



## From make-believe doctor to physician-scientist

BY KATIE SCARLETT BRANDT

**When Charis Eng was only 4, her father presented her with two gifts: a doctor's play set and a chemistry set.** 🧪❤️📖🔬

**E**ither might confound the average 4-year-old, but both ignited Eng's interest immediately. In fact, she found it impossible to choose one over the other—so she combined the sets and played with them simultaneously.

That desire followed Eng, PhD '86, MD '88, through the decades. Now in her 40s, she has combined scientific research and patient care to the benefit of both—and to a degree few physician-scientists can match.

Eng's new institute at the Cleveland Clinic in Ohio, which she grew from a staff of six to 90 in less than three years, is the only one of its kind in the country, proving Eng is a visionary who not only knows how to get what she wants, but also how to create it herself.

Eng joined the Cleveland Clinic in September 2005. Before that, she had created and run a cancer-genetics training program as the founding director of the division of human genetics at Ohio State University in Columbus. But the Cleveland Clinic made her an offer too tantalizing to pass up: to create a new

kind of clinical science center that would bring scientists, clinicians and patients closer together. She dubbed it the Genomic Medicine Institute.

"The Cleveland Clinic is a wonderful place and a very funny place," Eng said. "There was no human genetics research to speak of before I came. They seemed to look down on medical and human genetics."

But with a change of leadership about a year before she arrived, things changed. "And now that they've seen us in action," she said, "I believe they love the idea of genetics and genomics pervading all of medicine."

The institute, which fills the entire fifth floor of her building, focuses on all aspects of translational human genetics and genomics. In it, Eng has placed patient rooms side-by-side with laboratories.

The waiting room, for example, overlooks a lab. When patients sign forms indicating that their blood samples may be used for research, their minds don't wander to an image of some cold,

distant lab where stern scientists in sterile white coats hunch over test tubes and barely utter a word to anyone. Patients and researchers exchange hellos in the hallway, and patients know where their samples end up—right in the next room.

For some new patients, Eng said, the set-up can be intimidating initially. They admit that they're not sure why their doctors have sent them to this specific clinic and assume that something serious must be wrong. But after Eng describes her research and what it can do for the patient, "they say, 'My goodness, I wish I had known this beforehand. I was so nervous,'" she explained.

In its short history, the institute has served more than 2,600 outpatients. Eng, whose job carries mostly leadership responsibilities now, still sees patients one day each week and makes time for her busy research agenda. And she couldn't be happier.

"It's not possible for me to just be a physician alone or a scientist alone," she said. "I would feel that part of me is missing."

### A necessary hybrid

Clinical medicine and research had formed a hybrid in Eng before she could even explain what either was. By the time she turned 12, her play with the chemistry and medical sets had developed into something more serious. Her family moved from Singapore to Chicago in 1975 when Eng was 13, and her father entered the University of Chicago's doctoral program in economics of education. His low salary combined with the poor exchange rate brought pity from people closest to the Engs, and one neighbor—a graduate student at the university—donated his TV and radio to them.

Charis Eng, PhD '86, MD '88, (left) pictured with colleagues at the Cleveland Clinic, where she heads the Genomic Medicine Institute. Photos provided by the Cleveland Clinic

Eng had left the strict, all-girls school she'd known in Singapore and won a scholarship to a co-ed private school in Hyde Park—University of Chicago's Lab School. There, she could learn at her own pace, and reveled in taking 12th-grade honors courses as a freshman. She was also exposed to the world of genetics for the first time—and was captivated by genes.

After three years of self-described bliss, Eng's parents told her to pack her bags. Her father had his degree, and the family was going home. But Eng didn't want to leave. She thrived in the educational environment she'd found in Chicago, which offered opportunities she feared she wouldn't have in Singapore.

Eng's choice to stay in Chicago after her parents returned home was larger than any decision she'd made before. "I was a homely Singapore girl who liked living with parents," she once wrote in an essay. Now she was on her own—kind of.

As a high school student, she couldn't stay in the United States. So she applied early to the University of Chicago's undergraduate biological sciences division. She was 16, and the university accepted.

Though somewhat anxious and overwhelmed, Eng knew she was in the right place. She had long ago decided what she wanted to be when she grew up. In Singapore, there were doctors and there were scientists. But there were no doctor-scientists. At Chicago, she could make that combination a reality.

Only Eng and her parents knew what she potentially was giving up by remaining in the United States. Two of her uncles were very prominent scientists in Singapore—one was the prime minister's personal physician and a professor of medicine; the other was a professor and chairman of geography at

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a university. Eng could have ended up in a very different place had she returned to their support and guidance half a world away.

