospital in New York City in 1950, which included responsibilities in research, teaching and administration at New York University. Hubbard, who specialized in internal medicine, became part-time assistant dean at NYU, and eventually full-time dean. Even though his work was becoming more and more distant from clinical practice, he always remembered the needs of the patient. He explained in 1965:

I changed from general practice to internal medicine to be more effective in patient care. Then I went into teaching and research so that I could have a wider influence on care. I turned to administration to enhance teaching and research. I still find the greatest satisfaction in the relation between what I do and the care of the patient, even though it is increasingly indirect. [University of Michigan Medical Center Journal, 1965; v. 31, p. 241.]

Hubbard joined the University of Michigan in 1959 as professor of internal medicine and dean of the Medical School. At age 39, he was one of the youngest in the nation to hold such a position. He was the Medical School’s first full-time dean — without private practice and departmental administration responsibilities — and helped to redefine the role. Hubbard reorganized policy and practices at Michigan, emphasizing the importance of translating medical research advances into educational programs for students and practicing physicians. He was successful in involving the entire faculty in the affairs of the school and aimed to provide leadership that would help students and faculty work more effectively. Hubbard also directed a $33.5 million program to remodel existing buildings and construct new ones at the Medical School.
In 1969, the U-M regents made Hubbard the first dean of the Medical School to also have responsibility for directing the Medical Center. The logic behind this administrative restructuring was that teaching, patient care and research are inseparable, and the chief administrator should be responsible for the intersection of hospital and academic functions. A primary objective of this new position was to increase and efficiently utilize financial support for the Medical Center’s activities.

Within a year Hubbard had resigned, becoming vice president of the Upjohn Company in April 1970. Prominent in medical affairs at the national level, he often served as a consultant to government officials regarding health issues. Over the course of his academic and corporate careers, he served on the executive council of the Association of American Medical Colleges and as chairman of the board of regents of the National Library of Medicine. Hubbard’s energy, experience and interest in the problems of students and faculty were great contributions to the University of Michigan.

Following Hubbard’s resignation, John A. Gronvall was appointed dean of the Medical School and director of the Medical Center. Gronvall had joined the Medical School in the summer of 1968 as associate professor of pathology and associate dean of the Medical School. He became a full professor in 1972.

Gronvall led the Medical Center through a period of growth during his tenure as dean and director from 1970 to 1982. With support from the federal government, enrollment at the Medical School was increased to record levels. In 1978, the biggest year, the Medical School graduated 250 new physicians. Women entered the Medical School in ever greater numbers; by 1980 the enrollment was 30 percent female. The Inteflex program was started, in which 50 select incoming freshman could integrate their undergraduate and medical studies in a period of six years. There was new clinical emphasis on family practice and patient education. Under Gronvall’s deanship, recruitment of top-level faculty to the Medical School was increased as was involvement of faculty in patient care activities. Support for research in the Medical School was also increased. The Medical Library moved to the new A. Alfred Taubman Medical Library on Catherine Street in 1981, and approval was granted and construction started on the Replacement Hospital Project. Gronvall also helped obtain approval for the construction of a Medical Science Research Building (MSRB I).

John Gronvall was educated at the University of Minnesota, where he received his B.A. in 1953, his B.S in 1954, and his M.D. in 1956. He held an internship at Minneapolis General Hospital and went on to the University of Mississippi to become associate professor of pathology, associate dean of the Medical School, and associate director of the Medical Center. Gronvall also served as a consultant to medical divisions of the federal Department of Health, Education and Welfare and was frequently invited to speak on medical center administration and medical education at various national meetings. His published articles included “The Medical School Curriculum,” which he wrote with William Hubbard Jr. and George R. DeMuth for the Journal of Medical Education in 1970. In 1983 Gronvall resigned to take the position of deputy chief medical director at the Veterans Administration in Washington, D.C. He died suddenly in 1990 at age 59.

Following Gronvall’s tenure as dean, the position of a combined dean of the Medical School and director of the Medical Center was eliminated. A new position, vice provost for medical affairs, was created in 1983 to provide direct oversight to the dean of the Medical School and the director of the hospital; George Zuidema, M.D., was appointed to the new position. At this time, Peter A. Ward was appointed interim dean of the Medical School.
Ward, who earned his B.S. (1958) and M.D. (1960) degrees from the U-M, became professor and chair of the Department of Pathology at the University of Michigan in 1980, helping to strengthen the Department’s academic research programs. As Dean Gronvall had said of Ward, “His work has provided the scientific community with innovative techniques and basic information which have implications for a wide range of disciplines and disease processes.” [Hospital Star, December 1979.]

Ward was interim dean for three years, during which time he managed several important projects at the Medical School. He helped develop a process to reduce the size of the entering medical class by 30 students, necessary because of the changing patient population and patterns of health care delivery. The Neidhardt report on medical education, which would serve as a blueprint for curricular change, was approved by the executive committee. Under Ward, efforts were made to maintain the diversity of the class, including the implementation of the AIMED Program, a curricular innovation to support educationally underprivileged students. Ward also provided leadership during a Supreme Court case involving the University and an Inteflex student, which affirmed the right of professional educators to make academic decisions free from interference from the courts and determined that universities do not have a contract to guarantee the success of students. In addition, work on MSRB I continued, and construction was begun on MSRB II. Construction also continued on the new University Hospital and the Taubman Health Care Center. The Medical School received designation as one of a dozen Howard Hughes Medical Institute sites in the nation, and plans were made to locate it in MSRB I.

Ward returned to his responsibilities as chair of the Department of Pathology in 1985 and remains in that position today. He has conducted research on mediators and regulators of the inflammatory response, with special interest in cytokines, complement and protease inhibitors. He has also served on many national review boards and as president of the U.S. Academy of Pathology. Joseph E. Johnson III was appointed dean in May of 1985. Johnson had earned two degrees from Vanderbilt University, a B.A. in 1949 and an M.D. in 1953. In 1959 he joined the Medical School faculty and from 1969 to 1986 was director of the Rackham Arthritis Research Unit. In 1975 Bole became chief of the Rheumatology Division in the Department of Internal Medicine, a position which he held until 1986 when he joined the Dean’s Office. He served as the Medical School’s associate dean for clinical affairs, then as senior associate dean and executive associate dean until 1990.

During the period that Johnson was dean of the U-M Medical School, there were significant changes in medical education throughout the nation, with revisions to the medical school curriculum. For example, plans were made to put more emphasis on the importance of preventive care and to improve teaching in ambulatory care. The primary thrust of curricular reform, however, was to foster habits of critical thought and independent learning from premedical work through graduation. Johnson recruited eight new department chairs, and 11 endowed or collegiate chairs were established during his tenure. Research funding from external sources more than doubled, and the physical resources expanded as well.

Johnson worked to enhance the Medical Center. He was dean when the new University Hospital and A. Alfred Taubman Center opened in 1986. Several multidisciplinary “Centers of Excellence” were designated by the regents, including cancer and geriatrics centers. The Howard Hughes Medical Institute at U-M grew to 10 investigators, improving Michigan’s strength in molecular genetics. In addition, MSRB I was opened in 1986 and MSRB II in 1989, with planning begun for MSRB III. After completing his service as dean on June 30, 1990, Johnson remained on the faculty as professor of internal medicine.

Subsequently, Giles G. Bole was appointed dean. Bole spent nearly his entire academic career at the University of Michigan, earning his B.S. in 1949 and his M.D. in 1953. In 1959 he joined the Medical School faculty and from 1969 to 1986 was director of the Rackham Arthritis Research Unit. In 1975 Bole became chief of the Rheumatology Division in the Department of Internal Medicine, a position which he held until 1986 when he joined the Dean’s Office. He served as the Medical School’s associate dean for clinical affairs, then as senior associate dean and executive associate dean until 1990.

In 1990 Bole was appointed interim dean of the Medical School and was formally named dean in July 1991. The Medical School was recognized in several notable ways during Bole’s tenure, receiving a Robert Wood Johnson Clinical Scholars Program Grant and being redesignated one of the top members of the NIH Medical Science Training Program. The School was also refunded with the largest General Clinical Research Grant provided by the National Institutes of Health. The Medical
School moved up from sixteenth to ninth in the *U.S. News and World Report* rankings of research-intensive medical schools, and in 1996 it ranked ninth in total research funding from the National Institutes of Health. J. Bernard Machen, University provost, said, “Giles has an unusual grasp of the complexities of health care and has brought tremendous energy and leadership to his position.” [*University Record*, July 9, 1996.]

Bole also oversaw the appointment of 12 department chairs, as well as the appointment of the director of the NIH General Clinical Research Center and co-directors of the Mental Health Research Institute. In 1992, the School started using a radically new curriculum, and, to better serve the students, class size was reduced from 207 to 170. Near the end of Bole’s tenure as dean, the Medical School commissioned a cultural diversity audit, helping the School to critically assess itself and develop new ways of integrating the values associated with diversity into the School’s culture.

Bole’s leadership brought about improvement and growth in the physical plant of the Medical School and the entire University of Michigan Medical Center. Medical Science Buildings III was built, and the older Medical Science Buildings I and II were renovated and remodeled. The Medical School administration worked with the Michigan delegation in Congress to obtain funding for remodeling and reconstruction of the Ann Arbor VA Medical Center. Two other major construction projects were started: the Cancer and Geriatrics Centers building and the East Ann Arbor Health Center, a new ambulatory primary care facility. The Faculty Group Practice was organized in 1996.

In July 1996, Bole announced his intention to step down from the deanship and return to the faculty; he was named dean emeritus of the Medical School shortly thereafter. Upon Bole’s resignation, Homer A. Neal, interim president of the University, said, “His recent efforts have seen the Medical School respond to and meet the challenges of a rapidly changing health care environment. I know that I join his many colleagues and friends in thanking him for his years of service and dedication to the University community.” [*University Record*, July 9, 1996.]

Upon Bole’s resignation, A. Lorris Betz was appointed interim dean. Betz earned his bachelor’s, medical and graduate degrees at the University of Wisconsin, and did his residency in pediatrics at the University of California at San Francisco. He completed a research fellowship in pediatric neurology, also studying mechanisms of brain injury and edema formation in stroke and intracerebral hemorrhage, central control of blood pressure, mechanisms of cerebrospinal fluid production, and gene therapy to the central nervous system.

Betz had been appointed to the faculty of the University of Michigan in 1979 as assistant professor in the Departments of Pediatrics and Communicable Diseases and Neurology. In 1987 he was appointed as full professor in the Departments of Pediatrics and Communicable Diseases, Neurology and Surgery, and he became the director of the Crosby Neurosurgical Research Laboratories. He was named the first Crosby-Kahn Collegiate Professor of Neurosurgery and Neuroanatomy. From 1989 to 1993, Betz was associate chair for research in the Department of Pediatrics and Communicable Diseases.

Betz began his administrative career in 1985 as director of the Office of Research Programs in the Department of Pediatrics and Communicable Diseases. From 1993 to 1994 he was associate dean for faculty affairs, and he served as senior associate dean for academic affairs and executive associate dean before being appointed interim dean of the Medical School on August 1, 1996. J. Bernard Machen, provost and executive vice president for academic affairs, said at the time,

Lorris Betz is not only a respected member of the Medical School faculty, but he is experienced as a strong administrator. We are fortunate that he has agreed to serve in an interim role for the University as dean, and I look forward to working even more closely with him. He has been involved in all aspects of the administration of the Medical School, and I am confident that he will help us continue our leadership role as one of the top schools in the country. [*University Record*, July 9, 1996.]

