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PHOTOGRAPH BY JOHN EMERSON

CLINICAL CARE

TOP *of the* TOP

U.S. News & World Report identified more than 25 physicians from UMDNJ as being in the top 1 percent in the nation in their respective specialties. We're not surprised but we are very proud. We asked seven of these doctors why they think they were selected; and although they all deny being different from many other excellent physicians in their fields, the writers of this story recognized a pattern that might be called the anatomy of exceptional doctoring. Two of its primary components are passion for the work and a high degree of compassion for the patient. Read on to learn more.

Deborah Toppmeyer believes that it is her “sixth sense” — what she calls clinical acuity — that established her among the ranks of America’s top docs. It has also helped build her sterling reputation as an expert in breast cancer, breast cancer genetics and the design and implementation of clinical trials that offer promising new therapies targeted to specific types of breast cancer.

Yes, she has a very impressive resume. She joined The Cancer Institute of New Jersey (CINJ) in 1995 from the Dana Farber Cancer Institute at Harvard Medical School. Now she is chief medical officer and chief of solid tumor oncology at CINJ, director of the Goldstein Breast Cancer Center and the LIFE Center for Breast Cancer Awareness, and associate professor of medicine at Robert Wood Johnson Medical School. She has won awards and published scores of articles.

But to Toppmeyer, a great doctor is defined by EQ —

emotional intelligence — as well as IQ. “A good doctor must of course be competent in medical management,” she maintains. “A great doctor has an equally impressive emotional intelligence, listening to and understanding the patient with compassion and empathy.”

As Toppmeyer describes her clinical acuity, the end result is getting to know her patients and relating to each one, something she does well. Nothing could be a better measure of her own EQ. She understands not only the importance of a special relationship to the patient but also the opportunity to be part of the patient’s family. “They all look to you for guidance,” she adds. “You’re helping a patient transition to a very difficult stage of life. You’re giving difficult news. You must be honest and transparent. Patients need to know where they stand.” And Toppmeyer believes she needs to know where the patient is coming from.

Looking back, Toppmeyer remembers where she came from. Her commitment to a career in medicine came at a very early age. She was talented where it counted — in math and science — but just as interested in “giving back,” a combination that shaped her professional future. She fell in love with oncology during her residency. “You’re not just treating one organ system,” she explains. “You need all the skills, even though you’re

a sub-specialist. You're treating every aspect of the patient."

For Toppmeyer, oncology remains both intellectually challenging and rewarding, although not without its share of disappointment. "You can't cure every patient," she notes, "but you can help them live better and engage the family in that process." Not surprisingly the most rewarding part is the 50 percent of her time caring for patients at CINJ. The other half is spent discharging her administrative responsibilities, and although she admits to little patience with bureaucracy, she appreciates the trickle down to better patient care. "This is an amazing institution," she reports. "Everything we do here is for the patients."

Toppmeyer enjoys the academic research environment at CINJ, its diversity and the opportunities to develop new skill sets. She is excited about the progress research is making in better understanding cancer and in the impact that precision medicine and its targeted therapy is making on patient care. "You know how I feel about communications between doctor and patient," she says. "Just as important is communication between the clinic and our physician/scientists." She knows that discoveries in the clinic spur researchers to develop new therapies. "There are great people at CINJ and it's like working with family," she says. "I was here early on and it's been like shaping your child's future."

Speaking of which, Toppmeyer and her cardiologist husband are the parents of two teenage boys. The household also includes, according to her, "the best dog in the world." She manages the work/home balancing act well enough to allow for travel, golf and family ski trips. And she exercises and runs to "decompress."

She has been practicing for more than 25 years, yet she sees lots more ahead. She wants to spend more time mentoring junior faculty. "And I hope," she adds, "to find time to improve my golf game." ■

— Barbara Hurley

Passion Drives His Work

Lawrence Golbe never intended to be a researcher. In 1982, he was headed straight from his neurology residency into clinical practice. That's when he met Roger Duvoisin, MD, then-chair of neurology at Robert Wood Johnson Medical School (RWJMS), who in the late 1960s had been a member of the team that discovered levodopa, still the most effective and widely used drug for Parkinson's disease. "I was so impressed with his brilliant scientific mind," says Golbe. "He became my role model."

The young physician joined the RWJMS neurology department in 1983. And as they say, the rest is history. In this case, the medical school team helped rewrite the history of Parkinson's disease; and Golbe stepped up to play a leading role. Building on Duvoisin's suspicion that genetics might play an important part in the cause of Parkinson's, Golbe pushed forward. He led the clinical part of a decade-long effort to find the first Parkinson's disease gene. That effort paid off in 1998.

Golbe himself logged thousands of miles from 1986 to 1997, crisscrossing the Atlantic between the U.S. and Italy and traveling to many parts of this country, chasing down DNA samples in the hunt for the suspected disease-causing gene(s). His attention to detail made the critical link between two New Jersey families that were the basis of the "Contursi kindred," a group of six related families whose ancestral home was a town of that name in the hills a few hours from Naples, Italy. The first kindred member whom Golbe found, the son of immigrants, was under his care at RWJMS when he accidentally drowned. After the funeral, his brother, who also had Parkinson's, asked Golbe to be his physician. He extended the family tree horizontally and vertically by interviewing and examining those brothers' immediate relatives, finding six other affected family members. During that process, Golbe noticed that another patient of his at RWJMS had a strong family history of Parkinson's. Where was her family from originally, Golbe asked her? Contursi, Italy, she said. Eureka! He had connected the

dots and the research was on his way.