At Chicago, Eng started early on genetics research, prep work for a doctoral degree. In 1982, after completing her bachelor's degree, she continued at Chicago where she entered the combined MD-PhD program.

In the people around her, she found mentors. There was her genetics professor, Ed Garber, PhD ("He didn't travel like we do now—lucky him. He was in the lab everyday, and he'd sit right next to you and teach you," she notes); Janet Rowley, MD, now internationally famous for discovering translocations; and Funmi Olopade, MD, a fellow when Eng was a student and someone who, "has looked after me ever since."

## Research and patient care

In the early '80s, the concept of a physician-scientist still wasn't all that common when Eng enrolled in the MD-PhD program at Chicago which, at the time, was one of only a few universities that offered the dual degree. Popularity, however, didn't matter because Eng found herself shoulder-to-shoulder with others who wanted to see their research help the patients they treated.

In 1986, Eng completed her PhD; her MD came two years later. She then moved to Boston for a three-year residency at Beth Israel Hospital [at that time], where she learned about the Dana-Farber Cancer Institute affiliated with Harvard University. The institute provided clinical care for cancer patients and conducted research to help fight the disease. Eng set her sights on Dana-Farber and started there in 1991 on a medical oncology fellowship.

She realized then, as she said she still believes now, that "This is the future of all of medicine."

A year later, Eng accepted another fellowship to the University of Cambridge in England, where she was formally trained in clinical cancer genetics at the bedside and human cancer genetics at the bench. In 1995, she returned to Dana-Farber as an assistant professor of medicine and set out to put into practice everything she'd learned over the past 17 years.

"She wouldn't pose many research questions where she couldn't see the direct link between research and her patients," said Debbie Marsh, PhD, who joined Eng's lab at Dana-Farber as her first post-doc.

Eng focused on genetic links to cancer and in 1996, published a paper on Cowden syndrome, a rare disorder affecting one in 200,000 that increases the risk of breast and thyroid cancers. This study narrowed the search for the gene involved in Cowden to a location on a particular chromosome. That work, published in *Nature Genetics*, laid the groundwork for the discovery of a gene called PTEN, which was announced a year later by researchers at Columbia University. In a collaboration between researchers at Columbia, the Eng lab identified PTEN as the Cowden syndrome gene.

PTEN is a tumor suppressor gene whose normal function is to stop cell growth, enabling cells to repair damaged DNA, which is found in cancer cells. If the DNA is beyond repair, PTEN triggers apoptosis—a type of programmed cell death. In either case, the damaged DNA is eliminated and the cancer can't spread. The gene produces a protein that modifies other proteins and fats and may be involved in cell movement, cell adhesion and the development of new blood vessels—functions cancer cells often hijack.

But, as Eng discovered, PTEN doesn't always function normally. A few months after PTEN was identified, Eng found germline mutations in PTEN that predisposed patients to Cowden syndrome. Individuals with PTEN germline mutations are particularly susceptible to cancers of the breast, thyroid and uterus, Eng learned.

After Eng's discovery, she excitedly called all the patients who had participated in the research to share the good news. "Something we thought we wouldn't realize in 20 years, we came to within a few years and we could help the patients and others," Eng said. "My patients felt pretty good about that."

## A sense of pride

Eng's next move was to Columbus, Ohio. Within a few years, she had made the short list for several university jobs, but one was more appealing than the others.