Other transitions in the U-M Health System occurred as well. After the departure of George Zuidema in the mid-1990s, Rhetaugh G. Dumas, former dean of the School of Nursing, briefly held the position of vice provost for health affairs, reporting to the University provost. In 1997, review by the regents of the Health System’s executive structure resulted in the creation of the position of executive vice president for medical affairs, a position which continues to provide oversight to the dean of the Medical School and the director of the University hospitals while reporting directly to the University president. In September 1997, Gilbert S. Omenn, M.D., Ph.D., was appointed by the regents as the University’s first executive vice president for medical affairs. Omenn came from the University of Washington in Seattle where he had been dean of the School of Public Health and Community Medicine and professor of medicine (medical genetics) and environmental health.
During Lorris Betz’s service as interim dean, several new programs were started at the Medical School. The Biological Sciences Scholars Program was started to help recruit outstanding junior faculty in an institution-wide manner, and the Program in Biomedical Sciences was established to oversee the recruitment and admission of all Medical School graduate students. Also, the “white coat ceremony” was inaugurated for incoming medical students. After serving for more than two years as interim dean, Betz returned to the faculty; shortly thereafter, he was appointed senior vice president for health sciences and dean of the School of Medicine at the University of Utah in Salt Lake City.

Following Betz’s departure, Allen S. Lichter was appointed interim dean in December 1998. A native of Detroit, he earned two degrees at the University of Michigan: a B.S. in 1968 and an M.D. in 1972. He served his internship at St. Joseph Hospital in Denver, and completed his residency in radiation oncology at the University of California in San Francisco in 1976. Lichter went on to become the director of the radiation therapy section of the National Cancer Institute’s Radiation Oncology section, as well as a faculty member at the Johns Hopkins University School of Medicine.

Lichter is a professor of radiation oncology and served as the first chair of the department from 1984 to 1997. His clinical interests are in breast cancer, lymphoma and eye tumors. From 1984 to 1991, Lichter was director of the University of Michigan developed new three-dimensional X-ray imaging technology that allows physicians to guide radiation more directly to tumors, reducing damage to healthy tissue. He is a pioneer in three-dimensional treatment planning and conformal radiation therapy, especially for breast cancer. This technology is now widely used throughout the U.S.

On April 16, 1999, Gilbert S. Omenn announced that Interim Dean Allen Lichter would be recommended to the regents as dean of the Medical School. Lichter’s appointment as dean became effective May 1, 1999. The Dean’s Search Advisory Committee described Lichter as a “surpassing choice.”

At the time of Lichter’s appointment Omenn said about the new dean:

He is a wonderfully able, positive, and forward-looking individual with high values, keen interest in all of the missions of the Medical School and a commitment to diversity. I look forward to working with him as a key member of our Health System leadership team for many years to come.

The Medical School’s fifteenth dean, Allen S. Lichter follows his many able predecessors and becomes part of a long legacy of distinguished leadership in academic medicine in America.

Teresa Black, an Ann Arbor native, is a recent graduate, in anthropology, of New York University.
The chain ladder, revolutionizing our understanding of life insurance, was developed in the 1950s, demonstrating its importance in actuarial science.

Concurrent with an ambitious building program to build a new medical school, the University of Cambridge in England, the S.S. Kresge Foundation dedicated its new medical school building. This was a much-needed resource for the university, anticipating the explosive growth of medical research.

Changes included enlarging and refitting existing facilities and adding new ones, such as a new Outpatient Clinic Building, dedicated to improving medical care. The Medical School curriculum was expanded to include 24-hour emergency services.

Nobel Prize laureates contributed to the school's growth, including James Watson, pioneer use of radioactive treatments and James L. Wilson, at U-M Hospital.

Projects were underway in the U-M Medical School, the first in the U.S., and its contributions to medicine were recognized. The polio vaccine was deemed safe, effective, and potent, funded in part by the Buhl Foundation.

The Multi-Organ Transplant Program was established, funded in part by the Buhl Foundation, and was one of the nation's first facilities devoted solely to transplant surgery. It is the nation's first to open a center for research on human genetics, the Lawrence D. Buhl Center for Research on Human Genetics, in 1963.

The Lawrence D. Buhl Center for Research on Human Genetics, dedicated in 1966, deems the facility "one of the best equipped in the world in the field of human genetics.

Several projects descended from infectious disease research, including the Section of Thoracic Surgery, and the Department of Pharmacology, funded by the David Dickinson Trust fund. Its efforts are devoted to the treatment of hypertension, as well as malignant diseases with traditional radiation.

James W. Hubbard Jr. is appointed the first full-time director of the U-M Medical School, the first in the U.S., and was one of the first communists from all walks of life to be appointed chair. The Section of Thoracic Surgery, and the Department of Pharmacology, funded by the David Dickinson Trust fund. Its efforts are devoted to the treatment of hypertension, as well as malignant diseases with traditional radiation.

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The Lawrence D. Buhl Center for Research on Human Genetics, dedicated in 1966, deems the facility "one of the best equipped in the world in the field of human genetics.

Several projects descended from infectious disease research, including the Section of Thoracic Surgery, and the Department of Pharmacology, funded by the David Dickinson Trust fund. Its efforts are devoted to the treatment of hypertension, as well as malignant diseases with traditional radiation.

James W. Hubbard Jr. is appointed the first full-time director of the U-M Medical School, the first in the U.S., and was one of the first communists from all walks of life to be appointed chair. The Section of Thoracic Surgery, and the Department of Pharmacology, funded by the David Dickinson Trust fund. Its efforts are devoted to the treatment of hypertension, as well as malignant diseases with traditional radiation.

The multi-organ transplant program was established, funded in part by the Buhl Foundation, and was one of the nation's first facilities devoted solely to transplant surgery. It is the nation's first to open a center for research on human genetics, the Lawrence D. Buhl Center for Research on Human Genetics, in 1963.
Since its earliest days, the University of Michigan and its Medical School have benefited from the generosity of those individuals, foundations and corporations who have chosen to invest in the future of the institution by making private gifts. The Detroit Observatory, a historical landmark visible from many points on the medical campus, symbolizes not only the beginnings of the University as a major research institution, something clearly envisioned by President Henry Tappan, but the beginnings of private philanthropy as well. The Observatory’s name derives from the fact that individuals living in Detroit provided most of the money for the construction of the Observatory. Another early gift from New York state physician Elizabeth Bates to the Medical School was the first to establish an endowed professorship anywhere in the University.

In the second half of the 20th century, a number of significant gifts have made possible major construction at key points in the history of the Medical School. In chronological order and covering roughly the years of this issue’s timeline, they include gifts from:

The James S. and Lynelle A. Holden Fund

James Stansbury Holden, an early real estate developer in the city of Detroit, and his wife, Lynelle, through their private foundation, used much of their fortune to improve the quality of children’s lives, both during their lifetimes in Detroit and after their deaths in the 1960s. The Holdens were perhaps best known during their lifetimes for their many gifts to the Detroit Zoological Park. The Holden Fund’s gifts to the University of Michigan, totaling nearly $4 million, have also been largely designed to benefit children, beginning with a gift to establish the James and Lynelle Holden Perinatal Hospital in 1972 with a gift of $1.6 million. More recent gifts have included a gift of $1 million to support the James and Lynelle Holden Neonatal Research Laboratories. A gift of $200,000 from the Fund benefited the Center for Communications Disorders at the Kresge Hearing Research Institute.

The W.K. Kellogg Foundation

Will Keith Kellogg, without quite knowing it, launched a lucrative new industry in 1894 when he invented dried wheat flakes for the patients at his brother’s Battle Creek Sanitarium. Before long, W.K., as he was known, had also developed a highly marketable corn flake, followed not too many years after by Rice Krispies and All-Bran. His surprising marketing savvy, in combination with his great products, soon made him a very wealthy man. In 1930 he established a philanthropic foundation in his name with more than $66 million in Kellogg Company stock. Today the Kellogg Foundation ranks among the world’s largest private foundations.

Over the years the W.K. Kellogg Foundation has given more than $70 million in gifts to the University of Michigan to support teaching and research in such areas as public health, medicine, dentistry and nursing. One of the Kellogg Foundation’s largest single gifts to the University of Michigan, a $4 million gift, was made in the early 1980s to establish what is now known as the Kellogg Eye Center. One of the very first gifts made to the University by the Kellogg Foundation, in the early 1930s, was a gift to the Medical School to benefit the Department of Postgraduate Medicine, today known as the Department of Medical Education.

The Charles Stewart Mott Foundation

An early participant in the automotive revolution, Charles Stewart Mott’s success began in 1900 when he transformed the family business in Utica, New York, from the manufacture of wire wheels to the manufacture of axles. Soon he had moved the business to Flint to produce axles for the Buick Motor Company. In 1916 he became a vice president for General Motors. By 1926 his success had allowed him to found the Charles Stewart Mott Foundation, the central theme of which over its many years of existence has been the welfare of children. The Mott Foundation provided $6.5 million in the mid-1960s to help construct C.S. Mott Children’s Hospital, a $8.5 million project that opened in 1969.
In the otherwise quiet minutes before midnight on September 19, 1968, a surgical suite in Old Main bustled with activity that was about to make Michigan history. In a five-and-a-half-hour operation, Philip T. Barnum, a 49-year-old state employee from Kalamazoo dying of irreversible heart failure, received the heart of a 37-year-old Jackson prison inmate who had died of a stroke. It was the first human heart transplant performed in the state of Michigan.

Barnum lived only 15 months longer, but that extension of his life afforded him the opportunity to see his daughter graduate from high school and his son marry. That Barnum’s death on December 10, 1969, was due to infection and not rejection of his transplanted heart afforded hope and knowledge that even an organ so dynamic, complex, and imbued with connotation as the human heart could be replaced.

September, 1968
by David Stringer

Ed Bove’s exceptional abilities as a surgeon bring children and their grateful parents from all around the country and the world to Ann Arbor.

He’s pictured here in one of his trademark teddy-bear scrub hats. The custom hats, in a variety of patterns, are made for him and others by Betsy Hunsche, a medical assistant in pre-op at Mott Children’s Hospital.

Rebuilding Babies’

For pioneering pediatric cardiac surgeon Ed Bove, it’s a life rich in joy and triumph, but sorrow and defeat are part of what he lives with, too
Ed Bove’s first clinical rotation as a student at Albany Medical College in New York State in the early 1970s was in pediatric cardiology, where he saw his first “blue baby” — a child suffering from a heart defect known as the tetralogy of Fallot. The child’s dire condition made a strong impression on the young student, who soon after came upon the very same child on his next rotation in heart surgery. Bove had been leaning toward surgery as a specialty, but what he saw that day brought clarity to what had been only a tentative notion. “I scrubbed. I watched the surgery. I sat with him in the intensive care unit,” he recalls. “He was no longer blue! I was so overwhelmed, and I said, ‘That’s it — that’s what I want to do!'”

Bove (pronounced bo-vay) did his undergraduate work at the College of the Holy Cross in Worcester, Massachusetts. After graduating from medical school in Albany in 1972, he came to Michigan for his residency in general surgery and thoracic surgery, largely at the urging of the late Ralph Alley, M.D., then chief of thoracic surgery at Albany, who had taken Bove under his wing.

“At first he had seemed gruff and unapproachable,” Bove recalls. “But at the end of rounds one day, I got up the nerve to speak with him, and it was the beginning of a long friendship. He was a wonderful mentor to me over many years.” Alley suggested to Bove that he apply for his residency at either Duke, Massachusetts General, or the University of Michigan, and he tipped off the U-M interviewer to be sure to speak with Bove personally. Bove completed his residency at Michigan in 1980, and joined the Hospital for Sick Children in London, England, as a senior registrar, the equivalent of a fellow, for additional training in complex congenital heart surgery. Before returning to Michigan in 1985, he practiced at the Health Science Center of the State University of New York in Syracuse for five years.

