breakthrough

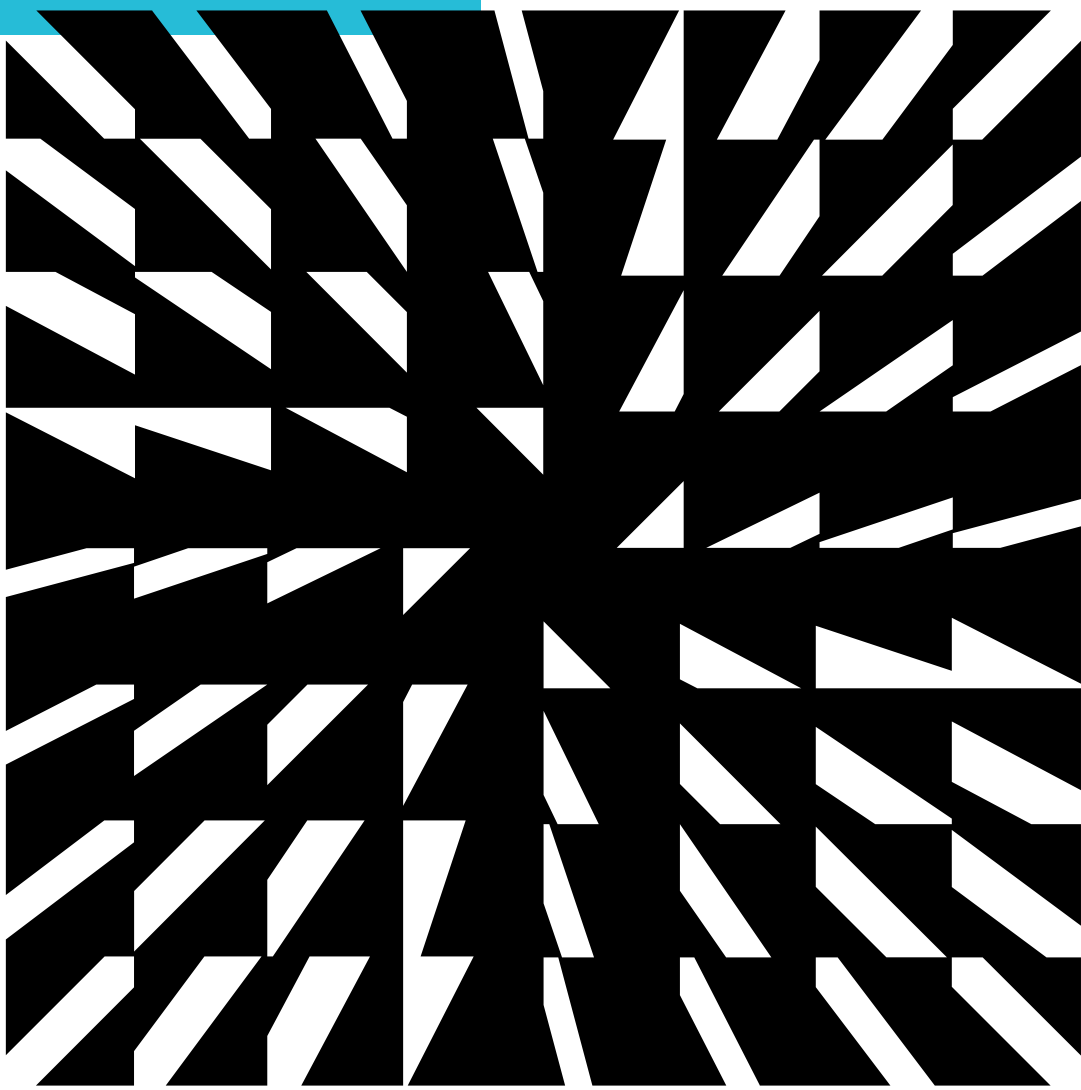
NUMBER 13 • SUMMER 2013

Is There Brain Injury?

What's Important to You?

The Brain in Your Gut

Helping Our Neighbors Get Healthier



Medicine is a public trust

THE JOHNS HOPKINS CENTER FOR INNOVATIVE MEDICINE

breakthrough

In this issue

David B. Hellmann, MD., M.A.C.P.
Aliki Perroti Professor of Medicine; Vice Dean, Johns Hopkins Bayview Medical Center; Chairman, Department of Medicine

"THE PRODUCTION OF HEALTH ITSELF"

As I write this, we have just celebrated two important events in our academic year: The Miller Lecture and the Miller Coulson Academy's Excellence in Patient Care Symposium (see Page 20). Our Miller Lecturer this year was Risa Lavizzo-Mourey, President and CEO of the Robert Wood Johnson Foundation. As I listened to her excellent lecture, I was pleased to hear that the goals she named for the future include many of the same things that we feel are important here at the Center for Innovative Medicine. Dr. Lavizzo-Mourey mentioned a Hopkins fourth-year medical student named Helen Prevas, who was shadowing Miller-Coulson Academy physicians in the clinic and was struck by how much their patients "adored and trusted" them. She asked one of her teachers how a student could ever hope to reach that point. Her teacher said, "I learn them inside and out as a person. The medical part comes afterwards." That is part of clinical excellence, and it is also the key to our Aliki Initiative (see Page 14).

Dr. Lavizzo-Mourey talked about food deserts and neighborhoods in the grip of urban blight. On Page 18 in this issue of *Breakthrough*, one of our CIM Advisory Committee members, Jacky Jennings, talks about the role of Hopkins faculty in making some exciting changes in Baltimore City. She talks about maintaining the health of the community, and on Page 10, another one of our CIM Advisory Committee members, Constantine Lyketsos, discusses how Johns Hopkins Bayview and Johns Hopkins Hospital are leading the nation in improving the health of our closest neighbors. The goal of doctors and hospitals is changing, she said, from taking care of sick and injured people to "the production of health itself." To me, that is what the CIM's core belief, that "Medicine is a Public Trust," is all about.

In this issue, we have exciting research to report on brain injury markers (see Page 4), some new thinking about finding the cure to diseases such as Alzheimer's (see Page 12), our world-renowned Scleroderma Center (see Page 16), and a new center of Neurogastroenterology – a long word for what its director, Jay Pasricha, describes as "the brain in your gut" (see Page 8).

Finally, I am honored to tell you that the Johns Hopkins Bayview General Internal Medicine Practice is the first academic primary practice at Johns Hopkins to be recognized as a Patient-Centered Medical Home by the National Commission for Quality Assessment. This remarkable achievement reflects the collaboration of our School of Medicine faculty in general internal medicine and members of the Johns Hopkins Community Physicians, many of whom have been written about in these pages over the last few years. It was truly a team effort.

Best wishes,

4

Is There Brain Injury?

Proteomics Center scientists may have found a new way to tell that the brain is in trouble, while there is still time to repair the damage.

What's Important to You?

Finding out from patients with a chronic illness how their lives are affected, and what they want to be able to do.

6

8

The Brain in Your Gut

Why the link between your belly and brain may be extremely important.

Helping our Neighbors Get Healthier

20 years. That's the difference in life expectancy between two sets of people who live right here in Baltimore.

10

12 Helping the Aging Brain

14 It's Just a Phone Call

16 Three Simple Rules

18 The Liquor Store Next Door

20 Creating A Culture of Health

WE BELIEVE

Medicine belongs to the public. Our mission is to create a different kind of academic medicine, to tear down ivory towers, share knowledge and dedicate ourselves toward one goal – making life better for patients.

BREAKTHROUGH is published by The Johns Hopkins Medical Institutions, Baltimore, MD 21287-2101.

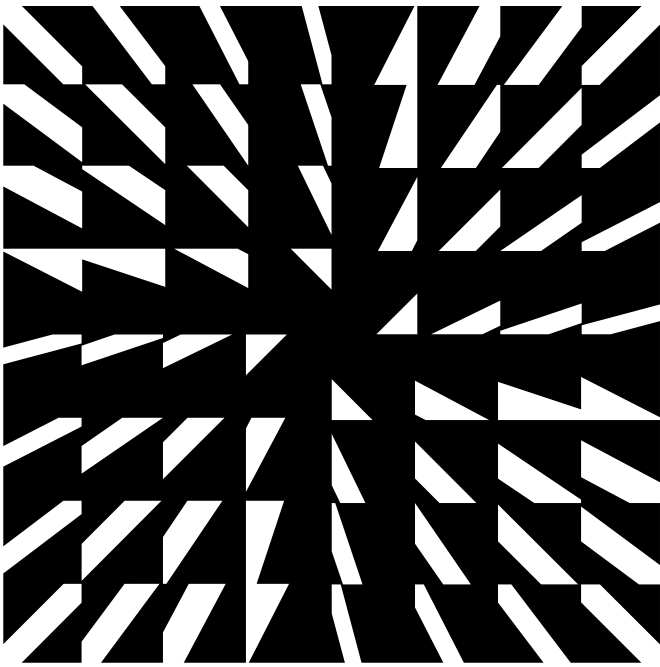
Director: David Hellmann, M.D.
Writer/Editor: Janet Farrar Worthington
Design: Skelton Design

on the web

If you'd like to learn more about the Johns Hopkins Center for Innovative Medicine, please visit our website: www.hopkinsmedicine.org/innovative

Is there Brain Injury?

Among their many other functions, proteins are the journalists of our bodies, sending out a constant and detailed description of what's happening in the cells. The tickertape may read simply that all is well. Or it could report that something is very wrong – a heart attack, perhaps, or loss of blood flow to the brain. When this happens, certain key proteins are released into the bloodstream, shouting their message that tissue is hurting, even if we can't feel it.



