

medicine

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Champions in the Fight against Depression

U-M's collaborative team takes the lead

H I G H P R

When the nation needs experts and leaders in medical science, it often

by Jeff Mortimer

Francis Collins puts it succinctly.

"Having University of Michigan faculty involved in policy matters in Washington, D.C., is good on two counts," says Collins,

who knows whereof he speaks: He's the director of the National Human Genome Research Institute, and he's on leave from the U-M Medical School's Departments of Human Genetics and Internal Medicine.



Francis Collins

"First, it's good for the country," he says. "There are many issues being debated here that require sophisticated intellectual input, and Michigan faculty can provide that expertise. The legislative and policy apparatus in our nation's capital is hungry for objective information to guide good decision-making. Second, it's good for Michigan to have its faculty in the thick of things, adding to the University's prestige and recognition and making sure that the University's interests are heard."

His field has a high profile these days, which has helped make Collins perhaps the most celebrated of the impressive list of biomedical Wolverines inside the Beltway. Some, like Collins, are on leave from the faculty. Others have formally left it. But all of them retain their ties with, and affection for, the University.

In addition to Collins, that list includes:

- **Josephine Briggs, M.D.**, head of the Division of Kidney, Urologic and Hematologic Diseases of the National Institute of Diabetes and Digestive and Kidney Diseases

O F I L E

en turns to Michigan

- **Kathryn Clark, Ph.D.**, chief scientist for human space flight, National Aeronautics and Space Administration
- **Elizabeth Nabel, M.D.**, director of clinical research at the National Heart, Lung and Blood Institute
- **Gary Nabel, M.D., Ph.D.**, director of the Vaccine Research Center of the National Institute for Allergy and Infectious Diseases
- **Paul Sieving, M.D., Ph.D.**, director of the National Eye Institute and
- **Jeffrey Trent Ph.D.**, scientific director of the National Human Genome Research Institute

With the exception of Clark, they all work within the National Institutes of Health. “There was a period when it seemed we were gradually taking over the place,” says Briggs, who has held her current job for five years and is on leave from the Departments of Internal Medicine and Physiology. “We had a pretty steady influx.”

Despite occasional appearances to the contrary, the government doesn’t hire these people and bring them to Washington so they can be ignored. “Scientists and other content

experts do in fact get a hearing,” says Collins, “often by staffers, not members of Congress, but it’s the staffers who often determine the outcome.”

Rebuilding the Nation’s Research Infrastructure

Just as the above list is not exhaustive, so the ways in which U-M faculty serve the government, and the public, are not limited to shaping the national research agenda and keeping Congress up to speed on it, important as those activities are. For example, U-M Executive Vice President for Medical Affairs Gilbert Omenn chairs an Institute of Medicine panel on quality oversight in federal health care programs, and he testified on behalf of increased NIH appropriations for research infrastructure construction.

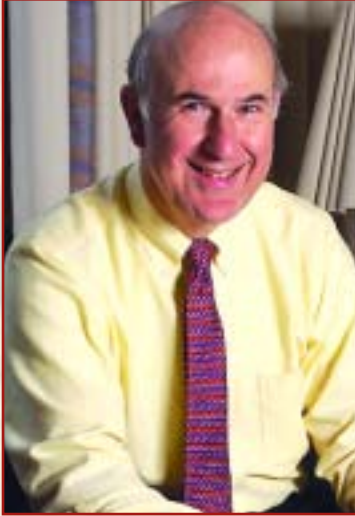
“The vast NIH budget is set up to support direct costs on individual research projects,” says Omenn. “Institutions are supposed to provide the facilities with which to conduct the research. The accumulated need in this country for new facilities and renovation of existing ones is in the hundreds of billions of dollars — such big estimates that NIH, the National Science Foundation, and the federal ▶



Josephine Briggs

ITS REPUTATION AND TRACK RECORD MAKE MICHIGAN A FORMIDABLE COMPETITOR FOR THE GLOBAL BENEFITS THAT FLOW FROM THE EFFORTS OF ITS PEOPLE IN WASHINGTON.