Bove’s experiences in medical school and during his residency at Michigan pointed him toward what is currently one of his specialties: hypoplastic left heart syndrome, where babies are born with the left side of the heart too small to be able to pump blood. “Going back a decade or so, death from this congenital defect was certain,” he says. “All that a physician could do was diagnose the illness and then inform the parents that their child was going to die.”

Bove, who first became interested in hypoplastic left heart syndrome in the early 1980s, soon experienced firsthand the terrible sense of defeat that came from watching these babies die. His first six operations to repair hypoplastic left heart syndrome were a failure. But with the seventh, the baby gained an additional two years of life. After the child’s death, his mother wrote Bove a letter of gratitude, thanking him for giving her two wonderful years and expressing the hope that he would continue to try to save other children.

It is his many subsequent successes — and the heart-wrenching appreciation he receives from even those parents whose children cannot be saved — that keeps Bove going. But the pain of the many failures is as acute as ever. “Sadly,” he says, “we lose some. It upsets me as much today as ever — just ask my wife. The high risk — it wears on you. Some days I’m high as the top of the world, but other days I’m deflated lower than the curb on the road.”

Today Bove is able to achieve an 85-85 percent success rate for hypoplastic left heart syndrome, a success rate that most of his admirers around the world would call phenomenal, but which he describes in characteristically modest fashion as “fairly good results.” The 15-20 percent of his patients that he loses is the dark reminder of how many more successes he would like to have.

The surgery Bove performs was once controversial. Heart surgery itself, he notes, has a history of less than 50 years and began in controversy in the 1950s. The questions raised about early heart surgery on adults were also asked when Bove began his high-risk surgery on babies, with many wondering how long the children would survive and what kind of lives they would have. Some worried that parents would be put through too much agony, only to have their hopes dashed.

Bove recalls giving a talk in London in the early 1990s when he was the only one at the meeting advocating the technique. With more and more successes, however, the controversy has died down, and Bove can now report that the procedure he performs for hypoplastic left heart syndrome is “routinely done.” He himself, however, is not viewed as “routine” by any of his admiring colleagues around the world, many of whom refer their most desperate patients to him because of his reputation and the pioneering work he has done in this field.

One such admirer is Dug Thiene, M.D., a pediatric cardiologist in Umea, Sweden, who came to Ann Arbor last year to present the case of a 12-year-old patient to Bove. Thiene had been to Ann Arbor in the past and had become a colleague and friend of Achiau Ludomirsky, M.D., associate professor of pediatrics and communicable diseases, through whom he met Bove.

Thiene’s patient, Jens Stalnacke, who lives above the Arctic Circle in the town of Kiruna, where his parents, Anita and Thomas, have a reindeer farm, had undergone his first heart surgery to replace a valve when he was three months old and underwent four subsequent surgeries...
Ed Bove’s files are filled with heartfelt notes from the grateful parents of the babies whose lives he has saved, often accompanied by photos offering adorable proof of the babies’ good health and happy spirits. Pictured here are (clockwise from top) Brynn Barckholtz of Cary, Illinois; Zachary Tucker of Colleyville, Texas; Joseph Gerardi of Fayetteville, New York; and Mary Margaret Davis of Brentwood, Tennessee.

Bove’s wonder babies also have their own websites: grateful father Russ Gillespie, who lives near Charlotte, North Carolina, has built a website to tell the happy tale of his son Joshua’s successful surgery in Ann Arbor to repair his congenital heart defect, the hypoplastic left heart syndrome for which Ed Bove is especially noted. The site can be visited at www.geocities.com/Heartland/8395.

“...BE SURE THAT WE WILL ALWAYS REMEMBER YOU…”

July 19, 1999
Dear Dr. Bove,
I know you’re really busy, so I’ll keep it short.
Enclosed is a picture of my son Benjamin (Benny) Brown, who will be two years old next week. You operated on him when he was nine days old and again when he was five months old.

I just wanted to say thanks for saving his life. Words can’t explain how grateful I am to you and all the wonderful people at the U of M. Instead of grieving his birthday (as we would be doing if he hadn’t received such excellent care) we are celebrating!

Benny’s turning into a great little kid! He’s totally fearless and tries everything his four-year-old brother does. He’s got a great sense of humor. He loves teenage girls and rubber snakes. He has the most beautiful strawberry-blonde hair. He sucks his fingers while he’s sleeping. Thank you for giving us the opportunity to get to know him.

I pray almost every day for blessings for you and the hospital. I’m so thankful God gave you the talent and courage to help such tiny people. Benny is such a blessing to me and so many others. He has taught us so much.

We know Benny has a fragile heart but we are letting him live his life just like everyone else. We’re setting limits on his behavior and raising him to be a kind and loving person. He’s not a cardiac cripple.

As we celebrate his second birthday we want to take time to remember all you have done. May God bless you.

Sincerely,
Brenda Brown

This letter from Benny Brown’s mother, Brenda Brown, of Buchanan, Michigan (just north of South Bend, Indiana) is typical of the many that Ed Bove receives. Benny underwent his third surgery with Bove in April.
surgeries. In the most recent of those surgeries, Jens’ aorta had been replaced with a prosthetic graft and the two coronary arteries had been sutured into this graft. The complications deriving from this surgery, including extreme scarring of the coronary arteries and their virtual invisibility from outside the heart, had made Jens’ surgeons in Sweden unwilling to attempt further operations on his heart. Yet his physical growth over many years necessitated his receiving a new graft. The challenge for Bove was to remove the coronary arteries and reattach them to the new graft without injuring them, a difficult procedure under the best of circumstances.

The only option Thiene and his colleagues in Sweden had seen was a heart transplant, which is why they sought Bove’s help. But in a seven-hour operation, Bove was able to successfully replace the valve. Jens, an enthusiastic snowboarder and skater, and his grateful parents, who describe Bove as “ödmjuk,” or “humble and compassionate,” were able to return home just two weeks after coming to Ann Arbor.

“Surgeons have a special bond with their patients,” Bove says. “They come to us because they trust us.” In Bove’s case, this is somewhat of an understatement. The trust of physicians and their patients in Bove’s life-and-death work extends far beyond Michigan, with about 40 percent of his patients coming from outside the state, and many, like Jens Stalnacke, from other countries around the world.

Amnon Rosenthal, M.D., U-M professor of pediatrics and communicable diseases, has high praise for his colleague: “Dr. Bove is a brilliant surgeon,” he says. “His technical skills are phenomenal. He has attained incredible surgical outcomes.” Rosenthal also speaks highly of Bove’s administrative approach, one focused on the teamwork necessary in the complex world of pediatric cardiology.

“He works very well with his coworkers,” says Rosenthal, “and has a wonderful team approach to the care of patients. Cardiac care involves many caregivers, including surgeons, cardiologists, nurses, anesthesiologists, social workers, technicians, and clerical personnel, and all have to work as one integrated unit focused on the patient.” Citing Bove’s humility, Rosenthal continues, “He has created a wonderful working atmosphere within the Michigan Congenital Heart Center, and he’s a very loyal institutional person. His administrative decisions always consider the perspective of the institution as a whole.” Rosenthal also commends Bove’s “commitment to training young surgeons in the field — highly qualified surgeons who are very much in demand.”

Susan Neilly, Bove’s secretary, underscores the gratitude her boss receives from the families he serves. “A lot of parents write to him and thank him for giving their child the gift of life,” she says, “and at holidays he gets cards and pictures.” She attributes this, in part, to the strength of his warm personality: “You can tell his compassion from the way he talks to people when he telephones families after a fetus is diagnosed with a heart condition,” she says. “And when a patient dies, he always writes the parents a heartfelt letter of condolence. He writes every one.”

The widely admired surgeon has no plans to ease his schedule. “I think I work too hard,” he says, “but I enjoy it. For me it’s either 110 percent or nothing. I can’t slow down.” Regarding the stress and the demands on his physical and mental stamina, especially the intense concentration required in the operating room, he says only, “Focus is terribly important, and I don’t want to lose my edge.” He still feels energized by the combination of intellectual, emotional, and personal challenge that he faces in his work, and he has no intention of slowing the pace. “It means a lot to me,” he says, “that babies benefit.”

Bove is proud of his own two children, both of whom are working in fields that contain elements of the medical and the high-risk. His daughter, Susan, 26, an associate scientist in preclinical research at Parke-Davis in Ann Arbor, is doing work on inflammation therapeutics related to osteo- and rheumatoid arthritis, and his son, Christopher, 23, is a paramedic training to be a firefighter in Chicago.

Bove, who grew up in New York City, is one of those lucky people whose talents and aspirations from an early age have been beautifully aligned — to his own deep satisfaction and to the extraordinary satisfaction of the many parents whose children are alive because of him. “As far back as I can remember I wanted to be a doctor,” he says. While it is his technical skills that make him a star in the surgical firmament, Bove still gleans his greatest pleasure and pride from the personal relationships that have been built on those skills. He is fond of a sentence from the classic essay, “The Care of the Patient,” delivered by Francis Weld Peabody, the highly regarded Boston physician and professor of internal medicine at Harvard University, to a medical school class in 1926: “The secret of the care of the patient is in the caring for the patient.”

The trust of physicians and their patients in Bove’s life-and-death work extends far beyond Michigan, with about 40 percent of his patients coming from outside the state, and many, like Jens Stalnacke, from other countries around the world.
“Just think of every one of your patients as another Norman Mette, a man whose quality of life was immeasurably enhanced by the kindesses and the dedication shown to him by his doctors and dentists.”

“You don’t need to thank the Mette Foundation,” Schettenhelm said to this year’s recipients, known as the Mette Scholars, who gathered with the trustees of the Mette Foundation for an annual dinner held in March at the Michigan League. “Just think of every one of your patients as another Norman Mette, a man whose quality of life was immeasurably enhanced by the kindesses and the dedication shown to him by his doctors and dentists.”

Mette had attended the University of Michigan for a single semester in the early 1930s, but in that Depression-era time did not have the funds to continue. The University represented for him, Schettenhelm says, the kind of excellence he aspired to and found in those who provided him with medical and dental care.

Though he lived into his 90s, Mette did not enjoy a healthy life. He underwent his first surgery for cancer at the age of 37, after which he was never able to work again, and underwent another seven surgeries for cancer over his lifetime. His niece, Marilyn Knickerbocker, a nurse at Sparrow Hospital in Lansing, remembers her uncle staying at her family’s house during his many recuperations.

His attorney, Karl W. Schettenhelm Jr., describes the late Norman H. Mette as a “very simple man, the kind of man who was embarrassed to say things about himself.” Mette, a frugal man who in his later years lived in a one-room apartment in the area of Detroit known as the Cass Corridor, did, however, have a dream. Thanks to his dream, more than 100 students in the University of Michigan Medical School and School of Dentistry have, over the past two decades, received more than $1.4 million in scholarship funds from the foundation in his name that he set up before his death in 1987, with about $1.1 million of the total going to the Medical School.

Mette Foundation trustees, from left, Paul Hoenle, head of the Johnson Smith Company in Bradenton, Florida; Marilyn Knickerbocker, a niece of Norman Mette and a nurse at Lansing’s Sparrow Hospital; John Snyder, a vice president of Comerica Bank and vice president of the Mette Foundation; and Karl Schettenhelm Jr., an attorney with the Southfield law firm of Raymond & Prokop.
How did he amass the funds to leave such a legacy to the Medical School? “He was extremely frugal,” Knickerbocker says. “He pinched pennies. And he made wise investments in the stock market. His brother, a successful Detroit architect with whom he lived for many years — neither of them ever married — left his estate to Norman, and he wisely invested that money and his own money, some of which he may have made mining out West in his 20s.”