Jenny Van Eyk, Ph.D., director of the Amos Family Proteomics Center and a pioneer in deciphering these exquisitely tiny protein signals, believes that the whole tale of every second of every day is there to be deciphered – if scientists can figure out what to look for and how to read it. Recently, she and Johns Hopkins Children's Center pediatric cardiologist Allen Everett, M.D., have made exciting progress in the area of brain injury in children. Their findings could have huge implications for adults, as well.

"We have found some proteins that we think are biomarkers of brain injury," says Everett. He and Van Eyk have been running studies to validate the significance of their findings in various clinical conditions. Their results have the potential to give doctors a new test – something new to look for, a new way to tell that the brain is in trouble, while there is still time to repair or minimize the damage.

What are these proteins? Well, there are several, and they have been identified in different groups of children, through different studies and with different assays. In particular, they come from glial cells – considered the "glue" of the nervous

system – which perform several critical jobs in the brain. They help neurons by supplying nutrients and oxygen and insulating them with a protective blanket called myelin. Some of these glial cells are star-shaped; these are called astrocytes, and they make glial fibrillary acidic protein (GFAP). When something bad is happening in the brain, GFAP shoots into the blood. As Everett and Van Eyk have discovered, it is a distress signal. For example:

- In one study of infants in the neonatal intensive care unit who had a loss of oxygen at birth, when blood levels of GFAP were elevated, serious brain injury was more likely to have occurred. "Biomarkers such as GFAP could help triage neonates" allowing doctors to identify infants with severe injury who need extra treatment, concluded Everett and colleagues in the *American Journal of Obstetrics & Gynecology*.

- In another study, published in *Pediatric Critical Care Medicine*, Everett and co-investigators found that elevated blood levels of GFAP in children who receive continuous cardiopulmonary bypass was "significantly associated with acute brain injury and death."

These proteins have the potential to give doctors a new test – something new to look for, a new way to tell that the brain is in trouble, while there is still time to repair or minimize the damage.

- Premature infants are at high risk of cerebral palsy, an often-devastating condition, traditionally is not diagnosed until weeks to months of life, when doctors use ultrasound to look for injury to periventricular white matter (this finding is called PWMI) in the brain. In an article just published in the *American Journal of Obstetrics & Gynecology*, Everett and colleagues reported that "the ability to predict PWMI with a blood test…shortly after birth opens the possibility for rapid identification of infants for early intervention."

"Two completely different projects collided to make something that's pretty cool."

Everett and Van Eyk have expanded their studies, and are looking at adults as well as children who are at risk of brain injury – including patients who undergo heart surgery, and adults who come to the Emergency Department with intracranial hemorrhage. "It's starting to evolve," says Everett. "We have more assays that we are developing that represent other cell types in other parts of the brain. We hope they'll give more of a complete picture of what the injury is to the brain."

Several of the proteins have modified forms; this happens through a process called citrullination, and it may allow for the brain marker tests to be even more specific. "Some of the citrullinated sites appear to be unique to different disease settings," says Van Eyk; a paper about this finding is due to be published soon. "We're hoping that these modified forms will be almost like a time stamp of injury, so we would have an additional ability to gauge not just the severity, but *when* the injury occurred. This becomes very important when we're talking about stroke, or monitoring after surgery. It's really a beautiful group of proteins." Johns Hopkins has provisional patents on these markers and has licensed them to a company called Veracis, Inc., located on the Johns Hopkins Bayview Campus.

Currently, GFAP is being measured in a blood test that's processed in the research lab. "It takes about two and a half hours from taking the blood sample to getting results," says Everett, but he and Van Eyk hope to reduce this time dramatically and to develop a "point of care" test, "to get a more rapid readout of when brain injuries are occurring." The goal is to detect the injury during that critical window of time before damage is irreversible. "This is basically like a heart attack of the brain," he adds. "The quicker you can intervene, the better the long-term outcome. Being able to learn this as quickly as possible becomes a real key."

CONTINUED ON PAGE 22

What's Important to You?

Alice has rheumatoid arthritis. When she visits her doctor, she is looking better, in terms of pain and inflammation, which is good. But she is not sleeping well, and the constant fatigue is interfering with her ability to take care of her husband, who is disabled. This is what matters the most to her. How can her doctor work with her so that she can achieve this goal?

Alice's goals may be different from those of Tim, who also has rheumatoid arthritis (RA), and is sitting out in the waiting room waiting for his own appointment. Trying to help both of these people reach their objectives is an example of personalized medicine. The Federal government thinks this aspect of the doctor-patient partnership is so important that it has created an entirely new grant-making mechanism devoted to it. One of the first pilot projects funded has gone to rheumatologist Clifton Bingham, M.D., Director of the Johns Hopkins Arthritis Center, who is studying methods to improve patient-centered care for people living with rheumatoid arthritis. The Patient-Centered Outcomes Research Institute (PCORI, pronounced "picori) funding that Bingham has received is for something critical to the wellbeing of people suffering from chronic illness: It's finding out from patients what specific aspects of their lives are affected by disease, what is most important to them, and what they want to be able to do.

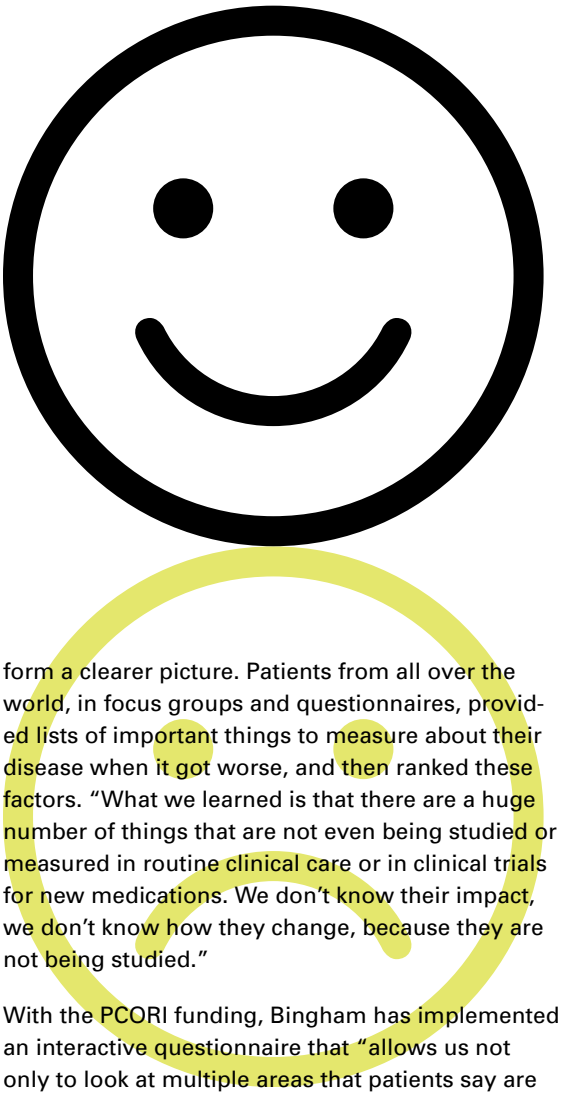
For example: Bingham takes care of many people like Alice and Tim. He has ways to monitor their physical signposts, like the number of swollen and tender joints; he has lab tests that quantify certain inflammatory markers in their blood. He can look at those numbers – determined by experts as the best outcomes to measure – and evaluate their responses to therapy, and based on these he might think, "Hey, they're doing well." But this may have little to do with what's going on in their lives and how they really feel.

With the funding from PCORI, Bingham has implemented an interactive, computer-based questionnaire that incorporates the perspectives of RA patients into their clinical care. "Instead of looking at abstract outcomes determined for groups, we need to start looking at the individual patient as the center of the disease," he says. "It's not enough for the doctor to say, 'This clinical trial says you have an 80-percent chance of getting 20 percent better in terms of your swollen and tender joints,' when the patient is wondering, 'Will this help me function better? Will I be able to do my job, or play with my children?'"

Already, after just a few months, he is seeing a changing dynamic in physician-patient communication at Johns Hopkins Bayview. This approach, Bingham notes, is stirring the pot nationally, "causing a tension between how things have always been done – measuring objective outcomes – and instead focusing more attention on the patient-centered view."

"A patient is feeling fatigued. Maybe that's coming from his rheumatoid arthritis. Then again, maybe it's because he's not sleeping well. Or maybe there's also depression.

Bingham has long been interested in this type of research. Several years ago, in a project for an international consensus organization called OMERACT (for Outcome Measures in Rheumatology), he led a work group that included patients from the get-go in planning a research study. One feature of a disease like RA is that "it is never static," Bingham continues. "Even when patients are feeling good, they have periods of worsening and improvement. We recognized that we did not understand how to study what we call a 'flare' of disease," and hoped that including the patient's perspective would help



form a clearer picture. Patients from all over the world, in focus groups and questionnaires, provided lists of important things to measure about their disease when it got worse, and then ranked these factors. "What we learned is that there are a huge number of things that are not even being studied or measured in routine clinical care or in clinical trials for new medications. We don't know their impact, we don't know how they change, because they are not being studied."

With the PCORI funding, Bingham has implemented an interactive questionnaire that "allows us not only to look at multiple areas that patients say are important, but to measure those with a high level of accuracy, and compare the level with that of the general population." For instance, 'we ask about pain, not only the amount of pain that people are having, but the impact that pain has on what they want to do. Our patients say, 'Don't ask me about the pain, ask me about what I'm *not doing* because of the pain.' Now we can assess that, and also look at sleep, physical function – what people can and cannot do – plus depression, anger, and anxiety that patients report are important pieces of their disease in various stages." The questionnaire also tackles life activities at home and at work, and how satisfied patients feel with their ability to perform in various areas.