Photo: Martin Vloet



Gil Omenn

government as a whole threw up their hands and said, 'There's no way we can make a dent.' "

Wrong. A dent, perceptible if not huge, has been made. "The program that was funded and increased each year — we took it from 10 to 30 to 75 to 100 million dollars in successive years — has been very helpful," says Omenn. "In contrast to so-called earmarked programs, where a senator or an expensive lobbying firm writes a specific building with no competition into the appropriations language, this is a competitive program requiring matching funds."

U-M has been among the beneficiaries. Grants from the fund have gone toward equipment for the Functional Magnetic Resonance Imaging Unit of the Department of Radiology, renovations to the Kellogg Eye Center, and enhancement of nuclear medicine equipment and facilities.

"Construction and renovation is the hardest funding to get," says Omenn. Michigan got it because it was a good competitor, not because Omenn was a player in the process. But the resources might not have been there in the first place if the latter weren't the case, and the case illustrates several points.

First, although it obviously gives Michigan better access to the national research conversation, having past and present faculty in Washington is not a route to "insider trading."

"Once you become a government employee, you cannot give preferential treatment to one university versus another," says Elizabeth Nabel, who formerly served as director of U-M's Cardiovascular Research Center. "Knowing what I know about Institute initiatives, I can't go back to the faculty or leadership of the U-M and say, 'Hey, six months from now, this proposal is coming down the pike and you should start putting a grant together.' That has to be avoided."

"We thrive on competition and peer review," says Marvin Parnes, U-M associate vice president for research and executive director of research administration, "so our interest is not in earmarking or getting special allocations for the University. Our interest is in ensuring that there are adequate funds for us to compete for research dollars in areas that we think are intellectually exciting and important."

Second, although it doesn't directly profit from its contracts (in fact, says Vice President for Research Fawwaz Ulaby, "By regental directive, the University does not lobby federal or

state sources of funding"), its reputation and track record make Michigan a formidable competitor for the global benefits that flow from the efforts of its people in Washington and their peers.

"Many academic medical centers are in financial trouble," says Omenn. "The U-M is looked to either with astonishment or plaudits for expanding our research, investing in the research base, drawing top students and residents and faculty, and delivering patient care in a competitive, cost-effective, financially sound, high-quality way. People take notice. We don't draw anywhere near as many patients from the rest of the country beyond our state as the Mayo Clinic or Mass General or Johns Hopkins does, yet we have this high national reputation."

Photo: Marcia Lanford



Marvin Parnes

And an investment in infrastructure helps float all boats: research, teaching and service — the three explicit missions of the University, all of which commingle and com-

plement each other, and all of which are also well served in other ways by the Medical School's Washington presence. "We're not trying to increase our funding or secure material gains for the University," says Ulaby, "but an integral part of our responsibility as an institution and as individual faculty within the institution is to serve the public. This is a form of public service, for the pure purpose of serving our broader community. Period."

"We have definitely made a contribution to biomedical research in this country by sending some of our best scientists and scholars to NIH," says Dean Allen Lichter. "These senior level positions often have profound policy implications."

Or, as Jeffrey Trent puts it, "I can think of very few institutions that can actually provide pretty compelling evidence that they've impacted the breadth of the field of biomedicine and biomedical sciences the way Michigan has."

That impact stems from decisions on what to investigate, the quality of the research itself, the effectiveness of its dissemination to peers and students, and the range and utility of its applications.

Expanding the Horizons of Biomedical Science

The Vaccine Research Center that Gary Nabel directs was established in 1998 primarily for the implementation of former President Clinton's mandate of an AIDS vaccine within

10 years, but its focus has broadened, both in terms of the diseases targeted and the collateral benefits of its work. Nabel became its head in 1999, after 12 years on the faculty of the Medical School's Internal Medicine and Biological Chemistry Departments. He also was the director of the Center for Gene Therapy and co-director of the Center for Molecular Medicine at U-M.

"Our primary emphasis is HIV/AIDS," Nabel says. But the ripples spread wide. "Our philosophy is that in the process of developing vaccines for one agent, we develop certain core technologies that could be applied to other vaccines," he says. "Obviously, we want to make the most of the scientific and financial investment, and we work with other people to help move their efforts forward as well. As we develop these concepts and strategies, I'd like to think we expand the horizons of what we can do scientifically."