Next, Golbe recruited collaborators at the University of Naples, who then traveled hundreds of miles on rural roads to bang on the doors of family members whose DNA might help fill out the family tree. Researchers also branched out to Argentina, Germany and northern Italy, where other Contursi family members had settled. The group found three separate families in Italy and three in the U.S. who shared a common ancestor but did not know one another. In total, they found 61 people with Parkinson's in the family, obtaining DNA samples on 20 of those and on hundreds of others without the disease. Golbe and his Italian counterpart established the full genealogy of this extended family through 12 generations to an ancestral couple who lived in Contursi in the late 1600s and early 1700s.

This neurologist-researcher is consistently poised to take that next bold step on behalf of his often-debilitated patients. And hope is one of those things that Golbe always finds a way to offer them.

Two geneticists working with Golbe at RWJMS, William G. Johnson, MD, and Alice M. Lazzarini, PhD, started to use the DNA samples to hunt for the culprit gene. The going was slow with the tools available in a small lab at that time, but the team was able to sift through markers on about half the genome before forming the collaboration with scientists at the NIH. Using their rooms full of state-of-the-art technology, they needed only nine days to find the general region of the gene on chromosome 4, a part of the genome not yet examined by Johnson and Lazzarini. This was published in *Science* in November 1996. A few weeks' additional work was needed to sequence the likeliest candidate genes in



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that region. It showed a mutation in one "codon," or "letter" of the genetic code, in the gene for "alpha-synuclein," a protein not previously suspected of a connection with Parkinson's. That was published, also in *Science*, in June 1997.

Within days of publication of this research, several labs tested the poorly characterized "blobs" of protein found in brain cells of those with non-hereditary Parkinson's — called Lewy bodies — and found alpha-synuclein to be their primary component. This demonstrated that even in Parkinson's sufferers who seem to have no genetic mutation for the disease, malfunction of alpha-synuclein is a fundamental step in the disease process, causing brain cells to die over a period of years. The Lewy bodies are especially prominent in dopamine-producing brain cells, and loss of dopamine is a prominent feature in this disease. Their findings were impactful.

"Currently, drug companies are working to stop the alpha-synuclein from forming abnormal clumps," Golbe says. "One change in this protein sets off a chain reaction that causes the normal alpha-synuclein to misfold. It then spreads from one brain cell to another. There is the same kind of chain reaction in Alzheimer's, Lou Gehrig disease and other neurodegenerative diseases, but with different proteins. If we can figure out an approach to stop the chain reaction in one of these diseases, maybe it can be applied to the others."

Golbe believes that as high-throughput screening speeds up the testing of drugs, scientists will figure out a drug that works to

prevent the spread of alpha-synuclein misfolding and then will figure out why it works and will finally tweak it to make it better.

In 2004, the RWJMS team discovered that a variant in the gene that codes for the enzyme glutathione-S-transferase (GST) affects the age of onset of Parkinson's in the Contursi family and several Greek families with the same gene mutation causing Parkinson's. The GST enzyme seems to detoxify one or more agents that speed up the loss of neurons in these individuals, explains Golbe, which is consistent with the theory that Parkinson's is at least partly caused by a toxin or toxins.

The neurologist has also become one of the world's experts on a lesser known neurological disorder called progressive supranuclear palsy (PSP), which seriously impairs behavior, eye movement, swallowing and balance. As in Parkinson's, a protein, this one called tau, "gloms up in the brain." In 2000, the RWJMS team found that a genetic mutation in the gene for tau plays a role in Parkinson's even though the tau protein seems not to aggregate in that disease. Alzheimer's disease, which also features tau aggregation, does not have this genetic defect shared by Parkinson's and PSP.

Golbe has developed a clinical rating scale for PSP that he published in 2007 and is now used worldwide. Although there are no effective treatments for the disease, he feels that giving patients an accurate diagnosis and prognosis is important psychologically and helps them avoid unnecessary diagnostic tests and useless treatments. The researcher now has a grant from a private foundation to build a National Online Research Registry for people with this disease.

He also worked with a drug company to help design a two-year clinical trial testing a fragment of a trophic factor that is administered via nasal spray, which is targeted to stopping the breakdown of microtubules in the brains of those with PSP. Results are due shortly.

But despite his "eureka" discoveries, there are many unanswered questions; and current therapies treat symptoms but do not cure Parkinson's. Golbe's decades of research, passion for patient care and attention to detail result in a singular level of doctoring. "There are so many drugs, so many potential complications, so many little differences between patients, and then there are changes from visit to visit. You always need to pay close attention," he says.

This attentiveness goes hand-in-hand with an ability to gently mention the personal concerns that a patient may not be able to broach — such as problems with bowel and bladder function, sex and depression. "Chronic disease — by definition — is not curable," he says. "But even if a patient is not responding well to treatment, there are things you can offer that may help him live his life."

Golbe, who heads the neurology residency program at RWJMS, teaches young doctors what Roger Duvoisin taught him 30 years ago. "When someone you don't know calls asking for advice in your area of expertise, don't ever say no. The taxpayers of New Jersey make it possible for us to have protected time to do research, read journals, write papers and go to conferences. There's always something you can offer them in return."

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— Eve Jacobs