Patients fill out the questionnaire before they see the doctor. Then they see the physician, as usual. The doctor and patient look at the questionnaire to see what they've missed. "Here's where the discussion becomes very interesting," says Bingham. "For example, we can identify that even though pain might be well controlled, a patient has significant levels of fatigue that can be incapacitating. Then, from the provider's perspective, the discussion becomes a need to understand what is driving that fatigue. Is it RA? Is it because the patient is not getting good sleep? Is it because there's a component of depression? We can see whether it's purely fatigue, or fatigue that tracks with depression and lack of sleep. This begins to allow not only an enriched conversation about what matters to the patient, but also about things that may not have come up in the clinical encounter. We have seen a number of patients in whom depression comes up at a very high level. It hasn't really been addressed in the visit, and the patient may not even have said anything about it. That's the power of this. It's not just that it's something to measure, it's that the measure enables conversation, understanding and, we hope, will lead to our ability to address these factors and improve quality of life."

"Will this help me function better? Will I be able to do my job, or play with my children?"

The patients seem to appreciate this extra dimension to their visits, Bingham says. "They say, 'Nobody's ever asked me this before,' or, 'Those questions were really hard. I have never even thought about these things.' There's an empowerment that comes from this."

Bingham believes this kind of discussion is a natural outgrowth of the Center for Innovative Medicine's projects, including the Aliki Initiative. "This is a philosophical change, part of everything David Hellmann's been doing so we can get to know our patients better and focus our treatment based on what they say is important. I am very hopeful that this project will move forward into other rheumatological diseases and be integrated into other clinical and research settings." ■

The Brain in Your Gut

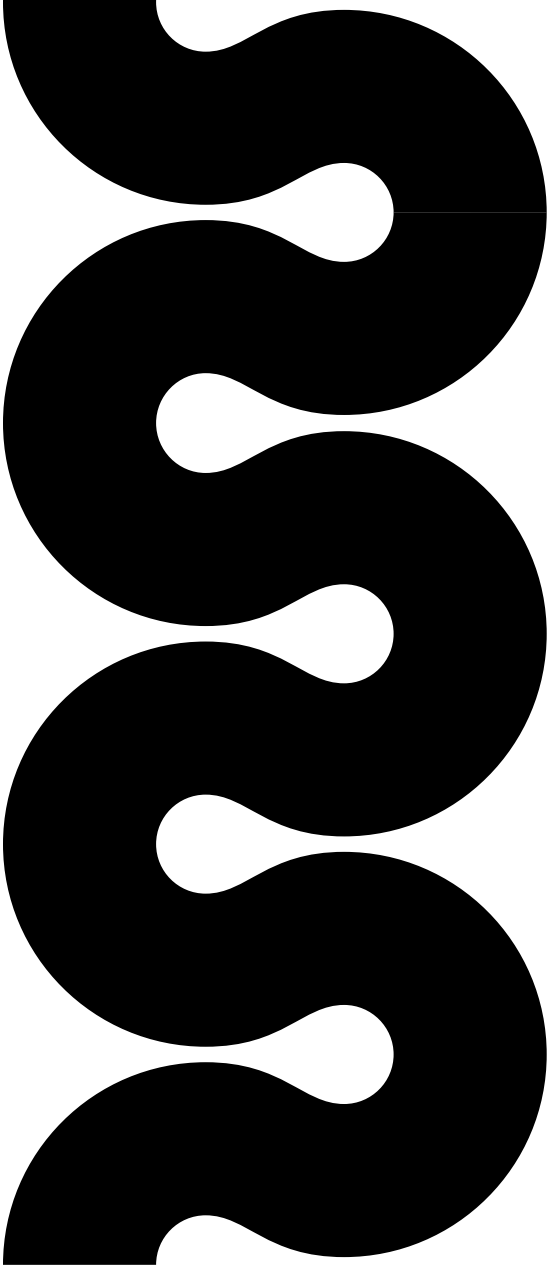
If you've ever had a gut feeling, felt butterflies in your stomach, or experienced cramps at times of high stress, then you know all too well that there's a link between the belly and the brain. But maybe you didn't realize how intricate and how very intimate this connection is – and how much scientists still need to learn about it. For instance:

- There are as many neurons in the gut as there are in the spinal cord.
- These intestinal nerve cells crank out 90 percent of the body's serotonin and half of its dopamine.
- Many of the same drugs used for anxiety and depression are used to treat irritable bowel syndrome and dyspepsia, although how they work is not well understood.
- As many as 40 percent of people who come to the doctor with gastrointestinal problems suffer from disorders like irritable bowel syndrome and gastroparesis that involve the enteric nervous system – the massive highway of nerve cells lining the muscular walls of the esophagus, stomach, intestines, and rectum.

"The gut has its own brain," says Pankaj Jay Pasricha, M.D., gastroenterologist and neuroscientist, director of the Center for Digestive Diseases at Johns Hopkins Bayview. Pasricha has recently created the Johns Hopkins Center for Neurogastroenterology and Gastrointestinal Motility Disorders, one of just a handful of such centers worldwide, to explore this gut-brain axis. "People think about the big brain," continues Pasricha, who also serves on the Advisory Board of the Center for Innovative Medicine, "but this little brain in the gut is very important, as well. These two brains talk to each other all the time. We now know that disturbances in the environment of the gut – tiny changes in the gut's microflora – can affect the mood, causing depression and anxiety." In turn, sadness, happiness, and all the emotions in between can influence the gut's motility. Motility, basically, is the functioning of the conveyor belt of muscle contractions and nerve impulses that moves food – like toothpaste through a tube – from one end to the other from swallowing to excreting, as the gut absorbs, digests, and processes everything we put into it. People who have irritable bowel syndrome, for instance, often experience diarrhea as well as constipation in response to changes in gut-brain communication; in gastroparesis, the stomach muscles, or the nerves supplying them, stop working. The conveyor belt is out of kilter, or the toothpaste tube stops being squeezed.

"The bigger picture here is enormous."

Exactly how the brain in the gut relates to the "big brain" is what Pasricha and his colleagues are working hard to find out, actively developing new drugs, testing the potential of never-before-recognized molecular targets for treatment of nausea, abdominal pain, and other symptoms that may arise when mind-gut pathways go awry. "The treatment of motility disorders really requires the art as well as the science of medicine, because every patient responds differently," notes Pasricha, who also heads an NIH-funded, multicenter gastroparesis consortium, and serves on the National Commission on Digestive Diseases. "Treating these patients can be very challenging, because if you don't fully understand what is causing the symptoms, you don't



really have effective treatments. In fact, there are very few effective treatments, and what works for one person might not be very helpful for another," which is why he believes that entirely new avenues of treatment might make a huge difference in care.

But better treatment for motility disorders is most likely just the tip of the gut-brain iceberg, Pasricha believes. The enteric nerves almost certainly play a role in obesity, diabetes, in pancreatitis; they may even be involved in Alzheimer's disease, some forms of cancer, and other diseases that aren't usually thought of as relating to the gut. "Nerves are involved in immune responses," he explains, "and this process, called neurogenic inflammation, is a problem in many disabling diseases." Signals from the enteric nervous system affect metabolism in the brain, liver, and elsewhere. Pasricha has focused much of his research on the pancreas, where these nerves have an impact on insulin

The enteric nerves almost certainly play a role in obesity, diabetes, in pancreatitis; they may even be involved in Alzheimer's disease, some forms of cancer, and other diseases that aren't usually thought of as relating to the gut.

resistance. "We anticipate that what we are learning about nerve signaling in the pancreas will lead to a new approach to diabetes therapy," he says. "At our center, we are putting in infrastructure for translational research, so we can take our new ideas and discoveries and bring them to the patients." In the lab, scientists are working to discover the molecular neuroscience of disorders of the gut's nerve cells. Also exciting: Research involving stem cells in the enteric nervous system may lead to the ability to regenerate cells in areas where function has been lost. "This center is going to make a difference and provide hope to patients who really suffer from what otherwise have been called intractable problems," Pasricha says. "The bigger picture here is enormous."

The new center offers a "soup to nuts" approach, Pasricha says – from research to the latest in diagnosis and treatment. "We have put together a comprehensive clinical program that allows us to provide state-of-the-art care for patients with motility disorders and functional bowel disease. This is multidisciplinary, because these disorders require a global and creative approach. It involves not just gastroenterology but psychiatry, nutrition, pain management, surgery, pelvic floor physiotherapy, allergy, internal medicine, psychology, and we are also working with practitioners of alternative medicine, including acupuncturists." ■

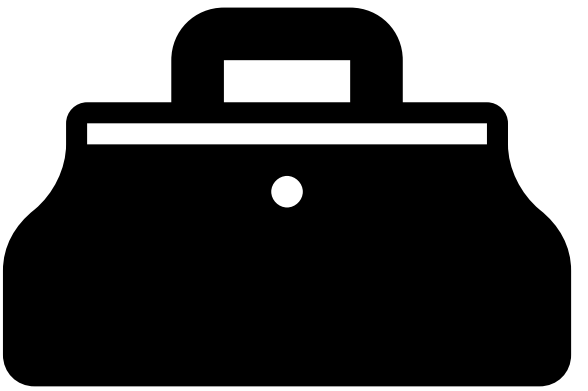
Helping our Neighbors
Get Healthier

Twenty years. That's the difference in life expectancy between two sets of people. They don't live in two different countries or separate parts of the world. These are people right here in Baltimore, and there are glaring health disparities between them. The longer-lived set lives in the more affluent parts of northwest Baltimore. The others are our closest neighbors, who live in some of the neighborhoods surrounding the Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center.