Those other efforts include developing vaccines that are unlikely to be profitable, and thus unlikely to draw much attention from the private sector. Although legion, the victims of scourges like Ebola and measles hardly constitute a lipitor-style market. While Ebola has been much in the news lately because of its potential as a bioterrorist weapon, Nabel has been on its trail since early in his U-M days.

"Markets can define society's medical needs to some extent, but they're not based on human health needs. They're based on economics," he says. "Ebola and other diseases like tuberculosis and malaria have ►



Jeffrey Trent



Gary Nabel

major impacts on world population, yet from a commercial point of view, vaccines for these microbial agents, or even an HIV vaccine, offer less incentive to the private sector. That's when we have to step up as citizens of the world and say this is important for people, and we're going to do our best to make something that will work. I'm all for letting the market do the job when the market can do it, but when it can't, when huge losses are sustained and there's no other way to deal with the problems, then we have to recognize that and do something about it."

Aside from a sense of social responsibility, why should this concern the First World? "The lesson that I learned by studying HIV beginning back in the 1980s is that any virus at any given point in time can evolve from being a rare isolated case to being a major worldwide human health problem," says Nabel. "Throughout human history, we have had to deal with outbreaks of different infectious organisms, and nothing magical has happened to say that era is behind us. We've had some remarkable successes with antibiotics, and we've saved a lot of lives with antibiotics, but you can go into any hospital any day and see people who are dying from resistant organisms. If we're lucky enough to develop a vaccine for AIDS in our lifetime, you can almost take it to the bank that there will be another epidemic, whether it's West Nile, Ebola, or an organism that we don't currently view as a threat."

Speaking of a widening ring of applications, being ready for that also means being ready for bioterrorism. "All the actions we need to

take to respond to bioterrorism outbreaks are those we need to take to respond to emerging infectious disease outbreaks," he adds. "One of the important challenges is not only that we develop vaccines for these untreatable diseases but that we develop approaches where we can make vaccines more quickly, identify emerging infections more rapidly, and protect the public health more effectively. In many ways, bioterrorism is just a form of a newly emerging infectious disease. Instead of emerging naturally, people are trying to take advantage of the biology of the organism and introduce it deliberately."



Paul Sieving

The Vision Thing: Impacting the National Research Agenda

Paul Sieving was named director of the National Eye Institute in 2001, having served on the Department of Ophthalmology and Visual Sciences faculty since 1985 and as

director of the Center for Retinal and Macular Degeneration.

Mastering the job is taking a while, he says, but he quickly understood that "the biggest part of it is the vision thing — the vision thing for vision," he chuckles. "And I'm beginning to enjoy that part of it. At the same time, there are realities in terms of budgets and space and people and energy and hours in the day. It's going to take a while to have everything converge on some products that I can hold up and say 'this is what I've accomplished.'"

The Institute released a much-publicized report in March predicting that the number of blind or visually-impaired Americans could double in the next 30 years as the baby boomers continue their implacable aging. "As the population gets older, the imperative for good vision care increases, and the Eye Institute and vision doctors and Kellogg Eye Center physicians and the Department of Ophthalmology at the U-M, all of us are going to be increasingly busy. I just hope that in the midst of being busy we don't lose sight of the fact of what the diseases are, so the next generation inherits some solutions from us."

Still passionate about his research, Sieving is dismayed by some current trends in that arena. "There's a lot of ego on the line in research, we all know that, but ultimately that research has to help people," he says. "When we set up potential theoretical roadblocks and 'protections of subjects' that are detrimental to finding answers that might help people, I'm bothered by that."



Elizabeth Nabel

Elizabeth Nabel says what attracted her to her current position was “the opportunity to have a beneficial impact on the national research agenda. I believe very passionately about the role of biomedical research in this country, and that we should be leaders in basic biomedical research and then translate those discoveries into new therapeutics that are going to benefit the public.”

On the other hand, she says, “While it allows you to establish a research agenda, I wear an Institute hat in making those research decisions. Often those are research programs or priorities that may not be aligned with my own personal interest, but I don’t wear an individual hat anymore. One must be a good steward of institute funds, which are taxpayer dollars. We have to ensure that those dollars are put to research programs that are going to directly impact the health and well-being of our public.”

