

FRESH PERSPECTIVE
BARGMANN AT HER HOME IN MANHATTAN, IN A MICHAEL KORS JACKET AND MARNI PANTS. PHOTOGRAPHED BY RALPH MECKE.

NEW FRONTIER

Cori Bargmann has quietly become one of the country's most respected neuroscientists. Now she's leading President Obama's \$100 million effort to solve the mysteries of the human brain. By **Rebecca Johnson**.

If Cori Bargmann weren't so nice to mice, she might not be where she is today. Back in the 1980s, when she was in her 20s and a graduate student in a lab at MIT, it was her job to give mice cancer. Ugly, suppurating, lethal tumors. Every time she did it, she started to cry. Her colleagues rolled their eyes. What kind of a scientist can't give a mouse cancer?

"I will defend to my grave the importance of animal studies," Bargmann says. "You cannot study metastasis in a dish. Nevertheless, I personally found it hard to do." And so Bargmann moved on to other animals. Worms. Not the fat, juicy ones you see in the soil but tiny nematodes: practically invisible squiggles of squirming lint that feed on rotting vegetation. When I visit her laboratory at Manhattan's Rockefeller University, overlooking the steely-gray currents of the East River, she places a dish of these worms under a microscope. Magnified, they are surprisingly nimble gymnasts somersaulting toward one another in graceful arcs of black and white. They look, I remark, like a tiny Escher

drawing come to life. "Yes," she agrees, "there's a reason their Latin name is *C. elegans*."

What drew Bargmann to worms at MIT was not their looks but their simplicity. Those feints and lunges weren't, she was convinced, random. The worms might be deaf, mute, and mostly blind, but something made it possible for them to find food and reproduce—the very activities most human adults do (or seek to do) on Saturday night. The golden grail for a neuroscientist is unlocking certain mysteries: How do thoughts become actions? What causes degenerative diseases like Alzheimer's? Parkinson's? Or psychiatric illnesses like depression and schizophrenia? The answers lie somewhere in the 10 billion neurons that compose the matrix of our brains. The worm, by contrast, has a mere 302 neurons. "If genes were words," she says, "it would be the difference between *Goodnight Moon* and Shakespeare." The worm, in other words, was knowable.

Bargmann's hunch paid off. Over the last 25 years, her work on the neural circuitry of worms has uncovered tantalizing clues to the role of genes, behavior, and environment that had previously only been guessed at. "A lot of people were looking at this before me," she says modestly. "What *C. elegans* was good for was closing the loop between genes, neurons, and behavior. With such a simple animal you can say, 'This gene is having this effect at this location and making this behavior occur.' It's a lot harder to connect all that in a larger animal."

For most of the last decade she has held a post at Rockefeller University, which accepts only graduate students and is generally considered, among scientists, a utopia for research, free of the infighting that characterizes so many academic institutions. She has received a flurry of awards—the Dart, the Kavli, and just last year the Breakthrough Prize, *lives* >180

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established by tech moguls Mark Zuckerberg and Sergey Brin (among others), which carries a \$3 million award, or roughly twice what the Nobel pays. "It was," she says, "like having a bag of money drop on your head out of the sky." Or, as one of her friends e-mailed her, "That's a lot of shoes" (a nod to her predilection for Christian Louboutin high heels).

Until recently, Bargmann has been famous mostly among other pointy-headed scientists. She tweets, but the content is usually something like "Very psyched about allele-specific single-stranded siRNAs that ameliorate mouse Huntington's-disease model." All that changed earlier this year, when President Obama announced the BRAIN (Brain Research Through Advancing Innovative Neurotechnologies) project, a \$100 million initiative designed to direct resources toward the most promising fields in neuroscience today. The effort, which the president boldly compared to the Apollo and Human Genome projects, will be directed by a committee of neuroscientists, led by Bargmann and Stanford neurobiologist William Newsome—what the National Institutes of Health director Francis Collins has called a "dream team."

As the daughter of German-born parents in Athens, Georgia, Cornelia Isabella Bargmann had a childhood that straddled the intellectualism of old-world Europe and the buoyant optimism of the American South. "It was the Cold War in the 1970s," she recalls. "Kids were expendable. We were always building rockets in science class and blowing things up." Her father, a translator at the Nuremberg trials, taught statistics and computer science at the University of Georgia, while her mother oversaw the cultural life of Cori and her three siblings by arranging piano lessons and reading aloud the work of writers like Konrad Lorenz, the Austrian ornithologist.