If, as the saying goes, "health is the first wealth," then something is wrong with our immediate picture, says Vice Dean David Hellmann, M.D. "Hopkins has not been very attentive in providing that first wealth for people in the neighborhood, although that's what we were founded for. We own the responsibility for trying to make this better."

And Johns Hopkins is doing just that with a huge, coordinated care initiative called the Johns Hopkins Community Health Partnership (J-CHiP), funded by a three-year, $19.9 million innovation grant from the Centers for Medicare and Medicaid Services. The grant is part of a $1 billion national Healthcare Innovation Challenge, whose triple aim is "improving the individual experience of care, improving the health of populations, and reducing the per capita costs of care for populations." Hopkins leaders believe J-CHiP is the long overdue opportunity to transform the health of our closest neighbors.

One major challenge is simply forging a cohesive system out of many health care organizations (see side story) that are accustomed to working as individual entities, says Constantine G. Lyketsos, M.D., Chairman of the Department of Psychiatry at Johns Hopkins Bayview. Lyketsos sits on the J-CHiP Operations Committee, charged with implementing the day-to-day functioning of this immense project, under the leadership of Dean and CEO Dr. Paul Rothman. A member of the Center for Innovative Medicine's Advisory Committee, Lyketsos believes that after the grant's three years are up, the changes will be sustained by the tremendous reduction in costs that will come from providing better health care. J-CHiP officials estimate that the initiative could save Medicare and Medicaid as much as $50 million during the first three years alone.



If health is the first wealth, "Hopkins has not been very attentive in providing that first wealth for people in the neighborhood, although that's what we were founded for. We own the responsibility for trying to make this better."

It Takes a Community to Help a Community

From the very top, the leadership of Johns Hopkins Medicine feels so strongly that the J-CHiP initiative is the right thing to do that the initial director of the grant was Ed Miller, M.D., the Dean and Chief Executive Office of Johns Hopkins Medicine. When he stepped down, his successor, Paul Rothman, M.D., assumed leadership of the grant, with Patricia Brown, president of Johns Hopkins Health Care, as deputy project director. The project is huge, and to make it happen, Hopkins has put together a remarkable network that includes Johns Hopkins University's schools of medicine, nursing, and public health; the Johns Hopkins Community Physicians, a large network of primary care providers in Maryland; the Johns Hopkins Home Care Group, a full-service home care provider; the Johns Hopkins Urban Health Institute; the state of Maryland; the city of Baltimore; Priority Partners, a Medicaid managed care organization that Johns Hopkins owns along with the Maryland Community Health System; five local skilled nursing home facilities; and community groups and advisory boards.

Another challenge and initial target for J-CHiP is getting early help to people who seem likely to become "hotspotters," Lyketsos explains. "Hotspotters are individuals with several chronic health conditions, who have poor health care outcomes and experiences despite consuming a lot of health care resources, largely because they're in and out of hospitals and emergency rooms." Working with risk prediction models developed by the late Fred Brancati, M.D., Professor of Medicine and Epidemiology, and colleagues, the J-CHiP team is systematically reaching out to "pre-hotspotters." An estimated 46 percent of this population had one or more hospital admissions in 2011, and 30 percent have six or more chronic conditions. The cost of care for this group in 2011 alone was $36 million, with, on average, $25,000 spent on each person in this group in a year.

"One of the really big innovations in J-CHiP is appreciation of the role of behavioral health conditions in people who are pre-hotspotters," says Lyketsos. These conditions include chronic psychiatric disorders like depression, anxiety or severe mental illness; also, substance abuse. "For younger people in our community this might be alcohol and opioids like heroin or cocaine; in older people, it is more likely alcohol and painkillers or sedatives." Health behaviors that make someone more likely to become a hotspotter include obesity, smoking, chronic pain, sleep problems, and "non-adherence" with medicine – basically, not taking medications as prescribed, or not keeping the prescription filled regularly. "Realizing that these behavioral health conditions – the addictions, the health behaviors and the psychiatric illness – are major drivers of why people have trouble, we are fully integrating behavioral health care within all levels where we provide health care: outpatient clinics, nursing homes, and inpatient units."

J-CHiP is not "calling these people out of the blue," but reaching out to them wherever they are receiving health care – in the hospital, the emergency room, a primary care clinic, or a nursing home. "Reducing readmission is only a small part of it," says Lyketsos. "The major effort is to improve the health of this population, to help these people before they are admitted by providing more intensive care in the community, because they are either having trouble managing their conditions, or their health care conditions are so complicated, they are at risk of going to the ED or hospital."

The project is only about six months old, so it's a bit early for results, Lyketsos notes. "But I can tell you some of the types of patients we're reaching out to," people with diabetes, heart disease, arthritis, lung disease, maybe cancer. "The typical patient, in addition, is overweight and/or maybe smokes, and/or is chronically non-adherent with taking medications or going to outpatient appointments." Another group includes people who have trouble with "self-management" of a health problem – "people who have not succeeded at quitting smoking, losing weight, or following through with treating diabetes or heart disease." And still another group includes patients with different complications that are equally difficult to treat, for example: "someone who has a relatively stable chronic condition, like diabetes, and also pretty severe arthritis, who is taking high doses of opioids for pain," says Lyketsos. "The painkillers are not helping; if anything, the pain is worse. The person develops depression, then withdraws to his house and periodically calls an ambulance to go to the emergency department, has a short admission in the hospital, and the cycle repeats itself, because in a brief hospital stay these issues cannot be addressed." ■

Helping the Aging Brain:
Why We Need a Fresh Approach

Richard O'Brien, M.D., Ph.D., is the chairman of the Department of Neurology at Johns Hopkins Bayview. His career has focused on studying how the brain adapts to change – how the brain's ability to cope, to form new connections and to recover from a stroke or disease, is affected by aging and by degenerative illnesses like Alzheimer's disease. A member of the Advisory Committee of the Center for Innovative Medicine, O'Brien is also an advocate of multidisciplinary collaboration and forming creative partnerships to solve tough problems. Recently, we interviewed him about research on the aging brain. Here's some of what he had to say:

What is the biggest problem in the brain as we age?

It loses its plasticity. Young children can have an entire half of their brain removed (a treatment in certain seizure disorders), and within three years you can't tell that anything had happened to those children. They're completely normal – they walk, talk, have fine motor skills – completely the same as someone who hasn't had their brain messed with at all. But in adults, a relatively small stroke is a devastating event. Adult brains don't have the same ability to find ways around problems. Their brains are just not adaptable, like a kid's.

Is there any way to turn back the clock?

That's what we need to do, is to find ways to turn old brains into young brains. In the last five years, people have put a lot of hope into stem cells, but I think the effect of stem cells is still very limited. Many good neuroscientists are now trying to find ways to make old neurons act like they're young neurons, and in that way, reactivate the things that older brains just can't do anymore. Honestly, I think that's something that's going to happen.

Cognitive reserve is improved by education, intellectual activity and social activity. People with high amounts of that show an ability to resist the damaging changes of Alzheimer's disease, probably because their brains remain young at heart.

What do you think happens to the brain as it ages?

My best guess right now is that as you age, the DNA in your brain becomes very heavily methylated and transcriptional elements just become sluggish. Your brain can't generate growth factors and other things the way it could when you were young. (*In chemical terms, a methylated gene becomes cluttered, and it is not easily translated into new*

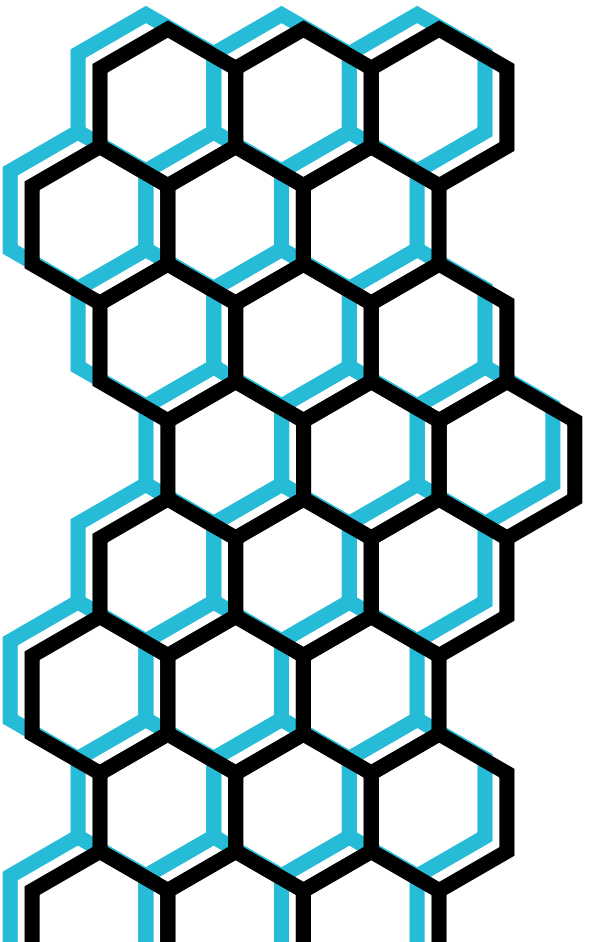
proteins. Methylation is like changing the tumblers on a lock so the key doesn't fit it anymore. When this happens to a gene, it loses its effectiveness.). Methylation is an important adaptation to age, because it puts the brakes on genes which might lead to cancer. But its downside is reduced plasticity.