Nabel has also made the health and well-being of patients in the clinical center of her institute’s intramural research program a top priority. “Since I’ve been here, I have put into place a system to support the conduct and monitoring of clinical research at the National Heart and Blood Institute to ensure that patients are adequately protected, that adverse events are promptly and responsibly reported, and that all research is being conducted in an ethical manner,” she says. “We have a responsibility to communicate this process to the public, so that the public can have trust in our ability to conduct and supervise clinical research in this country.”

That trust is undergirded by what might be called the ethical infrastructure, the design and support of which are integral components of the medical science enterprise. “As more and more of our ‘progress’ rests on science and research, it’s important to know what the social contract for research is and how it is formulated,” says Marvin Parnes. “What is the expectation attached to funding research? How do we manage the vision of the University as a place of great integrity, where it is only the pursuit of knowledge that should guide our activity, when that is intersecting with large amounts of federal funding? Is the understanding the same on both sides regarding what should be expected from that funding? You want the funding to be shaped by where the greatest good can be achieved.

“The perspective you gain as a researcher into what is truly required to advance knowledge is different than the view from the legisla-

ture,” he adds. “It takes someone who fully understands the complex interrelatedness of science to be able to articulate the agenda. For example, realizing how much discovery-driven rather than product-driven research has to go on to provide the necessary groundwork for disease cures, and that it might be less productive if one were only to focus on specific outcomes. We can’t neglect basic science and engineering funding if we want to address disease. Scientists understand this.”



Photo: Marisa Leiford

Howard Markel

A Real Obligation to Inform the Public

Although he’s still in Ann Arbor, Howard Markel (M.D. 1986), Ph.D., participates in the national conversation by writing for *The New York Times* and *Harper’s*, among other general interest publications. A professor of pediatrics and communicable diseases, director of the Historical Center for the Health Sciences, and the George E. Wantz Professor of ➤

the History of Medicine, Markel sees his role as a contributing medical correspondent and columnist as completely consistent with his other duties as a physician and scientist.

"Physicians in the academic arena, in particular, have a real obligation to make sure that the very wide constituency that we serve is informed about what we do," he says. "All of us who do research are serving the public."

He served the public in April 2001 by co-authoring a front-page story in the *Times* on studies showing that babies now start crawling later, if at all, due to being placed on their backs more to prevent sudden infant death syndrome. "A lot of parents worry about every little developmental milestone, and to be able to reassure people in this way was really quite gratifying," he says. "It was just fun to get the information out there. For me, my writing is an extension of my role as a professor. I'm an educator. Sometimes I educate in the classroom, sometimes in the clinic and sometimes in the journalism arena. They're all extremely legitimate and extremely important venues."

It's clear that the Medical School's national presence pays off for the public, the government and the research community. It's more difficult to specify how it's an advantage for the School. How does one assign a value to the experience of seeing Francis Collins end his remarks at the 2000 commencement ceremony by picking up his guitar and accompanying himself in one of his satirical songs? How does one prove he wouldn't have done the same at Harvard or Johns Hopkins?

But the payoffs are real, even if the evidence is anecdotal, and they range from sharing in the general societal benefit that that presence helps generate to knowing the person on the other end of the line when you need help from someone in Washington.

Says Gary Nabel: "We often can help triage when we talk to people and they say, for example, 'We're having a horrible problem finding a supply of nonhuman primates for x, y or z,' and I can tell them that's a global problem at NIH and these are the people that are dealing with it and this is how you might get some help. We can help direct people to the best sources of advice to solve a problem, whether it's an administrative problem or a scientific problem. As with most of academic medicine, the value of information and communication is really hard to overestimate. That's probably the most important way that we help one another."

Nabel says he has also steered some promising scientific talent toward Ann Arbor. "There are a lot of talented young investigators here at NIH," he says. "When they go off looking for opportunities in academia, we can point them back to Michigan and start to direct some of the newer talent to the University."

Paul Sieving views such nudging as at least appropriate, if not an actual civic duty. "I simply view the University of Michigan as a very strong university, and in terms of the educational needs of the country, having the University of Michigan even stronger makes it an even better national resource," he says.