Bargmann graduated from the University of Georgia, where she was the class valedictorian, and then went on to earn her Ph.D. at MIT. From the first, she stood out in a male-dominated field. "There were no real barriers for me," she says. "I don't remember ever being told that girls couldn't do science." In the 1980s the science writer Natalie Angier observed the MIT lab where Bargmann worked as they attempted to decipher the genetics of cancer oncogenes. In her book describing the search, Angier called the young scientist a "cool, competent sylph" who "may well be the brightest student at MIT" and "one of the few almost perfect people I have ever met."

Bargmann's husband, the Nobel Prize-winning scientist Richard Axel, confirms that his wife was an early phenomenon. "I told a friend I was going to MIT, and he said, 'There's a tall, thin blonde in Bob Weinberg's lab; go talk to her.' He didn't even know her name, but I did what he said."

Because she was tall, blonde, and thin? I ask, a little confused. "No!" he corrects me. "Because she was so *interesting*. The incisiveness of her mind was quite remarkable in one so young."

After MIT, Bargmann joined the faculty at the University of California, San Francisco, but in 2004 she was lured back east by Axel. The two wed in Paris in 2007. (It was Bargmann's second marriage; her first, to a fellow MIT graduate student, ended in divorce.) "I hesitated before asking her to leave San Francisco, because she had a very rich and interesting life

there," Axel says. "But very quickly Cori embraced the world of New York writers and artists. And they were intrigued by her. Science matters, but art matters, too."

They now live in one of those gracious limestone buildings lining Riverside Drive in Manhattan. The couple go to the opera about 20 times a year, attend the ballet regularly, and

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dine out every night—but rarely before 9:00. "When you visit Cori," says her sister Dorie, an investigator with the federal public defender's office in Austin, Texas, "you never know when you're going to eat." They also keep a house in East Hampton and share a passion for good clothes. His suits are custom-made; she is well known at the Armani store on Madison Avenue. The fourth e-mail Axel received after he won the Nobel Prize in Physiology or Medicine was from Vincenzo, Bargmann's personal salesperson at the store, reminding him that she was going to need some new gowns for the balls.

When the e-mail arrived asking if Bargmann would head up the BRAIN initiative, she hesitated for a few days. "It's more pressure, it's very public, and I have been very happy under the radar," she says. "We are committed to our laboratories," adds Axel. "It would be natural for someone in her stage of career to hesitate at assuming a more public role in science policy, which can be political and controversial. But Cori feels very strongly and thinks very hard about doing the right thing."

So far, the right thing has meant hours of work corralling scientists, answering e-mails, talking on the phone, and weathering a fair amount of snark and paranoia from scientists who fear that the money going toward BRAIN will mean fewer resources for their own work. "The sequester is hurting research very badly," she says. "If I thought this project was going to take resources away, I wouldn't be involved. I am doing this because I think it is going to be good for my field." She is even somewhat sympathetic to the snark. "There was no real plan," she admits of the early days of the project. "What's wrong with sniping about that?"

Making Bargmann cohead of the initiative was a clever way for Francis Collins, the NIH director, to quiet the critics, not just because she's a brilliant scientist but because she also has a reputation for being a stellar person. "Cori is a superb choice," says Marc Tessier-Lavigne, president of Rockefeller University, who once worked in an adjacent lab in San Francisco. "She's a remarkably deep and creative thinker, but she's also a wonderful colleague and mentor. Cori is very generous with everyone. I have long thought she would make a great leader."

"The initiative was initially so controversial, they needed somebody like her, who was beyond reproach," says Leslie Vosshall, a fellow professor at Rockefeller. "She's so perfect and relentlessly successful, we're all slightly afraid *lives* >186

of her. She stands out in every way. It's very difficult to keep up with the scientific literature in your own field, but besides neuroscience, she knows cancer, the immune system, and genomics. It's quite unusual to be so broadly read. She's like a walking supercomputer. I think at night she must download stuff straight into her brain from her magic notebook."