Does this just happen in the brain, or is this a general problem in the whole body?

Every organ has a different approach to aging. One of the points Toren Finkel at the National Institutes of Health recently made when he spoke at Bayview is that if you uncover the secrets to aging in the brain, they may be very different from the secrets in the aging heart, liver, the lungs, or the pancreas. Every organ faces its own age-associated changes, and we need to approach our research in this way.

So, how can you find out which things cause old organs to act old and not young?

That's a great question, and implied in it is the ability to manipulate those factors, so that people can enjoy more robust function of their heart or brain



I don't think that falling apart when you get old is something that has to happen.

into old age. There are some clues from interventions. There's plenty of good scientific data that exercise at mid-life or when you're young allows your brain to stay healthy when you're old. There's a study I read yesterday in the *Annals of Internal Medicine*, looking at the exercise capacity of people at age 50, and then comparing their Medicare records for dementia diagnoses 30 years later. Dementia was cut by more than a third in people who were fit as middle-aged adults. I think that's true for other organs as well. Already, people are keeping their brain or other organs young in midlife just by exercising, and probably by taking care of their general health, as well.

What does exercise do?

I'm sure it's not blood flow, but other things; for example, muscles certainly release and regulate the levels of good hormones in the blood. It's just a matter of figuring all that out at the molecular level. Another thing we are studying is called "cognitive reserve." It's an experimental paradigm. If you look at the brains of older people at autopsy, a lot of them have Alzheimer's disease, but only some have dementia, even with the exact same amount of Alzheimer's changes. Cognitive reserve is improved by education, intellectual activity and social activity. People with high amounts of that show an ability to resist the damaging changes of Alzheimer's disease, probably because their brains remain young at heart.

Will there be a fountain of youth?

When we talk about aging, none of us are looking to make people live to be 120 years old. But I think we'd all like people to be able to live well into their eighties and remain cognitively healthy and robust.

The other field that is obsessed with aging is geriatrics. In their field the paradigm revolves around a concept called frailty. That's what Jeremy Walston (*in the Division of Geriatric Medicine and Gerontology*)

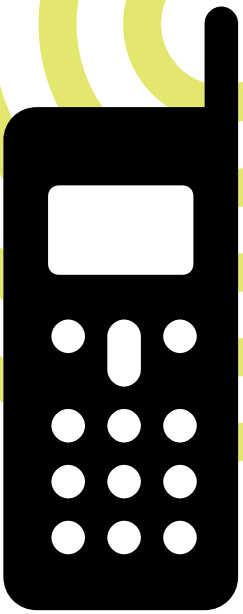
CONTINUED ON PAGE 23

It's Just a Phone Call

You might not think it would matter very much to patients if the doctor who took care of them in the hospital calls them after they get home. But it does. In a recent project done by the leaders of the Aliki Initiative, patients who received that call reported that they felt a closer partnership with their hospital physicians. "We found that of all the things we do on Aliki, the one that seemed to make the most difference was the phone call that the residents make to the patients after discharge," says Roy Ziegelstein, M.D., co-director of the Aliki Initiative.

The Aliki Initiative, begun nearly six years ago with support from the Greek philanthropist, Mrs. Aliki Perroti, is designed to help young doctors get to know their patients as a person – and, in so doing, to become more compassionate and caring physicians. Interns and residents on the Aliki Service have more time to spend with each patient, and the encouragement of their faculty leaders to put that time to good use for the patient's benefit.

The Aliki curriculum is a thoughtful compendium of little things that add up to being a better doctor – things like learning to ask a patient open-ended questions that promote conversation instead of yes-or-no ones that don't elicit nearly as much information. Or spending extra time on the often hectic day of discharge from the hospital to go over the list of medications the patient will be taking at home; making sure she knows why it's important to take this pill in the morning on an empty stomach, or that one at bedtime because it can make her drowsy. Running the Aliki program is a team that Vice Dean David Hellmann, M.D., the Aliki Perroti Professor of Medicine, likens to the Bell Labs, the renowned research and development think tank at AT&T that produced such innovations as the transistor, the laser, and the UNIX operating system. The Aliki think tank is small but mighty. The group – Ziegelstein and co-director Cindy Rand, Ph.D., Colleen Christmas, M.D., the Residency Program Director; Janet Record, M.D., a hospitalist; and Laura Hanyok, M.D., a general internist – meets every Tuesday morning around an actual round table in Ziegelstein's office, sometimes joined by Hellmann. "What this group is achieving in our Bell Labs of Aliki is transforming and energizing our young doctors and the faculty teaching them, and having a tremendous impact on our patients," Hellmann says.



This most recent research project came about after one of those roundtable discussions. "We were trying to study the impact of our new patient-centered discharge curriculum," says Record. "I had a particular interest in that because I deal with the discharge process all the time, and was motivated by personal experience of how difficult, challenging, complicated, time-consuming, and overwhelming it can be even for a provider. If it's hard for me as a physician to write a good set of discharge instructions, how hard is it for the patients to feel prepared as they leave the hospital to do what they should do? It shouldn't feel chaotic. It should feel understood. Patients should feel comfortable with what's happening."

One way the Aliki discharge has become more patient-focused is that doctors don't wait until discharge day to talk about life after the hospital. Aliki patients get a questionnaire – the best possible kind, because they don't have to write down any answers; they are just asked to think about them, and then talk with their doctor about them before they leave the hospital. (See side story.) The questions are written by the leadership team and designed to help young doctors learn to communicate and listen better. They are also written with the hope that patients will feel more empowered to take charge of their health.

In order to evaluate the impact of the patient-centered discharge curriculum, the leadership team administered a brief survey to patients who had been discharged from all four resident ward teams, of which the Aliki service is one. They wanted to find out how prepared patients felt for the transition home, whether their preferences had been considered, whether they had received a call from their doctor after they returned home, and whether they felt their doctor knew them as a person. "The post-discharge phone call became the most measurable and interesting result that we obtained," Record says.

But there were other important findings: Patients who received the follow-up call felt more informed and prepared to care for themselves at home, for one thing. For another, it turned out that residents were more likely to call their patients after discharge if they had been exposed to the Aliki curriculum than if they had never been exposed to it. However, notes Record: "Even house staff who had never rotated through Aliki gave their patients a post-discharge call 30 percent of the time, which we think is pretty high." In comparison, interns and residents who had taken part in the Aliki rotation called their patients at home 55 percent of the time, and those currently on the Aliki team, "where we're telling people, 'please call,'" called their patients at home 82 percent of the time.

Calling a patient who has left the hospital is not a standard of care required by any residency program, and "we can't find anything in the literature that comments on how frequently patients report receiving a call from their resident in internal medicine," notes Record. "We don't think it's out there." However, Johns Hopkins Bayview patients may be getting used to this idea. "There certainly has been diffusion of these patient-centered care skills into other teams and settings," Record adds. "The Aliki curriculum is having a lasting impact on residents' propensity to make a phone call to patients after discharge. When patients receive that phone call, they feel more prepared for that transition." When the Aliki program began, calling a patient at home "seemed so radical." Now it's becoming a good habit, "like wearing seatbelts." ■

Some Questions to Think About

Aliki patients receive a questionnaire that begins, "Your voice matters," and contains a few questions for them to think about. Later, with their doctor, they discuss their thoughts and concerns. The questions include:

- **What concerns do you have about leaving the hospital?**
- **What will be the hardest part of taking care of yourself?**
- **Will you have any support from family or friends? What can they help you with? Would you like us to talk to them?**
- **Do you have any worries about getting your new medications from the pharmacy, or getting to your follow-up doctor's appointments?**

Another set of questions is entitled, "Understanding Your Health," and is designed to make sure patients have all the information about their own health that they need. These include:

- **If you had to explain why you were in the hospital, what would you say?**
- **What are some warning signs to watch for once you leave the hospital?**
- **What are some things you can do (nutrition, physical therapy, etc.) to stay as healthy as possible?**
- **What can we explain better (medicines, diet, wound care, special equipment)?**

Patients do not leave the hospital until these questions have been answered to their satisfaction, and the Aliki team is sure that the patient is leaving feeling as empowered as possible, so they can do what they need to do to get better.

Three Simple Rules.
Result: International Success

If you have a rare disease, you probably know how difficult it can be to find someone with the expertise to give you the best treatment. You also probably know that when doctors, nurses and therapists specialize in that one disease and see a higher volume of patients who have it, they come to know that malady, and all its subtleties and offshoots, very well.

This was one of the big reasons why, in 1990, rheumatologist Fred Wigley, M.D., created the Johns Hopkins Scleroderma Center. Scleroderma is a relatively rare autoimmune disorder – affecting about 250 out of every million people – that attacks the skin and connective tissue, and the services that the Hopkins Scleroderma Center provides are so extensive that people from around the world seek treatment here. But Wigley also took one big step further toward curing scleroderma: With a critical mass of scleroderma patients to participate, he built up a database that is driving new research and shedding light on some of the greatest mysteries of this disease.

1

Build It Around Patient Care

"We started with the idea that in order to tackle a complex human disease, we had to aggregate the patients into one place, have doctors who specialized in that particular entity, and have a team of people around us who were knowledgeable about the disease," says Wigley, who has directed the Center for 23 years. "We believe that if we are going to have an impact, not only on helping people feel better but maybe even curing a rare disease, we have to do it through patient care. Physicians have to take care of patients who have the disease, and then that experience with the patients dovetails into and supports the research mission."