The brothers’ parents, Knickerbocker says, came to the U.S. from Germany, and the boys grew up as part of a large family in the town of Hancock in Michigan’s Upper Peninsula, where their father was the town banker.
Healing a Nation:
How Three Graduates of the U-M Medical School Wrote Their Own Chapter in the History of Civil Rights in America

by David Barton Smith, Ph.D.
For most of the 20th century, a quiet, largely private, and unheralded struggle was waged to end the division of patients and physicians in America’s hospitals by race. Three of the lonely champions central to this struggle were graduates of the University of Michigan Medical School. Each played a distinctive and key role in assuring its success.

One was an academic physician familiar with the political maneuvering that goes on inside the Washington beltway. The second was a community leader and practicing physician in a rigidly segregated southern community. The third worked as an activist, organizing northern liberal support for the cause of racial equality in medicine. Together, their individual sagas form a larger story of the civil rights struggle in America that has been largely left untold.

Paul D. Cornely graduated from the U-M Medical School in 1931. Like other black physicians, his choice of internship was limited to the few historically black hospitals that provided such training, such as Lincoln Hospital in Durham, North Carolina, where he did his internship. Frustrated in his subsequent search for a surgical residency, Cornely returned to U-M and earned his doctorate in public health.

Obtaining a faculty position in public health at Howard University, he began a career dedicated to documenting racial disparities in health care in America and exploring strategies for their elimination. He teamed up with Howard colleague and anatomy professor W. Montague Cobb in orchestrating a protracted legal and political campaign against hospital segregation. He began publishing the results of surveys of segregated practices in the nation’s hospitals and worked with Cobb in organizing a series of national conferences focused on ending hospital segregation.

Neither Howard University nor the Department of Health Education and Welfare dared provide space for them, fearful of the political backlash. Most conferences were held, instead, at a local church in Washington, D.C. The crusaders found encouragement in the 1954 Brown vs. Board of Education decision, appearing as it did to nullify provisions in the 1946 Hill-Burton legislation permitting the use of federal funds for the construction of hospitals on a “separate but equal” basis. The conferences led to court challenges and eventually to federal legislation, including Title VI of the 1964 Civil Rights Act that prohibits the allocation of any federal funds to any program or organization that discriminates on the basis of race.

A critical part of the story, however, involves Hubert A. Eaton, who graduated from the U-M Medical School in 1942. After leaving Michigan, Eaton returned to Wilmington, North Carolina, to assume his father-in-law’s medical practice. He had his own tennis court next to his home, and continued to play championship-caliber tennis. Such was his interest in tennis that he and his family welcomed Althea Gibson in her teen years as a member of the Eaton household in preparation for her debut on the world tennis circuit.

The photo at left, under the heading, “Physician-Pickets Demand Racial Equality in A.M.A.” appeared in the Thursday, June 20, 1963, issue of the New York Times. John L.S. Holloman Jr. (M.D. 1943) is pictured on the right, leading the pickets in Atlantic City in front of the Traymore Hotel, where the American Medical Association’s House of Delegates was meeting. Behind Holloman are Robert Smith, M.D., of Jackson, Mississippi, and Walter J. Lear, M.D., of New York. It would be another 22 years before an African-American, Lonnie Bristow, M.D., was elected as a trustee of AMA; in 1995 he became the AMA’s first African-American president.

The photo is courtesy of Patricia Holloman, who resides with her husband, now 80 years old, in Flushing, New York.
An incident in 1947, however, shifted Eaton's interests to other challenges. Called to testify in court concerning a liability case related to a patient, he suffered an indignity that was to change his life. The Bible he was to swear upon was switched awkwardly by the court clerk at the last minute, replaced with a beat up copy covered in dirty adhesive tape labeled “Colored.” It became a personal turning point for him and the beginning of a long, determined and often lonely battle to end racial discrimination.

Wilmington had two hospitals. One was a small substandard facility for blacks. The other, a more generously endowed facility, James Walker Memorial, maintained about 25 beds for black patients in a ward that had only two toilets and was completely separate from the main hospital building. In order to reach the delivery room, operating room or other diagnostic facilities, the black patient had to be wheeled or walked 30 yards across an open space. The medical staff didn't just deny black physician applications for privileges; the hospital actually had by-laws that restricted staff privileges to white physicians. Yet Walker Memorial paid no taxes and received public dollars for its support.

In 1954, Eaton, along with several other black physicians he had persuaded to join him, applied for privileges at Walker Memorial, with no illusions about the rejection that would, and did, follow. In March 1956, Eaton filed suit in U.S. Federal District Court, the first of its kind in the nation and a key test case, thus joining the hospital desegregation efforts supported by Cornely and his Howard colleagues. It took Eaton more than eight years, but in April 1964 he won a victory in the Federal Appeals Court. The case brought attention to the use of public funds in hospitals that discriminated against blacks and helped assure the passage of Title VI of the 1964 Civil Rights Act.

The transformation, under the threat of lost Medicare dollars, was remarkable. Almost 1,000 hospitals quietly and uneventfully ended segregated accommodations and discriminatory medical privileges, and the medical world was transformed. It would now be up to John L.S. Holloman Jr. to bring to final fruition the struggle begun by his fellow alumni, the Howard professor and the black practitioner in the segregated medical community of Wilmington, North Carolina.

Holloman graduated from Michigan in 1943, the year after Eaton. He practiced in New York, eventually becoming an active member of the Medical Committee for Human Rights (MCHR). The group would shock the medical establishment by picketing the American Medical Association meetings in 1963 for its failure to bar medical societies that refused to accept black physicians as members. In 1965 he assumed the presidency of MCHR, which sent volunteer civil rights hospital inspectors into the South during the summer of 1965. This hastily pulled together effort would serve as the blueprint for the Title VI Medicare certification process for the following year.

The group was frustrated by the federal inaction in addressing the clear violations they found in conducting their volunteer inspections. This culminated in a protest demonstration led by Holloman in the office of John Gardner, then secretary of Health, Education and Welfare, in December 1965. The pressure created by Holloman’s group helped; the Title VI certification effort for Medicare that was to start in July 1966 became a deadly serious one rather than a paper compliance charade. Holloman would serve as a consultant to the Office of Equal Health Opportunity responsible for making sure that hospitals receiving Medicare funds did not have segregated accommodations and did not discriminate against physicians in terms of privileges on the basis of race. The transformation, under the threat of lost Medicare dollars, was remarkable. Almost 1,000 hospitals quietly and uneventfully ended segregated accommodations and discriminatory medical privileges, and the medical world was transformed. It was almost as if, as one black physician observed, “it had always been this way.”
The University of Michigan Medical School’s sesquicentennial year coincidently marks the beginning of a national effort, Healthy People 2010. One of the key goals of this effort is the elimination of the remaining racial disparities in the U.S. in health use and outcomes by the year 2010. While clearly much remains to be done, the struggle waged by University of Michigan Medical School alumni Paul Cornely, Hubert Eaton and John Holloman Jr. did change the landscape of medical care in the United States forever. Three very different medical graduates worked as a team and won a remarkable victory. In the truest sense of the word, they each earned the title, “Champion,” that word so often embraced with enthusiasm in their alma mater’s fight song, *The Victors.*

References:


Author’s Note:

David Smith, who earned his Ph.D. from the University of Michigan School of Public Health in 1969, is currently professor and program director of the HealthCare Management Program at Temple University in Philadelphia. He is the author of *Health Care Divided: Race and Healing a Nation,* published by the U-M Press in 1999 and supported by a Robert Wood Johnson Health Policy Research Investigator Award. This article is based on his research for the book.

The U-M Kellogg Project collects oral histories about segregated hospitals in southeastern Michigan; visit its Web site for additional information: www.med.umich.edu/haahc.
**Whither the Residency? Newly Minted M.D.s Get the Good News**

Excitement, anticipation and jubilation were the overriding emotions on March 16, 2000, as the U-M Medical School’s Class of 2000 assembled to discover which residency programs would be theirs as they move on to the next important step in their medical careers. Of the 136 students who participated in the National Resident Matching Program, a computer-based selection process that pairs students with their preferred residency programs, 63 percent matched with their first choice and 13 percent received their second choice. Overall, four-fifths of the students received one of their three top choices of residency programs. An additional 23 students who participated in different matching programs, such as Ph.D. programs, post-doctoral programs or programs sponsored by the U.S. military, also attended Match Day.

Match Day is sponsored by the Medical Center Alumni Society, the Student Council and the Dean’s Office. In addition to celebrating their new residencies, students also celebrated the announcement of Heather Bunting as the recipient of this year’s Niland Award. Established by the Class of 1986 to honor class member Patrick John Niland, who was killed in a car crash in 1985, the Niland Award recognizes a senior student selected by his or her fellow classmates as best exemplifying the warmth and compassion for which Niland was known.
General Surgery
Brian T. Chin,
University of California Medical Center, San Diego
Naveen Gupta,
New York University Medical Center
Nicholas M. Lopez,
University of Kentucky Medical Center, Lexington
Elizabeth J. Renaud,
Boston University Medical Center
Aaisha K. Stimaq,
Graduate Hospital, Philadelphia
Alexander H. Toledo,
University of Maryland Medical Center, Baltimore
Dennis C. Tong,
Henry Ford Health Science Center, Detroit
Amy R. Woznick,
William Beaumont Hospital, Detroit

Internal Medicine
Nima Afshar,
University of California, San Francisco
Grant D. Barish,
University of California, San Francisco
Anne Y. Chen,
Henry Ford Health Science Center, Detroit
Madhavi Dandu,
University of California, San Francisco
David A. Deguzman,
University of Michigan Hospitals
Michele M. Doughty,
Emory University School of Medicine, Georgia
Steven M. Ewer,
University of Michigan Hospitals
Amit Gaggar,
University of Alabama, Birmingham
Saman G. Gupta,
University of California, San Francisco
Erin E. Hogan,
University of Michigan Hospitals
Renee A. Hoyt, St. Joseph’s, Wisconsin
Kevin T. Huang,
University of California, Irvine
Megan S. Jacobs,
McGaw Medical Center, Northwestern University
Peter V. Johnston,
Johns Hopkins Hospital, Baltimore
Jeffrey Jones,
McGill University, Montreal
Andrew C. Lee,
University of Washington Hospitals, Seattle
Robert H. Lee,
University of Michigan Hospitals
Grace A. Lin,
Barrow-Jewish Hospital, St. Louis, Missouri
Gregory J. Makris,
University of Illinois, Chicago
Randall S. Meisner,
McGaw Medical Center, Northwestern University
Aparna Padiyar,
University of Michigan Hospitals
Supriya Rajpal,
Hospital of the University of Pennsylvania, Philadelphia
Santosh K. Rao,
University of California, San Diego
James P. Smith,
University of Michigan Hospitals
Scott T. Sutton,
University of Colorado, Denver
Yuhjung J. Tsai,
University of California Medical Center, Davis
Rex T. Wang,
Harbor-UCLA Medical Center, California
Dana R. Wood,
McGaw Medical Center, Northwestern University
Jason C. Wood,
St. Mary’s Hospital & Medical Center, San Francisco
Theresa Y. Wu,
Harbor-UCLA Medical Center, California
Tina T. Wu,
California Pacific Medical Center, San Francisco

Family Medicine
Julia Bemer,
University of Michigan Hospitals
Heather N. Bunting,
St. Mary’s Health Service, Grand Rapids
Julia M. Dealmeida,
Rhode Island Memorial Hospital, Pawtucket
Manjushree Deshpande,
University of Michigan Hospitals
Jameelah J. Gater,
Emory University School of Medicine, Georgia
Dana E. Hawkins,
Sutter Health, California
Gregory S. Hylant,
St. Mary’s Health Service, Grand Rapids
Stacey L. Krause,
Exempla St. Joseph, Denver
Allison M. Leach,
Maine Medical Center, Portland
Jennifer L. Schafer,
University of Michigan Hospitals
Joshua D. Uy,
MacNeal Hospital, Berwyn, Illinois
Zoe J. Wardley,
Lancaster General Hospital, Pennsylvania

(Top) Pooja Mittal and James Broome, with Caroline Schreiber in the background.

