When Rob Langer was diagnosed with multiple system atrophy, a neurodegenerative disorder similar to Parkinson's disease, his physician Roy Freeman, M.D., could do little except manage his symptoms. As with Parkinson's, no treatments exist to cure or slow the disease, which impairs the body's autonomic, or involuntary, functions including blood pressure, heart rate, bladder function, and digestion.

For patients like Langer and their families, there are often too many questions and too few answers. "I think the only way to take full care of patients is to attempt to answer these unanswered questions," Freeman says. "It's also intellectually exciting. Whenever I have done anything, either in my outside interests or in research, I try to look below the surface and understand things at a deeper level."

As the director of the Autonomic and Peripheral Nerve Laboratory at Beth Israel Deaconess Medical Center, Freeman took that approach when he looked just below the surface of the skin for a potential clue to better diagnose Parkinson's disease (PD) and similar disorders. Building on a technique established by his group and others, he—along with colleagues Christopher Gibbons, M.D., and Ningshen Wang, Ph.D.—recently discovered elevated levels of alpha-synuclein in the skin of PD patients. Alpha-synuclein is a protein regularly found throughout the nervous system and is also the primary component of protein clumps known as Lewy bodies, which are considered the hallmark of PD. Their results, which were published in Neurology in October 2013, offer the first potential diagnostic biomarker to enable clinicians to identify PD with a simple skin biopsy well before it reaches an advanced stage. "This research is on the verge of making a real difference for patients," says Freeman, acknowledging that there is plenty of work to be done to replicate the study and investigate the results across various stages of the disease.

Parkinson's disease, which affects nearly one million individuals in the United States, is the most well known in a group of similar neurological disorders that feature the deposition of alpha-synuclein, called alpha-synucleinopathies. "We have a group of alpha-synucleinopathies that we know so little about," Freeman says of the list that includes multiple system atrophy as well as Lewy body dementia and pure autonomic failure. "We don't know the natural history, we don't know the risk factors that cause patients to progress slowly or to progress rapidly, and I think my group may have the tools to answer those questions."

When Freeman set out to find answers to better diagnose these neurodegenerative disorders, he had the support of a family who understood the value of those efforts. "The Langer Family Charitable Foundation really put this on the map," Freeman says. "It would not have happened without their support." In response to the care Freeman provided to Langer during his battle with multiple system atrophy, the foundation has contributed a large grant to support this research. "Dr. Freeman and his colleagues are doing such important work to help understand these devastating illnesses," Rob's wife, Carol Langer, says. "Our family supports his work in hopes that we can save another family from the debilitating effects of neurodegenerative illness."

Currently, PD is diagnosed only through clinical examination, often when symptoms are pronounced and advanced. Freeman says even expert clinicians can misdiagnose the disorder 20 percent of the time, particularly in the early stages of the
in integrated research, and the autonomic nervous system is the great integrator,” he says of the part of the nervous system that works automatically to regulate bodily functions like blood pressure, heart rate, bowel function, and sweating. The autonomic nervous system plays a vital role in maintaining homeostasis, or stability of the entire human body. “It integrates the internal and external environments, and it integrates multiple systems like cardiovascular, urogenital, and gastrointestinal systems,” he says. “And here we see how autonomic research integrates many aspects of the neurodegenerative disease field.” The investigation into alpha-synuclein in the skin is one of many major ongoing projects in BIDMC’s Autonomic and Peripheral Nerve Laboratory. Freeman is currently the principal investigator on several National Institutes of Health grants investigating the role of the autonomic and peripheral nervous system in central neurodegenerative diseases, like Parkinson’s disease and multiple system atrophy, and peripheral neurodegenerative diseases, like diabetic neuropathy. While Parkinson’s disease is primarily known as a movement disorder characterized by problems with tremor, rigidity, and postural instability, over the last decade, researchers have drawn attention to the non-motor features of the disease, some of which affect patients before the motor symptoms emerge. These premotor manifestations of PD can include cognitive problems and sleep disorders, but because of his expertise Freeman is most interested in those that affect the autonomic nervous system such as blood pressure control and temperature regulation.

CONTINUED ON P. 16

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— Carol Langer

NEWS OF NOTE

SILKEN BONDS
Using pure silk protein derived from silkworm cocoons, a team of investigators from BIDMC and Tufts University School of Engineering has developed a new type of surgical “fixation device” for bonding serious bone fractures. An alternative to the traditional metal alloy plates and screws, these new silk versions may offer improved bone remodeling following injury and can also be absorbed by the body over time, eliminating the need for surgical removal later on.