The Center has grown from "a one-man operation, which was me," to five full-time faculty and a clinical nurse who evaluate and manage about 10-15 new referrals and 60 return scleroderma patients each week from the U.S. and other countries, Wigley says. "There are features of the disease that are common, making it challenging to figure out who's got it and who doesn't have it." Once diagnosis is made, patients may need to see other specialists affiliated with the Center. "We have programs linked to each of the different problems these patients have," complications such as pulmonary hypertension, gastrointestinal motility issues, and heart-related problems.

"Every one of our patients who comes to the Center participates in our research activity. But we don't just say, 'Come give us a sample of your blood so we can study it.' We also take care of the patients, and that way we know the disease very well."

2 Establish a Research Program to Look for a Cure

"Every one of our patients who comes to the Center participates in our research activity," says Wigley. "But we don't just say, 'Come give us a sample of your blood so we can study it.' We also take care of the patients, and that way we know the disease very well." There are about 3,000 scleroderma patients in the Center's research database, and with this critical mass of patients, the Center has built a renowned framework for discovering the mechanisms, causes and new therapies for scleroderma. "In order to understand a disease and be able to study it in depth, you have to have lots of patients, and if you're only taking care of one patient, you don't have much of a view of things," notes Wigley. "The only way to get lots of patients in one place is to take good care of them, and to offer more than just the opportunity of being a research participant. The strategy is, on the one hand, be good doctors, and on the other, attract many people with a rare disorder – so you have lots of people in order to have a vision of what the disease is, to be able to study it well."

Linking this "exceptional data and sample resource to the discovery engine at Johns Hopkins has resulted in outstanding productivity," Wigley says. In exciting research, investigators at the Center have identified cancer as a potential trigger of scleroderma in some patients, "and we're now working on the actual molecular mechanisms for how that comes about." Scientists Ami Shah and Antony Rosen are working with oncologist Bert Vogelstein on the cancer connection. Zsuzsanna McMahan is doing translational research, and another clinical scientist, Francesco Boin, is "looking at the repertoire of immune cells" to understand what triggers the body's autoimmune response in scleroderma, "trying to figure out what our treatment does, to understand better what turns these cells on, and what we can do to turn them off." Other research, in collaboration with investigators including Paul Hassoun and his team at the Pulmonary Hypertension Center, is aimed at understanding why people who have scleroderma and pulmonary hypertension don't fare as well as other people; the culprit seems to be accompanying disease on the right side of the heart. "This is going to open up avenues of new treatment." The Center has also organized a multi-center program called "GRASP," linked with the National Human Genome Research Institute, to study genetic factors in African Americans with scleroderma. Other molecular research focuses on problems in tissue-repair cells, which might "be important drivers of ongoing injury" in scleroderma. A research collaboration with pediatric cardiologist Hal Dietz and scientist Elizabeth Gerber is shedding light on the basic mechanism of tissue fibrosis. "This (scar tissue and fibrosis in the skin) is the unique feature of scleroderma," notes Wigley. Dietz has a mouse model "that has given us incredible insight into how this is happening in these patients." Still other research is focused on clinical help – developing new diagnostic and monitoring tests, and coming up with new medications. Laura Hummers, who co-directs the Center with Wigley, organizes clinical trials, and Regina Greco leads the clinical and research staff.

"We believe that if we are going to have an impact, not only on helping people feel better but maybe even curing a rare disease, we have to do it through patient care. "

3 Be a Resource. Help Educate People About this Disease

"We have programs and activities for every level of learning," says Wigley. In addition to conducting clinical and basic science research, the faculty mentors students, residents, and postgraduate fellows, gives lectures at Hopkins and elsewhere, writes articles and textbook chapters, and Wigley is one of the editors of the leading textbook on scleroderma. "What we have here is an enterprise that's beyond just one person or even a few people," he says. "We have come a long way since 1990." ■

The Liquor Store Next Door

Location, location, location. Who would have thought the three most important things in real estate would apply to public health, too? And yet, they do, especially for children. Place is important. In fact, it matters desperately.

Jacky Jennings, Ph.D., M.P.H., director of the Johns Hopkins Center for Child & Community Health Research (CCHR), has devoted her career to understanding how social determinants – and place is a huge one – affect children and adolescents. Her work suggests, for instance, that an adolescent girl who grows up in one neighborhood has a tenfold higher risk of getting a sexually transmitted infection than another girl of the same age and identical risk factors, simply because of where she lives. Jennings' research is focused on children who are at risk of getting infectious diseases, becoming obese, being a victim of violence, developing asthma – and has found that these are "centrally linked to place." She believes that "if these things are important in the prevention of disease, they should also be important in the way that we design and build our cities and in the way that we treat and care for people. Often, our clinic models are not very sensitive to the environment where our patients live. When they come into a clinic setting, we don't know much about their neighborhood and environment." But, she says, we should.

Place matters, particularly where children live and play.

It's not that easy, for example, to tell a mom to serve more fruits and vegetables to her kids when she has no car and lives in a "food desert" – a neighborhood where the only grapes you can find within walking distance are in an overpriced can of fruit cocktail on a shelf in a convenience store, where the only greens you might possibly purchase come in a bag salad that, if you're lucky, doesn't taste too much like plastic. But if you want a beer or something even stronger – no problem; there's plenty.

Which brings us to certain liquor stores in the city of Baltimore. Jennings, who is also a member of the Center for Innovative Medicine's advisory committee, is adept at using tools that have been designed for research in other fields of science. One that she finds very useful is a health impact assessment (HIA). "The idea is along the lines of an environmental impact assessment," she explains. "If you want to build a bridge in a certain area, according to the National Environmental Policy Act, you have to do an assessment to determine the impact on the soil, fish, and local environment. In the actual legislation, people are supposed to be included, but they rarely are." The HIA highlights potential health consequences, good or bad, from a policy or program.

Baltimore City is in the midst of a rezoning effort, its first since 1971. Jennings and Hopkins colleagues received funding from Active Living Research, a national program of the Robert Wood Johnson Foundation, to conduct an HIA of the zoning code, "particularly as it related to outcomes like childhood obesity and violent crime." The team, including Rachel Thornton Johnson, project director, and Jonathan Ellen, principal investigator, from CCHR and the Department of Pediatrics, worked with Oxiris Barbot, the Baltimore City Health Department Commissioner, along with Laurie Feinberg from the Planning Department, and with George Nilson, the Baltimore City Solicitor, sitting at many meetings over the last two years to discuss the findings of their HIA. The subject of liquor stores, or "alcohol outlets," came up.

"Despite the fact that we've had a decline in population since the 1950s, we have maintained a high level of liquor stores in the city of Baltimore," Jennings says. "We have a very high per capita density of alcohol outlets." One of the city's "Healthy Baltimore 2015" goals is to decrease that density. The Hopkins team came up with three modifications to the zoning code that would help do this. They backed up their suggestions with a review of public health and criminal justice literature, specifically looking at the link between alcohol outlets and violent crime. "The overwhelming evidence suggests that there is a strong, consistent, and dose-response

relationship between the two," Jennings says. "We also conducted our own Baltimore City analysis," and found that "every increase in one alcohol outlet in a neighborhood is associated with a two-percent increase in violent crime."

But what can be done? These liquor stores have been there for years. They're fixtures. True – but really, according to the zoning code, they shouldn't even be there at all. "In 1971, a number of alcohol outlets that were in residential areas were grandfathered in," Jennings says. In other words, they were allowed to stay – but city officials thought that they might move or peter out on their own because they weren't in commercial areas. In fact, the opposite happened: These corner liquor stores had the local monopoly on alcohol "because no other businesses were allowed to be in those areas." Without competition, many of them thrived. Jennings' team's solution? Phase them out – or, in city zoning parlance, "amortize" them. "About 90 percent of these stores that are staged to be amortized are located in highly impoverished areas. So, in fact, we have allowed these alcohol outlets to be in areas that are already very disadvantaged. That's a real inequity issue. The idea that we would amortize them is really a positive equity issue. We're starting to level the playing field, if you will."

To clarify, these alcohol outlets aren't generally high-end establishments where, for instance, one might go and thoughtfully weigh the merits of various dessert wines to be served with a pear tart. Instead, says Jennings, "the ones we're talking about tend to be located in very impoverished areas. They

Certain liquor stores were grandfathered into the zoning code in 1971. But really, they aren't supposed to be in these residential areas at all.

have bars on the window, you basically walk in and there's bulletproof glass. You can't touch anything, and you ask the attendant for the liquor behind the counter." Although some of these stores aren't that dismal, "and you would look at them and say, 'they're really not problem liquor stores,' it's not so much about whether they are problems; they're just not in areas where they're supposed to be."

The plan would not take the owners' licenses away, Jennings points out, "but they would have to move their current business to an area where they're allowed to be." This proposal has generated a lot of controversy, "a lot of press, lots of blogs and tweets, and there's real opinion on both sides, as you might imagine. Of course, it's people's livelihood, so it's a real issue for the owners of the stores that may be closed. On the other hand, it's a real issue for people who live in those neighborhoods, where the alcohol outlet does, in fact, attract crime. The idea that you would raise a family right next to a liquor store is the whole reason we have zoning. Those shouldn't be next to one another."

If the City moves to adopt the idea to phase out the liquor stores, what next? One idea is to encourage people who want to fill the void with commodities those neighborhoods could really use – fresh produce stands, for instance. Other cities, faced with blocks of burned-out rowhouses or empty lots, have successfully repurposed that real estate in the form of community gardens.