(Bottom) Michele Doughty receives congratulations from MCAS President Jeffrey Dunn (Residency 1977), as Associate Dean of Student Programs Rachel Glick (M.D. 1984) looks on.
Obstetrics-Gynecology
Shaiba Z. Ansariali,
University of Illinois, Chicago
Jennifer E. Ballard,
University of Minnesota Medical School, Minneapolis
David W. Calton,
William Beaumont Hospital, Detroit
Aparna Diwan,
Brigham & Women’s Hospital, Boston
Michael D. Evers,
Indiana University School of Medicine, Indianapolis
Mei Ge,
UCLA Medical Center
Pooja Mittal,
University of Southern California, Los Angeles
Santosh Pandipati,
University of Washington Hospitals, Seattle
Shannon H. Panszi,
University of Massachusetts Medical School, Worcester

Ophthalmology
Mandar M. Joshi,
Tufts/New England Eye Center, Boston
Aaleya F. Koreishi,
Johns Hopkins/Wilmer, Sinai, Maryland
David M. Mills,
University of Florida, Gainesville
Leila Mokhtarzadeh,
Scheie Eye Institute, Philadelphia
Paul E. Nicholas,
University of Michigan Hospitals
Ehsan Sadri,
University of Maryland, Baltimore
Robert S. Wirthlin,
University of Miami, Bascom Palmer Eye Institute

Orthopaedic Surgery
John C. Austin,
University of Michigan Hospitals
Jessica S. Cooper,
University of Michigan Hospitals
Matthew J. Siskosky,
William Beaumont Hospital, Detroit
Samantha A. Spencer,
Harvard Combined Program, Cambridge
Brady T. Vibert,
William Beaumont Hospital, Detroit

Otolaryngology
Eric Bauer,
Washington University, St. Louis, Missouri
Matthew S. Pogodzinski,
Mayo Graduate School of Medicine, Rochester
Garfield Johnson,
University of Michigan Hospitals

Pediatrics
Melody D. Alger,
Medical University of South Carolina, Charleston
Craig A. Barkan,
Long Island Jewish Hospital
Heather L. Burrows,
University of Michigan Hospitals
Megan M. Edison,
Maine Medical Center, Portland
Andrea M. Hoogerland,
Medical College of Wisconsin Affiliated Hospital, Milwaukee
Sandhya H. Krishnan,
University of Chicago Hospitals
Damian J. Krysan,
University of Michigan Hospitals
Jin Shin R. Kwak,  
Children’s National, Washington D.C.

June A. Lee,  
Indiana University School of Medicine, Indianapolis

Carey N. Lumeng,  
Boston Combined Pediatric Residency

Crystal G. Martin,  
Wayne State University/Detroit Medical Center

Nelangi M. Pinto,  
University of Washington Hospitals, Seattle

Ena M. Randolph,  
University of California, San Francisco

Janice M. Rourk,  
University of Michigan Hospitals

Fabian Salinas,  
University of Michigan Hospitals

Ruth Scrano,  
Bethesda Naval Hospital, Washington, D.C.

**Plastic Surgery**

Jafar S. Hasan,  
University of Michigan Hospitals

Jonathan S. Wilensky,  
University of Michigan Hospitals

**Psychiatry**

Puneet K. Ailawadi,  
University of Michigan Hospitals

John W. Denninger,  
Massachusetts General Hospital, Boston

Virginia Matheson,  
Wright Patterson Air Force Base, Dayton

Chukwunweik Nwankwo,  
Massachusetts General Hospital, Boston

Eric A. Samstad,  
Johns Hopkins Hospital, Baltimore

David W. Sirkin,  
UCLA Neuropsychiatric Institute

**Radiation Oncology**

Scott G. Solty,  
Stanford University Hospitals

Amanda E. Bauer,  
St. Louis University, Missouri

Eric B. Callaghan,  
University of Iowa Hospitals, Iowa City

Gene A. Carpenter,  
Duke University Medical Center, Durham, North Carolina

Emma C. Diponio,  
Grand Rapids Medical Center

Eric A. Galino,  
University Hospitals of Cleveland

Thomas K. Song,  
Henry Ford Health Science Center, Detroit

**Surgery-Preliminary Year**

Martin Barrios,  
Stanford University Medical Center

Sharon E. Baughman,  
University of Michigan Hospitals

Eunice S. Chung,  
University of Michigan Hospitals

Alexander J. Fernandez,  
University of Michigan Hospitals

Rajesh G. Govindaiah,  
William Beaumont Hospital, Detroit

Kahlil Shillingford,  
University of Maryland, Baltimore

**Transitional Year**

Joseph Crow,  
Naval Hospital, Portsmouth, Virginia

**Urology**

Stefan Gutow,  
University of Kansas Medical Center, Kansas City

Jeffrey L. O’Connor,  
Vanderbilt University, Nashville

Michael Shulman,  
University of Texas SW Medical School, Dallas

Zachary L. Voeltz,  
Emory University School of Medicine, Georgia

Brian M. Yoder,  
University of Michigan Hospitals

"To the Class of 2000!"

(Above) Executive Associate Dean James Woolliscroft wishes graduating students a "lifetime of wonder, challenge and personal fulfillment."

(Left) David Morro and Charles Danek.
1950s

Michael J. Franzblau (M.D. 1952), clinical professor of dermatology at the University of California School of Medicine, San Francisco, has been given the Truth and Justice Award by the Anti-Defamation League and the Louis D. Brandeis Award by the Zionist Organization of America. Franzblau was given the awards for his efforts over many years to bring to international attention the role of Bavarian physician Hans Joachim Sewering in the 1940s in Germany in the killing of many physically and mentally handicapped children and adults as part of the Nazi government’s “racial hygiene” program. Franzblau’s efforts are featured in The Last Survivor: In Search of Martin Zaidenstadt by Timothy W. Ryback (Pantheon Books, 1999) and were described in a segment on CBS-TV’s Sixty Minutes in October, 1996. Franzblau can be reached at mfranzblau@aol.com.

Mark Menzel (M.D. 1959), an allergist in Boulder, Colorado, retired last fall from his practice with the Boulder Valley Asthma and Allergy Clinic, which he founded in 1966. A residency and fellowship at National Jewish Hospital brought him to Colorado in 1964. The photo here appeared in the Boulder Daily Camera last August when Menzel was featured in an interview about his career and his hobby, which involves researching the health of American presidents.

1960s

Herbert L. Cares (M.D. 1963), a Boston neurosurgeon, invites his classmates and others to visit his Web site at http://www.hlcares.com/. There he discusses and provides photos of his professional life and his work as well as his personal life, including his marriage last year to nurse Karen DiPietro, who shares his love of serious ballroom dancing.

The work of Irene Zsuzsi Danek (M.D. 1968) was featured in the December, 1999, issue of Michigan Medicine, the publication of the Michigan State Medical Society. Danek, who is on the staff of the private Interlochen Arts Academy south of Traverse City, specializes in a new field known as “arts medicine,” dedicated to the diagnosis, treatment and prevention of injuries common to dancers, musicians, singers and others in the performing arts. She is also conducting research on lung function in musicians.

Your bequest to Michigan will help keep the Medical School great for another 150 years

A bequest is a wonderful way to ensure that the Medical School’s future will be as bright as its past. For some, a bequest offers the opportunity to make a more substantial gift than would be possible during a lifetime. For others, it’s an opportunity to round out many years of giving with a lasting legacy to the Medical School to meet faculty, student and program needs, and to enjoy the financial advantages associated with a bequest to a charitable institution. If you’d like to support the work of the School by establishing a bequest, please call the Office of Medical Development and Alumni Relations at (734) 998-7705. We’ll be happy to send you all the information you need to establish a bequest to advance medicine at Michigan.

If you would like information on other ways to make a gift, please call and request a copy of Ways of Giving to Advance Medicine at Michigan, which includes information on establishing a charitable remainder trust, establishing a lead trust, participating in the University’s Donor Pooled Income Fund, making a gift of cash, appreciated securities, real estate or personal property, or leaving retirement assets to advance medicine at Michigan.
Danek herself is a pianist. She is married to Medical School classmate Charles Danek, who earned his M.D. from U-M in 1968 and completed his residency in physical medicine at Michigan in 1976.

Glenn Geelhoed (M.D. 1968) is the author of Out of Assa, Heart of the Congo, Medical Adventures in Central Africa (Three Hawks Publishing, April 2000). Geelhoed is professor of surgery and professor of international medical education at George Washington University in Washington, D.C. The book is an account of his volunteer medical work in Assa, a remote village in the Democratic Republic of the Congo in the summer of 1998. Henry Berry, editor and publisher of The Small Press Book Review, wrote about Out of Assa, “Geelhoed’s detailed, observant journal has an immediacy that will satisfy the arm-chair traveler or inform a reader looking for a picture of life in central Africa today… Geelhoed observes it all with a sharp anthropological eye, subtle humor, and humanitarian affinity.” The book may be ordered from the publisher (1300 Bishop Lane, Alexandria, VA 22302) or by e-mail at kej@3hawks.com. More information may be obtained by visiting the publisher’s Web site at http://www.3hawks.com.

1970s

Gary S. Kaplan (M.D. 1978) has been elected chairman and CEO of the Virginia Mason Medical Center in Seattle, Washington. Kaplan, a practicing physician in internal medicine, was elected to the four-year term by the Center’s member physicians. Kaplan has served in a number of senior leadership positions at Virginia Mason, where he began practicing medicine in 1978. As chairman, Kaplan assumes the helm of a health care system with annual revenues of $500 million providing health care to more than 150,000 residents of the Pacific Northwest.

1980s

Alice D. Ma (M.D. 1989) has been awarded a Junior Faculty Scholar Award by the American Society of Hematology. The award was presented to her at the 41st annual meeting of the Society last December in New Orleans. Ma, an assistant professor of medicine at the University of North Carolina at Chapel Hill School of Medicine, will use her award to study pleckstrin, a protein found in platelets and white blood cells. Ma’s study will focus on the DEP domain, a group of amino acids within pleckstrin, and its role in intermolecular interactions.

Ma earlier in her career received several honors including a Howard Hughes Medical Institute Research Scholarship at the National Institutes of Health, a Mentored Clinical Scientist Development Award from NIH and the National Heart, Lung and Blood Institute, and a University of Pennsylvania Pearls Teaching Award. Ma was a fellow and instructor in hematology at the Penn School of Medicine before joining the faculty at North Carolina in 1998.
Deaths
Richard E. Fry (M.D. 1978), on May 5, 2000, in Indianapolis. He served as assistant professor at the University of Texas Southwestern Medical School prior to moving in 1989 to Indianapolis, where he directed vascular surgery at St. Francis Hospital until his death. He was chief of surgery at St. Francis from 1997 to 1998, a member of its medical staff executive and policy committees, and a Fellow of the American College of Surgeons. He was 47.

Stay in Touch
Share your news with those with whom you trained at the University of Michigan. Please send news (and photos or other art) to Jane Myers, 301 E. Liberty, Ann Arbor, MI 48104-2251; fax: 734-998-7268; e-mail: jemyers@umich.edu.
Please include your name, Michigan affiliation, current practice, titles, awards, postal address, telephone and e-mail address along with your professional and personal news.