POISON’S POSITIVE POTENTIAL
A BIDMC research team has shown for the first time that carbon monoxide (CO), the highly toxic gas emitted from auto exhausts and faulty heating systems, may have a role to play in treating cancer. The surprising new findings reveal that in cell culture and animal models, CO can both prevent tumor growth in prostate and lung cancers and can amplify the effectiveness of chemotherapy 1000-fold—while sparing noncancerous tissue from chemotherapeutic side effects.

WINNING WEBSITE
BIDMC is one of 10 hospitals nationally and the only one in Boston to be named a winner of the URAC and The Leapfrog Group’s 2013 Hospital Website Transparency Awards. The BIDMC quality and safety website was the first in Boston to publicly report quality measures, specific clinical service volumes and outcomes, and patient experience and satisfaction metrics as well as report on efforts to improve safety and quality.

FIRST AID FOR THE HEART
In January, BIDMC became the first institution in the United States to use a new minimally invasive medical device, called the CoreValve System, since its recent FDA approval. The device treats patients with severely damaged aortic heart valves who are too ill or frail to have these valves replaced through traditional open-heart surgery. A multidisciplinary team of interventional cardiologists and cardiac surgeons performed the implant using a non-surgical, “transcatheter” technique to place the CoreValve in an 84-year-old man’s heart through a catheter inserted in his femoral artery.
“We thought that with the combination of autonomic involvement in PD, the presence of autonomic nerves in the skin, and the accessibility of the skin, why not look for the hallmark Parkinson’s pathology—alpha-synuclein—there?”

— Roy Freeman, M.D.

Freeman and his colleagues studied skin biopsies and motor and autonomic function testing from 20 patients with Parkinson’s disease and 14 control subjects. They focused on the sensory, pilomotor, and sudomotor nerves and found a significantly higher deposition of alpha-synuclein in the pilomotor and sudomotor nerve biopsies of the PD patients. The results also revealed a relationship between the amount of the protein in the skin and the severity of the PD and physiological measures of autonomic function, such as blood pressure and heart rate control.

Now the team is hoping to assess the validity of the alpha-synuclein biomarker as a predictor of Parkinson’s disease. “It is clear what needs to happen next,” Freeman says. “We know the experiments that need to be done. The biggest challenge for us is the funding.” Freeman and his team are expanding on these preliminary results by investigating biopsies of patients at an earlier stage of PD and patients with other alpha-synucleinopathies, like multiple system atrophy. They recently received grant support from the Michael J. Fox Foundation.

Freeman and his team are also investigating the post-mortem tissue of patients who had a confirmed autopsy diagnosis of PD to look for similar levels of alpha-synuclein in the skin compared to what they found in their recent study. “Parkinson’s disease is a devastating illness,” Freeman says. “There is still much work to be done, but this is a first step to find an accessible biomarker to confirm a diagnosis very early in the course of the disease.”

In Memoriam
Jane Fialkow, 1927-2013

With sadness, the BIDMC community reports the loss of Jane Fialkow on January 23, 2013 at the age of 86. A longtime friend of BIDMC, she was the loving wife of Jay Fialkow, a BIDMC trustee emeritus and former member of the Trustee Advisory Board.

Born in New Haven, Conn., to the late Belle and Julius Marx, Fialkow met her future husband when she was a student at Emerson College in Boston. He was studying at Harvard College. They resided for most of their lives in Newton and Key Biscayne, Fla., before settling in at NewBridge on the Charles in Dedham for the past three years.

Beloved by many, her 86th birthday party included 250 of Jane’s family and closest friends celebrating the theme of “Everybody Loves Jane.”

Along with her philanthropic support of the medical center, Fialkow graciously donated her time as a BIDMC volunteer. She was also actively involved with numerous organizations in the greater Boston community, including Jewish Family & Children’s Service and Combined Jewish Philanthropies.

“Jane, who had such a kind, caring, and generous spirit, will be remembered for her empathy and for the way she always looked out for others,” says Kristine Lapin, senior vice president of development at BIDMC. “She was beloved by many and an inspiration to all of us, and is greatly missed.”

Fialkow is survived by her husband, Jay; daughter Linda Sternberg, a BIDMC overseer; daughter Debra Zabludowski and her husband, Dan; and son David, also a BIDMC overseer, and his wife, Nina. She also leaves behind six grandchildren and her brother, Fred, of Boca Raton, Fla.