Having the opportunity to work on something that has the ability to effect large-scale positive change "has been amazing," Jennings says. "It's taught me so much about how you bring social determinants to the policy arena. It's just fascinating, and so important, because that's where we all hope that we can move with our work – to actually make a difference." ■

Creating A Culture of Health

Risa Lavizzo-Mourey, M.D., M.B.A., at Johns Hopkins Bayview in April to deliver the 10th Annual Miller Lecture, came with a mission. The President and CEO of the Robert Wood Johnson Foundation invited the audience of physicians, students, house officers, patients, and community leaders to "build some bridges, cross some bridges, and question the status quo.... If all goes well, we'll end up sharing a vision of the future that calls on each of us to play a part in building a new national culture of health."

Lavizzo-Mourey said that when she was fresh out of medical school, she "didn't have a clue what to do, or any incentive to go find out. After all, we were medical doctors, not social engineers. And one has nothing to do with the other. Right?" But she kept seeing things that bothered her. There was one patient she saw during her internship at Brigham and Women's Hospital (which included a rotation at the West Roxbury, Mass., VA Hospital), whom she thought of as "the VA Lady," a military veteran, homeless, with swollen feet and painful leg ulcers. "She'd been to the VA many times before. We did for her what they always did. A few hours in a warm bed, some antibiotics, a decent meal. The next morning we had to let her go. We needed the bed for patients with more acute problems. Sure, she was a military veteran with health coverage. But we were bit players in a system that was not equipped to protect our patient from the harshness of her life outside the hospital – a harshness that was destroying her health and shortening her life. She limped back into the same problems she had before – no home or job, lousy food, cast-off clothing, no social network to come to her aid, no one of her own who cared for her. And we went back to our same old business as usual."

Lavizzo-Mourey was learning a powerful lesson: "We were up against social, economic, and environmental conditions... and they were winning. The truth is these forces will always win. Our care began and ended at the front door of the hospital. At Morning Report, no one taught us that how and where we live, learn, work, and play have more to do with our health and patients' health than the treatments we were diligently learning to apply."

After her training in internal medicine and geriatrics, Lavizzo-Mourey joined the faculty at Temple University's School of Medicine – a first-class teaching hospital in a very poor neighborhood of about 20,000 people, mostly African Americans and Latinos, some of whom lived without indoor plumbing, with "no place for families to buy healthy foods, fresh fruits and vegetables at a reasonable price." Lavizzo-Mourey recalled one young girl "who didn't hold a real banana in her hand until she was in third grade... Just a few miles from the Liberty Bell and Independence Hall it was a veritable food desert. Fast food and takeout, bodegas and high-price corner stores, they all were stocked with everything that's bad for you – cigarettes and junk food – and almost nothing that's good for you. The neighborhood was a self-contained incubator for childhood obesity." It was, she realized, "the VA Lady syndrome writ large."

"Tinkering at the margins is not a solution."

But Philadelphia began to change for the better, as green grocers, farmers' markets, community health initiatives, and 30 miles of new bicycle paths began "pushing back the desert" and lowering childhood obesity rates. Lavizzo-Mourey used lessons from the "Philadelphia Story" and elsewhere to illustrate new ways of thinking about the health of the community. Among some "basic realities" of our current situation are that "spending more doesn't translate into better health and quality care; acute care trumps preventive care in the struggle for resources; and tinkering at the margins is not a solution."

"For a decade, we have been better physicians, and physicians in training, because of the initiatives made possible by the Miller Family," says Vice Dean David B. Hellmann, M.D. Mrs. Anne Miller's concern that gifted, compassionate physicians such as the renowned Johns Hopkins internist, Phil Tumulty, seemed the exception and not the rule led to many discussions with Hellmann about the qualities that make up a great clinician. This led to the first Miller Lecture in 2004. The Miller Family then created an endowed professorship, the Sarah Miller Coulson and Frank L. Coulson, Jr., Professorship, which helps support the work of Roy Ziegelstein, M.D., a cardiologist who is also the Miller Scholar and "one of our outstanding clinicians and teachers," says Hellmann. There are four Miller Coulson Scholars: Colleen Christmas, M.D., Steven Kravet, M.D., S. Chris Durso, M.D., and Scott Wright, M.D., – a team whose work in defining the qualities of clinical mastery laid the groundwork for The Miller-Coulson Academy of Clinical Excellence, a signature program sponsored by the Center for Innovative Medicine. "This is such an exceptional family," says Hellmann. "Their sustained generosity has enabled us to become a better public trust."

The Academy's mission is to recognize master clinicians. Based on the efforts of the Miller Coulson Scholars, the Academy developed a rigorous process to identify exceptional clinicians, a clinical portfolio that assesses clinical accomplishment. The portfolio of each candidate nominated for membership in the Academy is reviewed and scored by an external committee of respected physicians at top academic medical centers, and then by an internal selection committee. "We hope that by acknowledging our most clinically excellent physicians, the Academy will not only celebrate the accomplishment of these individuals, but will provide inspiration to all clinicians," says Scott Wright, the Academy's director. Each year, the Academy sponsors an annual symposium devoted to excellence in patient care, highlighted by the induction of new members. This year's new members are:

- **Alfredo Quinones-Hinojosa, M.D., Professor of Neurosurgery and Oncology**
- **Vani Rao, M.D., Associate Professor of Psychiatry & Behavioral Sciences**
- **Satish Shanbhag, M.D., Assistant Professor of Medicine & Oncology**

Members in the Academy contribute to a blog, "Reflections on Clinical Excellence," which draws readers from around the world into discussions and sharing of perspectives on being a better doctor and taking care of the whole patient. Among other efforts, the Academy offers a curriculum to help physicians move toward clinical excellence; an elective for Johns Hopkins medical students; Academy-hosted Medical Ground Rounds; and journal articles related to medical excellence.

The Frank L. Coulson, Jr. Award for Clinical Excellence

Last year, the Miller-Coulson family and the Academy created a new annual award for house officers who have shown clinical excellence. It is named for Frank Coulson, who died two years ago after a battle with cancer. The Frank L. Coulson, Jr. Award for Clinical Excellence honors his life, his personal commitment to professional excellence, and his great interest in clinically excellent physicians.

This "important award in clinical excellence allows us to recognize outstanding residents at all of the programs at Johns Hopkins Hospital and Johns Hopkins Bayview," says David Hellmann, M.D. The awards "recognize the compassion, humanism, professionalism, and wisdom that these doctors have already exhibited early in their careers," says Scott Wright, M.D. The Miller Coulson Academy is proud to recognize this year's recipients:

Daniel Calva-Cerquiera
Plastic and Reconstructive Surgery

Molly Cavanaugh-Hussey
Dermatology

Christina Cinelli
Radiology

Alison Dolce
Pediatric Neurology

Matthew Finn
Internal Medicine

Ian Han
Ophthalmology

Kendra Harris
Radiation Oncology

John Holst
Emergency Medicine

Sofia Lyford-Pike
Otolaryngology-Head and Neck Surgery

Payam Mohassel
Neurology

Jeffrey Mullins
Urology

Kelly Olino
Surgery

Fernanda Porto-Carreiro
Internal Medicine

Nathan Smith
Pathology

Ben Stein
Orthopedic Surgery

Caleb Ward
Pediatrics

In the future, she hopes that for doctors and care organizations the "professional purpose is redefined from the treatment of illness and injury to the production of health itself. The line will blur between patient-centered care and population-centered care. You'll influence decisions made by schools, by zoning boards, by urban planners, and budget-makers. Where you deliver care will shift from doctor's office and clinic or hospital bed to the home, workplace, school – wherever people live their lives."

For a decade, the Miller Lecture has brought the Johns Hopkins medical community together each year "to think about good medicine, and to inspire us to be better doctors," says David Hellmann, M.D., the Aliki Perroti Professor of Medicine. It is made possible by the generosity of the Miller family: Thomas and Anne Miller and their daughters and sons-in law, Sarah Miller Coulson and the late Frank L. Coulson, Jr., Leslie Anne Miller and Richard Brown Worley. Worley has served on the Board of Trustees of the Robert Wood Johnson Foundation. ■

CONTINUED FROM PAGE 5

One day, this and other biomarkers being developed might be of use to adult and child athletes who are injured on the field. Is it a concussion? If so, how bad is the damage? And when is it safe for the athlete to start playing again?

Van Eyk and Everett have been working with Howard Katz, Ph.D., in material medicines at The Johns Hopkins University to develop a biosensor that could electrically sense these proteins in the blood, with the goal of being able to monitor what's happening in real time. Ideally, says Everett, "you wouldn't even have to draw blood, you'd just be able to look at the monitor and see the levels of these proteins circulating. That would be of particular value in patients having heart surgery, where your blood has to circulate through the cardiopulmonary bypass machine." The scientists envision using such a device to help clarify what's going on in people who come to the emergency room with a headache or double vision – worrisome symptoms that might mean a stroke, a mini-stroke or some very subtle brain injury that can produce damage over the long-term, or even something completely different, like a migraine. One day, this and other biomarkers being developed might be of use to adult and child athletes who are injured on the field. Is it a concussion? If so, how bad is the damage? And when is it safe for the athlete to start playing again? Van Eyk is interested in exploring "alternative matrices," such as a saliva test that could give a quick result, and if it's positive, could be confirmed with blood or imaging tests.

"None of this has any value unless our biomarkers end up being really good clinical predictors," says Everett. The scientists are not just trying to find the best test, but honing their findings – looking to see whether using a panel of tests might produce a more complete picture, and focusing on whether certain proteins are better at showing particular types of injury, and whether they're more helpful in adults or children.