Corrections
Pictured above right is Fred Hodges, head of roentgenology (radiology), featured as a 1931 entry in the historical timeline of the Medical School. A photo of William A. Frayer, professor of history who left the U-M faculty in 1929, was mistakenly used to represent Fred Hodges in the Winter 2000 issue.

The error was noted by William C. Frayer (M.D. 1945), who recognized his father as well as remembered what Fred Hodges looked like, based on his own 1945 group class photo in which Hodges was present.
Michigan’s Continuing Medical Education Calendar, Summer 2000

**JUNE**
- 19-23 35th Annual Northern Michigan Summer Conference
  Shanty Creek, Bellaire
- 22-24 First International Conference on Pediatric Continuous Renal Replacement Therapy (PCRRT)
  Marriott Inn, Orlando, Florida
- 23-24 Advanced Trauma Life Support (Student Course)
  Towsley Center, Ann Arbor

**JULY**
  Grand Traverse Resort, Grand Traverse
- 13-15 Psychopharmacology Update
  Grand Traverse Resort, Grand Traverse
- 14-15 Annual Sheldon Society Meeting
  Towsley Center, Ann Arbor
- 14-16 Advances in the Management of Infectious Diseases
  Grand Hotel, Mackinac Island
- 22-23 Endocrinology and Diabetes Update 2000
  Boyne Highlands, Harbor Springs
- 27-30 Internal Medicine Update
  Grand Hotel, Mackinac Island
- 28-30 Endoscopic Sinus Surgery, Comprehensive Sinus Surgery
  Towsley Center, Ann Arbor

**AUGUST**
- 11-13 Update in Office Gastroenterology
  The Inn at Bay Harbor, Bay Harbor
- 18-20 Cardiology Update
  Grand Hotel, Mackinac Island
- 31-1 Critical Clinical Issues in the Care of the Elderly
  (Location to be determined)

**SEPTEMBER**
- 7-8 22nd Annual Seminar in Diagnostic Ultrasound
  Towsley Center, Ann Arbor
- 13-14 Sports Medicine (Location to be determined)
- 15-16 Advanced Trauma Life Support (Student Course)
  Towsley Center, Ann Arbor
- 17-22 The 13th Annual Pediatric Board Review
  Crowne Plaza, Ann Arbor
- 21-22 Complementary Therapies in Clinical Practice: An Evidence Based Approach
  (Location to be determined)
- 23 Cancer Symposium/Field of Dreams
  (Location to be determined)

Course dates may change. For verification or more information about course locations and content, call or write: Office of Continuing Medical Education, Department of Medical Education, University of Michigan Medical School, Box 1157, Ann Arbor, MI 48106-1157
Charles M. Boyd, M.D. (Residency 1998), clinical assistant professor of otolaryngology and dermatology, has been selected to participate in the American Medical Association Glaxo Wellcome Emerging Leaders Development Program. The Program's goal is to offer tools to help physicians better meet the challenges facing them individually and collectively in the legislative/regulatory, organized medicine, and managed care arenas. Only 50 physicians from across the U.S. were selected to participate, chosen for their demonstrated leadership potential, commitment to leadership development, participation in organized medicine, and the diversity of their leadership experience.

Mary-Margaret Brandt, M.D., clinical instructor in the Department of Surgery, Division of Trauma, Burn and Emergency Surgery, and Mary M. Johnson, clinical assistant professor in the Department of Internal Medicine, were selected as recipients of the University of Michigan Traditions of Leadership Award. The award offsets expenses associated with attending the Association of American Medical College’s Professional Development Seminar for Junior Women Faculty and is made possible through the Medical School Gender Equity Fund and the University of Michigan Alumnae Council.

George J. Brewer, M.D., Morton and Henrietta Sellner Professor of Human Genetics and professor of internal medicine, was presented with the American College of Nutrition’s Master’s Award at the College’s 1999 meeting. Only the seventh Master’s Award in the College’s 40-year history, it recognizes a lifetime of excellence in research in the area of nutrition. Brewer was selected on the basis of his long-term work on zinc and copper, and, more recently, on molybdenum compounds. In 1998, Brewer received the Raulin Award of the International Society for Trace Element Research in Humans. The Raulin Award is the Society’s highest honor and recognizes lifetime achievement in research on trace elements.

Theodore M. Cole, M.D., professor emeritus and retired chair of the Department of Physical Medicine and Rehabilitation, was honored with the 1999 Distinguished Member Award from the American Academy of Physical Medicine and Rehabilitation. The award honors members who have provided invaluable service to the specialty of physical medicine and rehabilitation primarily through participation in related organizations. The Academy is the national medical specialty society of more than 6,000 physical medicine and rehabilitation physicians.

Arnold G. Coran, M.D., professor of surgery and head of the Section of Pediatric Surgery, recently completed a term as chair of the Executive Committee of the Surgical Section of the American Academy of Pediatrics. Under Coran’s direction, several innovations were made to the annual meeting program, including State of the Art lectures delivered by professor Jose Boix-Ochoa from Barcelona, Spain, and Agostino Pierro, from London, England.
Melody Neely Is First Recipient of Ward MacNeal Award

The first Ward J. MacNeal Distinguished Dissertation Award for best dissertation by a student in the Department of Microbiology and Immunology was made to Melody Neely (Ph.D. 1998) at a ceremony in March, 2000, for her dissertation entitled “Functional and Genetic Analysis of the Lambdoid Bacteriophage H-198, A Natural Vector for the Shiga-like Toxin Genes.” Neely’s work focusing on the causes of infectious diseases mirrors that of Ward MacNeal (A.B. 1901, Ph.D. 1904, M.D. 1905, Hon. Sc.D. 1939), an eminent pathologist who was a leading authority on bacteriophage and who served as professor of bacteriology and director of bacteriological services at New York Post-Graduate Medical School from 1912 to 1946.

Currently a post-doctoral fellow in the Department of Molecular Microbiology at Washington University School of Medicine in St. Louis, Neely was chosen for the MacNeal Award based on overall scholarly credentials, degree of innovation and insight, and the scope and importance of her work. The Ward MacNeal Distinguished Dissertation Award is made possible by a gift from the estate of Charlotte Etzold MacNeal, the wife of Ward MacNeal’s son, Perry S. MacNeal (M.D. 1936, Residency 1940).

Josef Miller: He’ll Help Pick Nobel Prize Winners

Josef Miller, Ph.D., was appointed as a foreign adjunct professor at Sweden’s prestigious Nobel Prize-granting Karolinska Institute in Stockholm in recognition of his long-standing research with the Institute and the new research and training programs he developed there during his recent sabbatical. He is one of only 10 Americans to hold the title. Among his duties, he will nominate and vote on candidates for the Nobel Prize in Physiology or Medicine.

Miller is the Ruth and Lynn Townsend Professor of Otolaryngology and an adjunct professor in psychology at the U-M. He is a member of the Neuroscience Program faculty and of the Center for Biomedical Engineering. From 1984 to 1999, he was director of the Kresge Hearing Research Institute; he is currently director of the Center for Communication Disorders.

In addition to his doctorate in physiology, Miller has received two honorary medical degrees from the Universities of Goteborg in Sweden and Turku in Finland. In 1997, he received the Presidential Citation of the American Academy of Otolaryngology — Head and Neck Surgery. He served as chair of the U-M Research Priority Committee and received the Regents Distinguished Service Award for his work in establishing the National Institute of Deafness and Other Communication Disorders, the 13th Institute of the NIH.

Jeffrey A. Fessler, Ph.D., associate professor of internal medicine, of electrical engineering and computer science, and of biomedical engineering, recently received the University’s Henry Russel Award. The annual award, established in 1925 with a bequest from Henry Russel of Detroit, is given to young faculty members for scholarly achievement and promise. “His research in tomographic medical imaging, iterative estimation and statistical inverse problems is absolutely first rate and has given him exceptional visibility in academia and industry at a relatively early stage of his career,” the selection committee noted. Fessler joined the U-M in 1993.

Sid Gilman, M.D., William J. Herdman Professor of Neurology, chair of the Department of Neurology, and director of the Michigan Alzheimer’s Disease Research Center, has been named a Fellow of the Royal Society of Medicine, effective February 1, 2000. The Royal Society, based in London, publishes research books and journals, sponsors lectures and conferences, and maintains the leading medical library in Europe.

Mark A. Helvie, M.D. (Residency 1983, 1986), associate professor of radiology (not pictured), and Jon A. Jacobson, M.D., clinical assistant professor of radiology, received the 1999 Radiology Journal Editor’s Recognition Award for Reviewing with Distinction. Helvie and Jacobson were among 70 reviewers chosen from a field of 985 for this recognition; their names were listed in the January, 2000, issue of Radiology. Radiology is a monthly journal devoted to clinical radiology and allied science, published by the Radiological Society of North America.

In addition to his doctorate in physiology, Miller has received two honorary medical degrees from the Universities of Goteborg in Sweden and Turku in Finland. In 1997, he received the Presidential Citation of the American Academy of Otolaryngology — Head and Neck Surgery. He served as chair of the U-M Research Priority Committee and received the Regents Distinguished Service Award for his work in establishing the National Institute of Deafness and Other Communication Disorders, the 13th Institute of the NIH.
in the nation devoted to education regarding surgery of the hand, the oldest organization Louis was president of the American Society in underdeveloped areas of the world. In 1997, a group devoted to education and patient care Surgery Societies and by Physicians for Peace, sponsored by the Egyptian Orthopedic and Plastic Herpes Foundation provides the Elion Award to performing scientific research. The American herpesvirus and immune disorders. Elion, who discovered acyclovir, entered the field at a time when most employers would not hire women to perform scientific research. The American Herpes Foundation provides the Elion Award to foster awareness and treatment of herpesviruses and to honor outstanding research in the field.

Ellion received the Nobel Prize in 1988 for her work on life-saving medicines for leukemia, herpesvirus and immune disorders. Elion, who discovered acyclovir, entered the field at a time when most employers would not hire women to perform scientific research. The American Herpes Foundation provides the Elion Award to foster awareness and treatment of herpesviruses and to honor outstanding research in the field.

Qingxue Li, Ph.D., research investigator in the Department of Microbiology and Immunology, received the 1999 Herpes Foundation Gertrude Elion Award for distinguished contributions in herpesvirus research. This is the top national award given annually to two early-career investigators in honor of the Nobel Laureate, Gertrude Elion. It includes a $10,000 award ($5,000 to the department and $5,000 to the investigator) and is presented to outstanding female scholars in herpesvirus research.

Juanita Merchant, M.D., Ph.D., associate professor of internal medicine, is being honored for her contributions to science and technology in the field of nitric oxide biochemistry. Impression 5 Science Center created the Tribute to Science and Technology Award program in 1981 to honor individuals who have made significant contributions to science and technology in Michigan. Emphasis is given to individuals who also serve as models for post secondary students.

JAMA is the world’s largest federation of scientists, as well as publisher of the journal Science.

Michael A. Marletta, Ph.D., John G. Searle Professor of Medicinal Chemistry and professor of biological chemistry, was recently named Michigan Scientist of the Year for 2000 by the Impression 5 Science Center in Lansing. He was selected for his numerous contributions to the field of nitric oxide biochemistry. Impression 5 Science Center created the Tribute to Science and Technology Award program in 1981 to honor individuals who have made significant contributions to science and technology in Michigan. Emphasis is given to individuals who also serve as models for post secondary students.