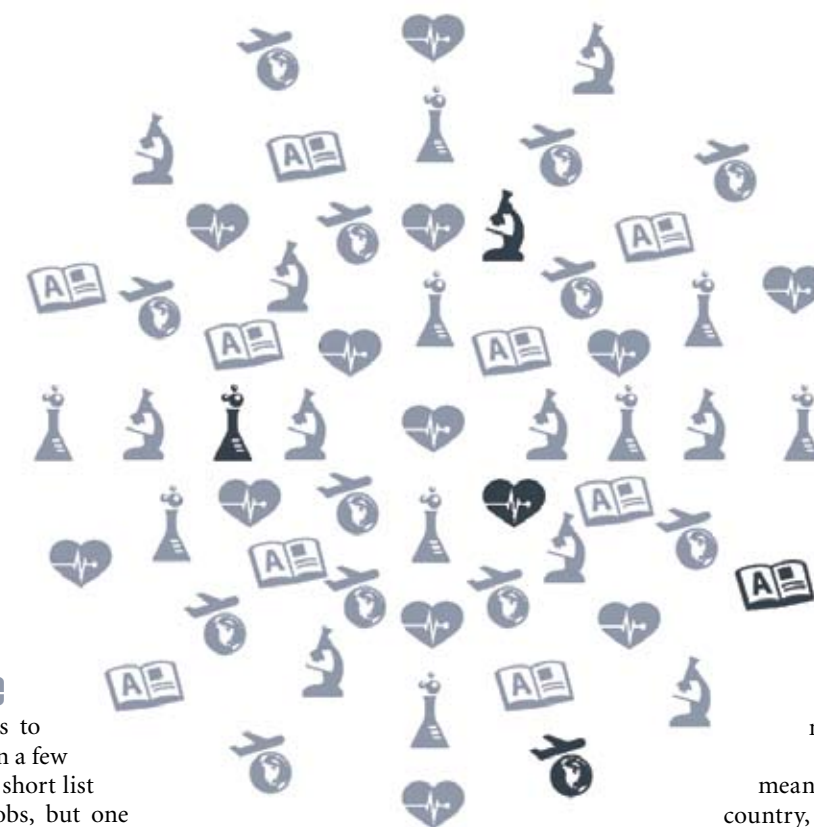
Ohio State University wanted Eng to create a top clinical cancer genetics program and recruit more people like her. Since there was a paucity of clinical cancer geneticists, Eng proposed creating the nation's first clinical cancer genetics training program there, to offer the type of educational experience Eng had to go to England to get. Beginning in 1999, she would teach others how to translate science into patient care in cancer.

On the clinical side, Eng saw patients from OSU's James Cancer Hospital, providing genetic counseling to people with a high risk of heritable cancers. In the lab, she pursued her studies of PTEN, work that led to the better tests to identify germline PTEN mutations in patients before they developed cancer. Knowing of their increased risk, patients can work more closely with doctors to prevent the disease—or at least catch it early.

Eng was at the top of her game. She had wanted to do something good for the country who had adopted her for her unique education. So, the moment her five years on the green card arrived, she immediately applied for U.S. citizenship. Calling on her knowledge of American history and politics, lessons she learned at the Lab School and the College, she was prepared for her citizenship exam. By the time test day arrived, Eng's old knowledge of American history had returned, especially her favorite topic of the key battles that led to Cornwallis' surrender to Washington at the Battle of Yorktown.

When the proctor laid the exam in front of her, deep disappointment washed over Eng. "They asked the simplest questions," she said. Instead of political and cultural history, the test required Eng to "write down the number of colors in the American flag."

Yet, when Eng received her passing grade and took the oath of citizenry, she couldn't deny her sense of pride—not so much for her newly acquired knowledge of American history, but the knowledge that she'd contributed to her country as a physician and a scientist. She was sworn in during an emotional



ceremony held in downtown Columbus just two months after Sept. 11, 2001.

Becoming a U.S. citizen meant Eng could remain in this country, but it also meant she could

bring her parents to live in Ohio. Her father, Soo-Peck Eng, PhD '79 had long since

retired and he and Eng's mother, Siok-Mui, were living in Vancouver. Having them nearby was a great relief to Eng.

Her strong sense of family enables her to work well with families in her clinical practice. It also endears her to those who work alongside her.

Kristin Waite, PhD, who joined Eng's lab at OSU in 2001 as a research scientist, called Eng innovative, loyal and "scary smart." Eng's commitment to her patients and her staff led Waite to follow her when she left OSU in 2005 for the post at the Cleveland Clinic.

"For someone who is not married and who does not have kids, Eng is very cognizant of family values and the impact that work has on family," Waite said.

Micheala Aldred, PhD, can attest to Eng's values. She was the first scientist Eng recruited for the new institute in Cleveland. "In building her department, Charis looks more at people's motivations rather than their research topics," she said. Aldred studies chromosomal deletions implicated both in Wilms tumors, a rare childhood cancer, and also in a rare but devastating childhood condition. Her work has little in common with Eng's research, but the underlying theme is the same. "She wants people to be interested in translational medicine."

Eng is definitely doing something right. While other scientists fear for the state of science in America and struggle to find funding, Eng has been extremely successful, and is "just grateful."

She still relishes every moment of work, and just as she did after she discovered the link between PTEN and Cowden syndrome, Eng continues to share news from the bench with patients in her clinic, which she said gives them an important sense of contribution.

So, though she's all grown up, Eng in many ways is still the little girl who found a way to play doctor and scientist at the same time.