In September, Bargmann and fourteen other scientists on the committee are scheduled to release a set of goals that they believe represent our best hope for figuring out how the brain works. Scientists around the country will then apply for grants in the areas the committee has identified. All of this is happening, Bargmann explains, in a promising moment for the field, partly due to simple improvements in existing technology—microfabrication gets better every year; electrodes get stronger and thinner, making it easier to measure more nerve cells; and computers can handle even larger sets of data. Perhaps more important, there have been what she calls "mind-boggling" advances in procedures like optogenetics, in which scientists use light to activate different sets of neurons, then observe how the animal responds. "This technique," she says, "really marks a shift in neuroscience. Now we're not just watching the flow of information but trying to change it. We might have done this and the animal would have a seizure and fall over, but that's not what happened. Instead, you get this sensible, well-organized behavior that you can interpret."

Bargmann, like most experienced scientists, is careful not to make promises about real-life applications for her research. "There's always this urge to tell people that you'll be able to help them," she says. "But it takes a long time to do the research." Indeed, her characterization of the scientific life is almost comically grim: "Being a scientist is extremely boring and frustrating. You have a good idea and it doesn't work; you write a grant and it isn't accepted; you submit a paper for publication, it's rejected. You basically have to be able to delay gratification indefinitely." Press her, however, and she will talk about some possibilities for fields that could benefit from work funded by the BRAIN project. There is, for example, the dismal state of the psychiatric drugs being taken by millions of people across the world. "The drugs used in psychiatry now were basically discovered accidentally in the search for heart medications in the 1970s. There hasn't been a fundamentally new discovery since then, only improvements in existing kinds of drugs. If we understood the rules and processes of how the brain works normally, we'd be able use more rational approaches in developing medications."

inevitably, young female scientists look to Bargmann as a role model, a phenomenon she seems to regard warily. After all, no one is truly perfect. She is afraid of spiders, and jet lag causes her to experience a deep, debilitating depression. "I was giving a speech to a group of girls at Stanford." She stops herself, clucks with disapproval, and corrects the noun. "I was giving a speech to a group of women, and they asked me these questions I found so touching." She rifles through her desk and returns with a stack of index cards.



DOWN TO A SCIENCE

"I HAVE BEEN VERY HAPPY UNDER THE RADAR," SAYS BARGMANN, WEARING MICHAEL KORS. PHOTOGRAPHED AT THE HOWARD HUGHES MEDICAL INSTITUTE AT ROCKEFELLER UNIVERSITY.

Handwritten on each are questions about her research, the state of science, but also her own career, many of which come down to a somewhat plaintive "How did you do it?" I pick a card at random and read it aloud.

Can you please comment on this: A woman scientist can only choose two out of the following: scientific life, personal life, family life.

"I would say," she answers, "you can have a scientific life and hobbies. You can have a scientific life and a family, but it's probably true that you can't have all three and feel good about them. But that's true for men, too. The problem is being a human being." I look around her pleasantly crowded office. One table is filled with snapshots of her parents, her sisters, her niece, and her goddaughter. Artworks by friends fill the walls. Lined up on the windowsill are empty champagne bottles, each one representing the successful completion of a Ph.D. by one of her graduate students. It is the room of a person who is connected to and adored by many people, but not her own children. Very gently, I approach the fact that she is, at the age of 52, childless and likely to remain so.

"This is really easy for me," she answers without hesitating. "I never wanted to have children a single day in my life. It's why my first husband and I broke up. He thought I would grow out of it, but I never did. Now he's married with lots of children, and I am happy for him. Temperamentally, I'm just not drawn that way. The only time I feel bad about it is when I am talking to young women scientists and I know they are looking at me, thinking, Oh, she gave up kids to be a scientist, and I want to tell them, 'No, I didn't!' I am very happy with my personal life."

Of course, when your life is dedicated to science, the personal and the professional are, by definition, inextricably intertwined in a way that others can find hard to fathom. "Science," as Bargmann explains, "is a community enterprise. I have this romantic view that we are all like workers building a medieval cathedral. Some people are making a saint in a crèche, another person is making a cool gargoyle that no one sees, and others are doing the boring work of laying the bricks for the structure. But even that is interesting. And when it's all done, together we'll have built one of the great accomplishments of humanity." □