Juanita Merchant, M.D., Ph.D., associate professor of internal medicine in the Division of Internal Medicine, has been chosen to receive the sixth Henry Wagner Jr. Clinical PET Award from the Institute for Advanced Medical Technology. Minoshima was chosen for his scientific contributions, including the development of stereotactic image analysis of brain PET/SPECT and applications to PET activation studies, discovery of posterior cingulate gyrus hypometabolism in Alzheimer’s disease, and the proposal and development of “diagnostic” statistical mapping techniques for functional brain images. His methods are currently used at 40 institutions in 11 countries.

Thomas L. Schwenk, M.D., professor and chair of the Department of Family Medicine, has been elected to the board of directors of the American Board of Family Practice.

Jean Robillard, M.D., professor and chair of the Department of Pediatrics and Communicable Diseases, has been elected a Fellow of the American Association for the Advancement of Science. He was recognized during a ceremony at the Association’s Annual Meeting on February 19, 2000, for “important contributions to understanding renal development and maturation of kidney function and for leadership in the discipline of pediatrics.” AAAS is the world’s largest federation of scientists, as well as publisher of the journal Science.

Mark B. Orringer, M.D., John Alexander Distinguished Professor and head of the Section of General Thoracic Surgery, was elected vice president of the Society of Thoracic Surgeons at the Society’s 36th annual meeting in January, 2000. Orringer will assume the presidency of the Society in 2001. The Society’s primary objective is to improve the quality and practice of thoracic and cardiovascular surgery. It is the largest professional society of cardiothoracic surgeons in the world and has a combined national and international membership of approximately 4,000 surgeons.

Satoshi Minoshima, M.D., Ph.D., associate professor of internal medicine in the Division of Internal Medicine, has been chosen to receive the sixth Henry Wagner Jr. Clinical PET Award from the Institute for Advanced Medical Technology. Minoshima was chosen for his scientific contributions, including the development of stereotactic image analysis of brain PET/SPECT and applications to PET activation studies, discovery of posterior cingulate gyrus hypometabolism in Alzheimer’s disease, and the proposal and development of “diagnostic” statistical mapping techniques for functional brain images. His methods are currently used at 40 institutions in 11 countries.

Gregory Wolf, M.D., has been invited by the Department of Surgery, University of Hong Kong, to be an External Examiner of the Dental Examination (BDS Third Examination). In conjunction with this honor, Wolf will also be guest lecturer at the Hong Kong Surgical Forum, a postgraduate course sponsored by the University of Hong Kong’s Departments of Surgery and Medicine. Following the Surgical Forum, Wolf will travel to Xian, China, as an invited speaker at a Joint Surgical Convention held in conjunction with the Fourth Military Medical University.
George J. Brewer Installed as First Sellner Professor of Human Genetics

George J. Brewer, M.D., professor of human genetics and a specialist in the treatment of Wilson’s disease, was installed as the first Morton S. and Henrietta K. Sellner Professor of Human Genetics at a ceremony held at the Gerald R. Ford Library on April 24, 2000.

A member of the Medical School faculty since 1965, Brewer has been director of an interdepartmental graduate training program in genetics since the program’s inception 22 years ago. His research, which he describes as “opportunistic pursuit of interesting projects, particularly those with an opportunity for new disease treatments,” has largely focused on copper metabolism. Experimenting with zinc as a therapy for sickle cell anemia, Brewer discovered that zinc caused copper deficiency. This led to a new treatment for Wilson’s disease, an inherited condition of copper accumulation and toxicity. The FDA in January, 1997, approved zinc as therapy for Wilson’s disease based almost entirely on the work of Brewer and his research team.

The Sellners, whose son, Ascher, was diagnosed with Wilson’s disease in 1971, established the professorship to recognize and encourage Brewer’s work and to honor his care of their son. Ascher Sellner, M.D., now 58, is a gynecologist in private practice in Brookfield, Connecticut. The Sellner’s gift of $1 million in the form of a charitable remainder trust will be matched with $750,000 from the Medical School; an endowed research fund will accompany the professorship, encouraging research and treatment efforts in genetic diseases.

Dixon Named to National Academy of Sciences

Jack E. Dixon, Ph.D., the Minor J. Coon Professor of Biological Chemistry and chair of the Department of Biological Chemistry, was recently elected to the prestigious National Academy of Sciences. Academy members are elected in recognition of distinguished and continuing achievements in original scientific research.

“For a scientist, election to the National Academy of Sciences is the highest recognition short of the Nobel Prize,” said Gil Omenn, M.D., Ph.D., executive vice president for medical affairs. “Jack Dixon is one of the nation’s pre-eminent biochemists, and we are very proud to have him on the Medical School faculty.” Dixon studies the structure and function of the protein tyrosine phosphatases, or PTPases, and their important role in cellular signaling.

Dixon is a Fellow of the American Academy of Arts and Sciences, a member of the Institute of Medicine, and past president of the American Society for Biochemistry and Molecular Biology. He also serves on the National Scientific Review Board of the Howard Hughes Medical Institute. Dixon was named Michigan Scientist of the Year in 1994. In 1997, he received the U-M Distinguished Faculty Lectureship Award in Biomedical Research. In 1999, he was chosen as the Henry Russel Lecturer, the highest honor the University gives to a senior faculty member. Dixon also chaired the faculty advisory committee for the U-M’s new Life Sciences Initiative.
In the lives of both people and institutions, there are moments of special significance, times of celebration and reflection on what has passed and what is still to come. The Sesquicentennial Celebration and All-Classes Reunion of the University of Michigan Medical School, to be held Friday and Saturday, October 13 and 14, in Ann Arbor this fall is such an occasion.

For a century and a half, the University of Michigan Medical School has held a secure place among the most esteemed medical schools in the country, providing inspired leadership in the education of America’s physicians, in the understanding of the underlying importance of basic and clinical research to progress in medicine, in the early realization that true medical education required that students have the opportunity to work with patients in a clinical setting.

The weekend in Ann Arbor will be an opportunity to join your fellow alumni/ae, faculty and friends in celebrating both the glorious past and the promising future of the Medical School. The weekend will begin with a fascinating look at the School’s history with Howard Markel, M.D., Ph.D., pediatrician, medical historian and director of the School’s Historical Center for the Health Sciences, and with the announcement by George Morley, M.D., professor emeritus of obstetrics and gynecology, of the first inductees to the School’s new Hall of Honor honoring outstanding faculty and graduates of the past.

Noted alumni Donald S. Fredrickson (M.D. 1949) and Marshall W. Nirenberg (Ph.D. 1957), both of whom were awarded honorary doctor of science degrees by the University of Michigan in 1977, will present addresses on Friday. Fredrickson has, in the course of his distinguished career, served as head of the National Institutes of Health and the Howard Hughes Medical Institute. Nirenberg was awarded the Nobel Prize in 1968 for his early work on the genetic code and its role in protein synthesis.

Friday evening everyone will gather for a reception and gala dinner featuring entertainment by U-M Music School faculty members William Bolcom and Joan Morris, the husband-and-wife team noted internationally for their interpretations of American popular songs from the 19th century through the 1920s and 1930s.

Saturday will feature a tailgate brunch followed by the Michigan-Indiana football game in Michigan Stadium with a special halftime performance by the Michigan Marching Band honoring the Medical School’s Sesquicentennial.

An exhibition at the University of Michigan Art Museum, open during the weekend, will celebrate the School’s sesquicentennial by featuring images and objects offering both historical and cultural perspectives on medicine. A Thursday evening reception hosted by Dean Allen S. Lichter at the Museum, including the unveiling of a series of portraits of the deans of the Medical School, will also be open to those who will be in town.

If you have not already received a registration packet for the Sesquicentennial Celebration/All-Classes Reunion, or if you have questions, please call the Medical Development and Alumni Relations Office at (734) 998-8107 or (800) 468-3482.

Ways to Register

There are four ways to register for the Sesquicentennial Celebration/All-Classes Reunion: by mail (U-M Medical Development and Alumni Relations Office, 301 E. Liberty, Suite 300, Ann Arbor, MI 48104-2251), by phone at the above numbers, by fax at (734) 998-7268 or on the Web at www.med.umich.edu/medschool/mcado/reunion.htm. All registrations and payments must be received by the first week of September. Registration as soon as possible is recommended to ensure receiving desired hotel reservations and football tickets.
They learned muscles and vessels, and nerves and bones,
  And proteins and acids and lipids and carbs,
  And slides with stains and cultures of strains,
  And bugs and drugs and heme and derm,
  And hearts and lungs and kidneys and livers,
  And neuro and psych and endo and repro…

From “Joseph’s Coat”
The 82nd annual Galens Smoker, *Joseph and the Amazing Monocolor White Coat*, brought a return to the time-honored Smoker tradition of looking to Broadway for inspiration, with the performance borrowing from Andrew Lloyd Webber and Tim Rice’s 1973 musical, *Joseph and the Amazing Technicolor Dreamcoat*. In the program notes, the Smoker “czars,” Craig Barkan, Pooja Mittal, Erik Bauer and Mandy Bauer, noted the theme: “While what goes around comes around, some ties, like those in your family — or with classmates — are stronger than even the all-too-human desire for revenge. We also learn that the seemingly unattainable can sometimes fall within our grasp: it is indeed possible for a Smoker to have a plot.”

The production was presented to enthusiastic audiences on April 21 and 22 at the Lydia Mendelssohn Theater. The annual Silver Shovel Award, first conceived by J. Robert Wilsson, president of Galens in 1937, as a tribute to the popularity and teaching ability of radiologist Fred Jenner Hodges, was presented by last year’s honoree, endocrinologist Robert Lash, to Andrew Flint, professor of pathology.
Greeting members of the MCAS Board and their guests at a special dinner on March 17, 2000, to celebrate the Alumni Society’s 40th anniversary, Medical School Dean Allen S. Lichter proclaimed his belief that even with 150 years of illustrious history to its credit, “the best years of our Medical School lie ahead of us.”

Praising MCAS as an organization that helps keep the Medical School vibrant and thriving, Dean Lichter and Gil Omenn, M.D., Ph.D., executive vice president for medical affairs, congratulated MCAS on its own four decades of history and its superlative record of involvement in the affairs and future direction of the School.

(Top) Lynne and Raymond Ruddon (M.D. 1967), and Jeffrey Dunn (Residency 1977)

(Above left) Fourth-year student Samir Gupta, George Blum (M.D. 1955, Residency 1957), John and Mary Weg

(Above right) Fourth-year student Craig Barkan, Tom Varbedian (M.D. 1956), and Jaime Baker Knauss (M.D. 1981)

(Right) George Morley (M.D. 1949), David Burkons (M.D. 1973), and Gordon Kauffman (M.D. 1972)
In the past year, the more than 140 alumni/ae of the Medical School listed below volunteered to serve as a resource to Medical School students in the coming year through the Alumni Host-Resource Program, please contact Michael DeBrincat at (734) 998-8107.