"I'm all in favor of keeping the energies flowing both ways, from the University into me and those of us who have moved on, and back to the University. One wants always to be careful not to overtly favor the institution one came from, but the reality is there are a limited number of very strong places in the country, and new young strong scientists need to make contacts back into that strong bed of institutional science in order to develop as fully as they can."



Kathryn Clark

The 'Halo Effect'

What might be called the "halo effect" can also be useful in luring luminaries. "The University of Michigan becomes more visible at NASA because of my presence there," says Kathryn Clark, on leave from the Department of Cell and Developmental Biology, "and Michigan has the ability to dance on that a little bit because NASA is hands-down the

government's favorite entity. The NASA logo — we call it the meatball — is the most recognized non-corporate logo in the world. I have been told that even among corporate logos, the only one that beats us is Mickey Mouse. So there is some visibility for the University to have somebody stationed there, especially as chief scientist."

People from U-M, in turn, are clearly attractive to Washington. "Because of its strong research programs, it's a source for NIH of people who are both superb scientists and have worked in a complex institution as managers," says Marvin Parnes. "It's the right constellation of talents. Much like our provosts go off and become presidents: if you can run something here, you can run something anywhere."

Michigan's emphasis on interdisciplinarity is another high card in the deck. "It is very critical, with the kind of science that has to happen nowadays, to not approach the problem with the perspective of any one discipline," says Josephine Briggs. "At Michigan, certainly in the Department of Internal Medicine, we were eager to be as non-discipline-bound as possible. That certainly continues to be a focus here at NIH."

It's a focus for Clark, too. "My job is to represent all the science possible on the space station at advisory committee meetings, in the general world, in talking to engineers," she says. "My knowledge in physiology was helpful but I was responsible for everything that went into the space station, so I had to learn all of it."


And then there's, well, the vision thing. "It was an absolutely terrific experience to be surrounded at Michigan by outstanding scientists who had the vision to want to affect their fields more broadly," says Jeffrey Trent. "Michigan provided a venue to do that in allowing a number of these people [who are now in Washington] to be involved in major program initiatives there."

The word "fun" frequently surfaces in their conversations, but so does the challenge of juggling their own research activities with the exigencies of managing such large operations. Says Briggs: "That's one of the challenges of these jobs — the administration of science, which is really what we do here, requires real active proximity to the scientific issues. I think if you have people who function just as administrators and aren't centrally engaged in the questions, the quality of the administration would not be as good."

"Right now, I am needing to let go at some level of my own research agenda and see that agenda being accomplished by other people," says Sieving. "At the same time, I can never let go of that agenda because scientists thrive on science."

The Medical School's "faculty alumni/ae" don't let go of their ties to Michigan, either. Although Gary Nabel says his job at the Vaccine Research Center has been "a very fulfilling experience and a unique opportunity; it's not very often that you can build a new effort literally from the ground up," he also says, "we [he and Elizabeth Nabel are married] didn't

leave Michigan lightly. We loved it there, and we still think very fondly of our days in Ann Arbor. If it weren't for the fact that we would be unable to do what we're doing in any other way, I don't think we would have come."

"I bet you can't find any of us that don't look back fondly at our time at Michigan," says Trent, "and the longer we're gone, the more we miss it." 

ON THE 'FINAL FRONTIER'

Kathryn Clark met John Glenn when she was a 10-year-old girl in Silver Lake Village, Ohio, and she hasn't been the same since.

"It was so inspirational to me that I still carry the picture of the two of us in my wallet," says Clark, "and it's been a long time since I was 10. I want to be an astronaut in the biggest way. I started to apply to the astronaut corps several years ago and continue to update my application every year. I have friends who applied for up to 14 years before being successful," she says, "so I'll just keep on trying."

In the meantime, she has at least made it to the National Aeronautics and Space Administration, where she's worked since 1998 while on leave from her position as a research investigator in the Department of Cell and Developmental Biology. Clark joined NASA as the first woman to serve as the International Space Station's senior scientist, a job limited to two years so it can be rotated among specialties as well as individuals. At the end of their term, "Most people retire or go back to their home institutions," she says.