This work started when Everett and Van Eyk were taking part in a study funded by the National Institutes of Health, and by the National Heart, Lung, and Blood Institute's Proteomic Innovative Center, which has made possible much of the proteomic discovery work in Van Eyk's program. The scientists were looking for blood biomarkers to show brain injury in children with sickle cell disease, "because there is an ongoing, continuous risk of stroke in anyone with sickle cell disease," Everett notes. "The peak of stroke in sickle cell disease is before you're 10 years old. Many of these children have evidence of subclinical brain injury, micro-infarcts, before they have an overt stroke." Van Eyk's proteomics technology identified circulating proteins that seemed to be elevated when these children had brain injury. The result of that study, published in the journal *Acta Haematologica*, showed the promise of elevated levels of GFAP as a way to predict stroke. This research was also supported by the Biomarker Development Center, part of the Johns Hopkins University's Institute for Clinical and Translational Research which, in turn, is funded by a Clinical and Translational Science Award from the National Institutes of Health.

"None of this has any value unless our biomarkers end up being really good clinical predictors."

"I don't know if it was a lucky or a 'eureka' moment," says Van Eyk, "but we had developed these technologies in a project to study auto-immune diseases, and two completely different projects collided to make something that's pretty cool." ■

CONTINUED FROM PAGE 12

studies. Why do some people become so brittle when they get older? When older people are susceptible to all kinds of problems, especially infections; when muscles break down, causing weakness; when bones thin, causing fractures; and it all seems to happen together – that condition is called frailty. What are the signals that underlie that? I don't think that falling apart when you get old is something that has to happen. If we can understand the mechanisms involved in frailty, we'll be able to maintain people's quality of life longer. A very interesting thing is that when people get into their eighties, they don't tend to get cancer or have heart attacks anymore; what happens instead is that they start developing frailty and degenerative diseases of the brain. That's what tends to kill older folks – not the things that kill middle-aged or younger people. They have their own set of disease processes.

You have said that we need to change our approach to research on aging. What do you have in mind?

At Johns Hopkins Bayview, we have a lot of resources that no one else has. We have the Hopkins Geriatrics program, the National Institute on Aging, the Memory Center, and Geriatric Psychiatry. We have a lot of people interested in this thing called aging from many different angles. We need to bring these people together and get them to start sharing ideas. For example, as I've thought more and more about Alzheimer's disease, to me it seems to be so related to aging that I believe you can't understand Alzheimer's without understanding brain aging. We're spending as much effort looking at the differences between young and old as we do between people with and without diseases. The majority of studies of elderly people with Alzheimer's disease compare patients with Alzheimer's to people of the same age without it, to see what the differences are. Now, we're switching our emphasis – not so much looking at the disease group, but looking at the difference between older people and young people. We assume that whatever we see happening to the brain with age is going to apply to Alzheimer's disease, simply because age is such a huge risk factor for it; that anything we discover with aging is a prime candidate to be a cause of dementive disorders. Fifty percent of 90-year-olds have dementia, 35 percent of 80-year-olds have it. Age is such a huge risk factor for these diseases that I think you have to study the aging process, not just the disease process.

Are you thinking that maybe we will be able to reverse the damage of a disease like Alzheimer's?

I think the most important thing is not to reverse the damage but prevent it from happening. To understand what goes on and then try to not allow it to happen. On the other hand, if someone has a stroke, you'd like to know why an older brain can't work around that stroke. We're studying stroke in several models to understand how mice are able to regenerate their function when they're young but not when they're old. Our view is that it's probably not going to be a just one growth factor or two, but large systems that need to be modified. Luckily, certain gene regulation molecules can control vast numbers of responding genes. I am confident we will understand these processes over time.

Fifty percent of 90-year-olds have dementia, 35 percent of 80-year-olds have it. Age is such a huge risk factor for these diseases that I think you have to study the aging process, not just the disease process.

What about diet?

Here's an example: One study done in Indiana recently compared African Americans living in Indianapolis to their ancestral populations in Africa. The incidence of dementia was half in Africa compared to those folks living in the U.S. I do think there is a significant role for environmental factors in Alzheimer's Disease. We just don't know what they are yet. The bottom line is that if you're going to try to find treatments and preventions for the diseases of older folks, you've got to think about the aging process itself, not just the disease. ■

Medicine is a public trust

THE JOHNS HOPKINS CENTER FOR INNOVATIVE MEDICINE

4940 Eastern Avenue
B1 North, Suite 103
Baltimore, Maryland 21224
410-550-4098

IF YOU DO NOT WISH TO RECEIVE THIS NEWSLETTER
PLEASE WRITE TO US AT THE ADDRESS ABOVE.

FRIENDS

OF THE JOHNS HOPKINS
CENTER FOR
INNOVATIVE MEDICINE

"We were up against social, economic, and environmental conditions... and they were winning. The truth is these forces will always win. Our care began and ended at the front door of the hospital.... No one taught us that how and where we live, learn, work, and play have more to do with our health and patients' health than the treatments we were diligently learning to apply."

Risa Lavizzo-Mourey, President and CEO of the Robert Wood Johnson Foundation, at the 10th Annual Miller Lecture.

Mr. & Mrs. George Aidinis
Mr. Aristidis Alafouzos
American Legacy Foundation
Mr. Daniel P. Amos,
Daniel P. Amos Family Foundation
Mr. & Mrs. Paul Amos,
The Paul & Courtney Amos Foundation
Anonymous
Mr. & Mrs. Charles R. Ballard, Jr.
Mr. & Mrs. David Bentz
Mrs. Caryl and Mr. George Bernstein
Drs. Joel and Risa Bordman
Drs. John and Lynda Burton
Mrs Joan Carl and Mr. Bernard Carl
Ms. Dana L. Case
Clearshot Holdings
Mr. Roger M. Cline
Dr. Christopher J. Conners
Mrs. Eleanor Conners*
Mr. & Mrs. Hugh C. Cosner
Mr. Frank L. Coulson* & Mrs. Sarah Miller Coulson,
Frank L. & Sarah Miller Coulson Foundation
Mr. & Mrs. George Coumantaros
Ms. Lavinia Currier
Mr. & Mrs. Neil Dahlmann
Mr. & Mrs. Michael J. Davies
Mr. David B. Ford
Mr. & Mrs. David B. Ford, Jr.
Mr. & Mrs. Brian Finn
The family of Mr. & Mrs. Leonard S. Fiori, Sr.
Lema Corporation
Mr. Michael Fiori
Ms. Lenora Irwin
Mr. Seth E. Frank,
Georges Lurcy Charitable & Educational Trust
Mr. & Mrs. Bernard Garil, Elmwood Country Club
The Deane A. and John D. Gilliam Foundation
Mr. & Mrs. William Gooch
Mrs. Clairborne W. Gooch III
Mr. & Mrs. William O. Goodwin
Mr. & Mrs. Steven T. Gorski
Jerome L. Greene Foundation, Inc.
Dr. & Mrs. Barry Halpern
Dr. Sidney Harman*,
Harman International Industries
Dr. & Mrs. David B. Hellmann
Ms. Virginia Henderson
Mrs. Wilhelmina C. Holladay and Mr. Wallace F. Holladay, Sr.*
Mr. & Mrs. Scott Jacobs,
Rosenthal and Jacobs Foundation Fund of the Greater New Orleans Foundation
Mr. & Mrs. Robert J. Katz
Mr. Christos D. Lambrakis *
Mr. & Mrs. L. Douglas Lee
Stanley M. Levenson, M.D.
Mr. & Mrs. Adam M. Lewis
Mrs. Fotini Livanos
Mr. & Mrs. David L. Lowe
Mr. & Mrs. Edgar L. Lowe,
Edgar L. Lowe Family Trust
Mr. Harvey M. Meyerhoff
Mrs. Anne G. Miller and Mr. G. Thomas Miller
Mrs. Leslie A. Miller & Mr. Richard B. Worley,
Miller-Worley Foundation
Mr. & Mrs. Fred Mirmiran,
The Mirmiran Foundation
Mr. & Mrs. George Miron
Dr. & Mrs. Mack C. Mitchell, Jr.
Mrs. Betty & Mr. Walter S. Montgomery, Jr.
The Arkwright Foundation
Mr. Melvin C. Muntzing
Mr. & Mrs. C. Patrick Oles, Jr.
Ms. Jenny Pao and Mr. Bo Shao
Esther S. Pearlstone,
The Pearlstone Fund, Inc.
Mrs. Aliki Perroti
Mr. Max S. Pudelkewicz and Family
Mrs. Marjorie S. Roosevelt
Mr. Robert R. Rosenheim
Mr. & Mrs. George M. Ross
Mr. and Mrs. Mark E. Rubenstein
Mr. & Mrs. Charles H. Salisbury, Jr.
Dr. Gary P. Schoppert
Mr. Alan A. Shuch
Mrs. Claudia Serwer and Mr. Michael Skol
Sonosite, Incorporated
Mr. & Mrs. Stelios Spiliadis
Mr. & Mrs. Richard L. Storch
Mr. Ram Sundaram
Ms. Nina Tao
Mr. David Tepper
Mr. & Mrs. Richard D. Thurman
Mr. Dimitris H. Varvatsoulis
David and Sue Viniar
Meredith & Peter Wellington
Ms. Christie Weiner and Mr. Richard Paisner
Mr. & Mrs. A. Morris Williams
Mr. & Mrs. Gregory Zehner
Dr. & Mrs. Jonathan Zenilman

* Deceased