**1940s**
- Ada G. Yancey Sr. (M.D. 1941), Atlanta, Georgia
- Donald Cooper (M.D. 1942, Residency 1950), Devon, Pennsylvania
- Paul E. Hodgson (M.D. 1945, Residency 1952), Omaha, Nebraska
- Martin E. Feferman (M.D. 1946), South Bend, Indiana
- Robert P. Dobbie (M.D. 1946, Residency 1953), Lincolnshire, Illinois
- Ruben S. Kurnett (M.D. 1948), Birmingham
- Joseph H. Leek (M.D. 1948), Duluth, Minnesota
- George W. Morley (M.D. 1949), Ann Arbor

**1950s**
- William A. Anderson (M.D. 1950, Residency 1954), Orange, New Jersey
- Allen Susin (M.D. 1952), West Bloomfield
- Robert D. Currier (M.D. 1952, Residency 1957), Jackson, Mississippi
- William H. Bartlett (M.D. 1953), Madison, Wisconsin
- Allan D. Weiner (M.D. 1953), Farmington Hills
- William L. Kopp (M.D. 1954, Residency 1962), Jackson, Michigan
- Gerald A. Abrams (M.D. 1955, Residency 1957), Ann Arbor
- George L. Blum (M.D. 1955, Residency 1957), Southfield
- Thomas G. Varbedian (M.D. 1956), Bloomfield Hills
- John C. Floyd Jr. (Residency 1957), Ann Arbor
- Gerald O. Strauch (M.D. 1957), Winnetka, Illinois
- Thomas C. Murphy (M.D. 1957, Residency 1960), Evanston, Illinois
- Neal A. Vanselow (M.D. 1958), Residency 1963, Rio Verde, Arizona
- Herbert Kauffer (M.D. 1958, Residency 1964), Lexington, Kentucky
- Bruce A. Work (M.D. 1959, Residency 1967), Augusta, Georgia

**1960s**
- Melvin H. Johnson (M.D. 1960), Battle Creek
- Grant L. Hailer (Residency 1961), Chaker Heights, Ohio
- Robert P. Christopher (Residency 1963), Memphis, Tennessee
- William H. Gaasch (M.D. 1963), Auburndale, Massachusetts
- Brian L. Hotchkiss (M.D. 1963), Grand Rapids
- Raymond W. Rudden (M.D. 1967), Skillman, New Jersey
- Harold M. Frideman (Residency 1964), Hanover, New Hampshire
- Walter D. Dishell (M.D. 1964), Encino, California
- James E. Delavan (M.D. 1964, Residency 1971), Grand Rapids
- Lance A. Talmage (M.D. 1964, Residency 1973), Toledo, Ohio
- Dennis W. Shermata (M.D. 1965, Residency 1971), Sedona, Arizona
- Harvey E. Dondershine (M.D. 1966), Palo Alto, California
- Paul Helman (M.D. 1966), Evanston, Illinois
- Glenn Peter Verbrugga (M.D. 1966), Cadillac
- Gary D. Maynard (M.D. 1966, Residency 1971), Dallas, Texas
- Elizabeth L. Schmidt (M.D. 1966, Residency 1967), Dearborn
- W. Kirt Nichols (M.D. 1966, Residency 1973), Columbia, Missouri
- Eugene M. Esiner (M.D. 1967), Miami, Florida
- John E. O’Malley (M.D. 1967), Marrero, Louisiana
- Michael R. Pappaci (M.D. 1967), Dunwoody, Georgia
- Charles W. Newton (M.D. 1967, Residency 1972), Grand Rapids
- Gary S. Gutow (M.D. 1967, Residency 1973), Nashville, Tennessee
- Bruce Avery (Residency 1968), Knoxville, Tennessee
- Shirley B. Avery (Residency 1968), Knoxville, Tennessee
- Jack L. Berman (M.D. 1968), Los Angeles, California
- Irene S. Danek (M.D. 1968), Traverse City
- Charles J. Danek (M.D. 1968, Residency 1976), Traverse City
- Mortiz M. Ziegler (M.D. 1968), Boston, Massachusetts
- Kenneth C. Hilt (M.D. 1969), Ludington
- Alan Sugar (M.D. 1969, Residency 1970), Ann Arbor
- Michael E. Johns (M.D. 1969, Residency 1975), Atlanta, Georgia

**1970s**
- Harry Applebaum (M.D. 1970), Northridge, California
- Norman T. Berlinger (M.D. 1970), Minnetonka, Minnesota
- Raymond J. Weitzman (M.D. 1970, Residency 1975), West Bloomfield
- Richard L. Bucciarelli (M.D. 1970), Traverse City
- Marvin Bittner (Residency 1979), Omaha, Nebraska
- Susan B. Perry (M.D. 1979), Davenport, Iowa

**1980s**
- Jeffery A. Mono (M.D. 1980), Des Plains, Illinois
- Lindsay Carol Thomas (M.D. 1980, Residency 1984), Minneapolis, Minnesota
- Jamie Baker Knau (M.D. 1981), San Marino, California
- Timothy J. Laing (M.D. 1981), Ann Arbor
- Archebald J. Pequet (M.D. 1981), Waukesha, Wisconsin
- Jeffery K. Clark (M.D. 1982), Bloomfield Hills
- Martha Yacoos Daly (M.D. 1982), Los Altos, California
- Claude Fanelli (M.D. 1982), Wormleysburg, Pennsylvania
- Scott R. Pynnnonen (M.D. 1982, L’Anse
- Peter B. Manning (M.D. 1982, Residency 1988), Cincinnati, Ohio
- Charles A. Bush-Joseph (M.D. 1983), Hinsdale, Illinois
- David E. Goldath (M.D. 1983), Barrington, Illinois
- Frederick C. Green Jr. (Residency 1984), Phoenix, Arizona
- Jacqueslyn G. Lockhard (M.D. 1985), Farmington Hills
- Nicholas C. Saenz (M.D. 1986), San Diego, California
- Donald D. Thomas II (M.D. 1986), Burr Ridge, Illinois
- Alan J. Ruby (M.D. 1987), West Bloomfield
- Thomas D. Starkey (M.D. 1988, Residency 1990), Nashville, Tennessee
- Rakesh K. Gupta (Residency 1989), Dayton, Ohio
- Judith A. Shubitowski (M.D. 1989), Ann Arbor

**1990s**
- Alexander J. Lin (M.D. 1990), Chisinau
- James F. Chmiel (M.D. 1991), Cleveland Heights, Ohio
- Howard K. Weiner (M.D. 1991), Ann Arbor
- Norman Pflaster (Residency 1992, East Moriches, New York
- Charles C. Flippe (M.D. 1992), Indianapolis, Indiana
- C. Randall Smith (M.D. 1992), Athens, Georgia
- Vicken R. Vorperian (Residency 1993), Madison, Wisconsin
- Steven E. Dentz (M.D. 1993), Alexandria, Virginia
- David B.S. Dyke (M.D. 1993), Ann Arbor
- Melissa J. Howell (M.D. 1993), Fernport
- Robert D. Janke (M.D. 1993), San Antonio, Texas
- Ravindra V. Prasad (M.D. 1993), Durham, North Carolina
- Daniel R. Pritchett (M.D. 1993), Brooklyn, New York
- Bithika Sophat Kheterpal (M.D. 1993, Residency 1997), Ann Arbor
- Michael J. Harmoning (M.D. 1994), Grand Rapids
- John E. LaGorio III (M.D. 1994), Muskegon
- Stephen W. Brotz (M.D. 1995), San Francisco, California
- Carl A. Buccellato (M.D. 1995), Clinton Township
- Sandra L. Najarian (M.D. 1995), Lakewood, Ohio
- Corrinne Zachery (M.D. 1995), Delray Beach, Florida
- Bradley R. Bartos (M.D. 1996), Grose Pointe
- Elizabeth A. Bishnoi (M.D. 1996), Middleton, Wisconsin
- Louis J. Cubba (M.D. 1996), San Francisco, California
- Jayson S. Greenberg (M.D. 1996), Houston, Texas
- Michael J. Faulkner (M.D. 1996), Baltimore, Maryland
- Michael W. Schifere (M.D. 1997), Madison, Wisconsin
Message from the Executive Vice President for Medical Affairs

I am pleased to share with you the findings and recommendations of our year-long strategic planning effort for the U-M Health System. More than 125 people, as members of the strategic planning committees, participated in the planning process, and many others contributed valuable comments as well. According to our consultants, The Lewin Group, we had a most unusual degree of engagement of people throughout the Medical School, Hospitals and Health Centers, M-CARE, and other units of the University.

Our goals were to:

- Develop a shared vision and a common direction for the U-M Health System.
- Develop an integrated strategic plan linking education, research and patient care.
- Anticipate/assess future scientific, clinical, educational, organizational and financial opportunities and partners, as well as threats and competitors.
- Create an appropriate decision-making and conflict-resolving mechanisms.
- Provide a basis for setting priorities, allocating resources and deciding on investments.
- Lay a foundation for ongoing planning.

I believe we’ve made excellent progress addressing these goals. We are determined to “shape a positive future for academic medicine,” as my co-authors Allen Lichter, Larry Warren, Lee Bollinger and I outlined in the February 16, 2000, special issue of the Journal of the American Medical Association that was dedicated to the University of Michigan Medical School and its Sesquicentennial celebration.

The key themes of the strategic plan include creativity, innovation and integration; measurement of all aspects of operational and financial performance; fiscal soundness to enable success in meeting our mission and to permit investment; and greater satisfaction of patients, families, referring physicians, faculty, staff, students and others.

The strategic plan highlights our shared commitment to:

1. Continue to improve service to patients and their families through concerted efforts and positive attitudes of all Health System staff, upgraded systems, and improved signage.
2. Assure that our clinical programs and M-CARE remain competitive in quality, price, service and quantity so as to sustain positive operating margins, however tough the payment world. Compare ongoing clinical and operational redesign with best practices of regional competitors and national peers.
3. Expand development of comprehensive care centers that capitalize on clinical excellence and the technological and organizational advances of our research and medical management programs. Plan investments in comprehensive centers for cardiovascular disease, women’s and children’s health, transplantation, and depression, along the lines of our Cancer Center; additional possibilities are neurosciences and musculoskeletal.
4. Ensure we are making optimal use of existing facilities in all clinical, research, and educational programs. Reallocate space to improve productivity and accommodate additional grants to current faculty, while preparing to recruit new faculty for the U-M Life Sciences Initiative. Invest in information systems to enhance patient safety, quality, integration, and productivity across the Health System.
5. Enhance our Medical School ranking in research, based on proxies of NIH funding, citation indices, and competitive renewals of grants. Recruit additional excellent faculty, initiate more interdisciplinary proposals, utilize existing space as intensively as possible and create new research space in the future Life Sciences Institute and Medical Research Laboratory Facility.
6. Periodically enhance the curriculum to better integrate basic science and clinical education (starting clinical clerkships in mid-year II/inserting transitional science courses in year IV), utilize new technologies, create more self-learning and small-group experiences, and create lifelong learning relationships (Web-based and in-person) for graduates, resident alumni, referring physicians and others.
7. Improve our ability to attract, develop, and retain outstanding faculty, staff, and medical, predoctoral, and postdoctoral students. Expand the Biological Sciences Scholars Program. Participate very actively in the Life Sciences Institute, Initiative, and Corridor programs. Clarify faculty career ladders, enhance mentoring of faculty, staff and predoctoral and postdoctoral students, and provide greater recognition of outstanding performance in clinical, educational and research domains.
8. Streamline decision-making processes throughout the Health System and its units. Integrate operating and capital budgeting processes to achieve greater discipline and synergy in maximizing return and moderating risks from our investments.
9. Intensify the use of measurement of performance by a much broader array of Health System leaders as an essential element of planning, budgeting and rewarding performance.
10. Significantly increase philanthropic support to advance the full range of educational, research, clinical, and community service missions for both the Medical School and the Hospitals and Health Centers. Draw upon the loyalty, interest and generosity of alumni, patients and their families, faculty, staff, and other current and prospective benefactors.

For those currently within the Health System, the strategic plan can be accessed on the Web at: http://www.med.umich.edu/i/omenn/strategic. If you would like a print copy of the Strategic Plan, please call (734) 615-0574 and a copy will be mailed to you. I welcome your comments.

We are doing well in a very challenging and exciting time for academic medicine. Best wishes to all of you.

Gilbert S. Omenn, M.D., Ph.D.
U-M Executive Vice President for Medical Affairs
and CEO, U-M Health System