But the agency had other plans. "I was getting ready to go back to Michigan," Clark recalls, "and my boss [Joe Rothenberg, associate administrator for the Office of Space Exploration] walked into my office and said, 'What do I have to do to keep you here at headquarters?' And I said, 'Give me a job.' So they created my current position."

Her intergovernmental personnel agreement, the formal procedure whereby faculty are granted leaves for such service, was renewed for two more years, and she became chief scientist for Human Exploration and Development of Space, one of five so-called "enterprises" (*Star Trek*, anyone?) within the agency. The others are Biological and Physical Research, Earth Science, Aeronautics, and Space Science.

Clark's father was a physician "and I worshipped him," she says, "so I was interested in how things worked in the body — and then broke — from a young age." She came to Michigan for graduate school in 1981 from the College of Wooster, earning an M.S. in education from the School of Education's Department of Physical Education and a Ph.D. in kinesiology after that department became the School of Kinesiology. "I actually got to help with that change," she says, "and I never moved."

CLARK'S PRIMARY SCIENTIFIC INTERESTS ARE NEUROMUSCULAR DEVELOPMENT AND ADAPTATION TO ALTERED ENVIRONMENTS, SO IT'S CLEAR HOW HER EXPERTISE FITS WITH NASA'S MISSION.

Her primary scientific interests are neuromuscular development and adaptation to altered environments, so it's clear how her expertise fits with NASA's mission. But what she really likes to do is educate, formally or informally, within or outside the walls of the agency, whether it's fourth graders in a classroom, members of the U.S. Congress, the movie and television producers for whom she consults, or the scientists all over the world that she meets with as part of her job.

While Clark was deputy director of the Center for Microgravity Automation Technology, a NASA commercial space center in Ann Arbor, she assisted with a ladybug experiment that flew on the 93rd space shuttle mission and served as a pilot for a larger education program aimed at inspiring students to study math and science. "A group of girls from Chile designed the experiment to see if ladybugs could still eat aphids, and therefore act as a natural pesticide, while in microgravity," Clark says. "The answer is yes, they can. But there is also some indication from the experiment that aphids breed faster in space than on the ground."

The project, one of seven that she's flown on the space shuttle, had other results, too. Although the Center for Microgravity Automation Technology faded into history shortly after Clark left it to go to Washington, the education program survived. It's now called Launching Education into Orbit, and

plans are in the works to get student experiments to the International Space Station.


Even commuting time can be valuable. Clark returns virtually every weekend to the Ann Arbor home she shares with her husband, Robert Ike, M.D. (Residency 1985), an associate professor of rheumatology in the Department of Internal Medicine. "I fly with a lot of the congressmen," she says, "which can be kind of a benefit."

A pilot herself, she's also an avid cyclist, swimmer and cross-country skier, and was one of the first inductees when the National Women's Museum opened in Dallas in 2000. "I've never put much time into worrying about being a woman in anything I do," says Clark. "Some people tell me that this is why I have my job, because they needed a woman. Other people tell me that I must have to struggle hard because I'm a woman. I feel that if you do your job well and with enthusiasm and you're not obnoxious, nobody really cares."

It's spreading the word that lights her fire. In addition to "KC," a high school nickname that stuck, she's also been dubbed a "space station ambassador," having logged more than 600,000 miles, worked at 16 shuttle launches, given more than 100 speeches and briefings, and brought together scientists in 10 fields from 16 countries to work on getting science into the space station.

"I spend most of my time talking to other scientists, both around the agency and around the world, about ways to collaborate in how we're going to explore," she says. "Going to Mars, going to Europa, the Hubble Telescope, all the things related to exploration, I get to talk about. It's phenomenal. It's

absolutely great. I've been all over the world. I've done only five continents — I haven't yet dipped into Africa or the South Pole, but I have been to the North Pole."

And Hollywood. She was the technical consultant for the feature films *Mission to Mars* and *Space Cowboys* and is currently working on a pilot for a television series, as well as with director James Cameron, of *Terminator* and *Titanic* fame, on a movie set on Mars. "When you take the elevator up to Jim's office, the actual terminator is standing right in front of you as you exit. And the hand that's at the end of the first Terminator movie is actually sticking out of his desk," she says.  —JM



Kathryn Clark at age 10, with John Glenn