Some Good Chemistry

Guts and chance led a teenage immigrant to lab success. BY ESTHER LANDHUIS

IT WASN'T SUPPOSED TO HAPPEN.

Scientific experiments rarely work the first time, and this one seemed to stand little chance at all. "It was a crazy idea," says biosciences doctoral student Mireille Kamariza.

Yet in fall 2015, she peered into the microscope and saw "squiggly green things"—a model for tuberculosis bacteria set aglow with a just-created chemical dye. Developed with hopes of speeding diagnosis in poor countries struck hard by the disease, the new method for detecting culprit bugs in patients' sputum "could turn out to be one of the most impactful things we've done in TB since the beginning of my career," says chemistry professor Carolyn Bertozzi, Kamariza's adviser. "I couldn't believe it worked so well, since there were many arguments for why it might not."


BERTOZZI

> The new method could become 'one of the most impactful things we've done in TB.'

Turning this boon into a useful diagnostic needs more work, but for now the bigger surprise is how 27-year-old Kamariza got here in the first place.

She grew up with three older brothers in Burundi, a small African country embroiled in civil war. The family moved a lot; people around them died of malaria and AIDS. A close relative succumbed to TB, one of the world's deadliest infectious pathogens. In 2015, TB sickened 10.4 million people and killed 1.4 million—a toll worse than that of AIDS. "Living in Burundi, I went to a lot of funerals," Kamariza says.

In those conditions, you might think science was a faraway dream—a distant world—and you'd be mostly right. "In my country, there were no research labs," Kamariza says. "Science was something Europeans and Americans did. It was for other people—not for me." One of her first, perhaps only, exposures to science came through reading books about planets. As a kid, Kamariza says, "I wanted to go into space."

She didn't make it that far. But in fall 2006, 17-year-old Kamariza packed her bags and flew with one of her brothers to California. They crammed into an older brother's studio apartment near San Diego Mesa College, working and "taking classes here and there between jobs," Kamariza says. "When you're an immigrant, you start really low."

A year later, one of her chemistry professors, a fellow French-speaking African, saw potential in Kamariza and persuaded her to focus on school. The hard work paid off. In 2009, Kamariza earned a spot at UC-San Diego and dropped her Safeway job.

Kamariza calls herself shy. Yet chatting one-on-one she smiles easily and freely shares her journey's twists and turns. She's quick to acknowledge others who paved her way, wanting to "give credit where credit is due." Her life teems with examples of tribulation turning into triumph. She tends to gloss over how her own instinct and initiative drive the process. Kamariza is a quiet maverick.

Transferring to a big school like UCSD, especially as a young minority woman, "you don't have any friends. You don't know what to do," Kamariza says. She confided this to a math classmate whose parents were from India. The pair didn't wallow in pity. They created a mentoring program, which they called Open Doors, to match incoming transfer students with current students. It was "just an idea," Kamariza says—a "peer-to-peer thing" to enfold transfer students and help the university welcome diversity.

But their efforts spawned other programs that continue to this day, such as symposia that introduce prospective transfer students to faculty and help them find summer research opportunities. Kamariza "is one of my all-time favorite students," says David Artis, dean of undergraduate research initiatives at UCSD. "She was accomplished and dedicated to the success of many besides her own."

Still, when she came to the Bertozzi lab (then at UC-Berkeley) as a prospective PhD student in summer 2012, Kamariza struck the professor as reticent and nervous—not so unusual, perhaps, for students from large schools, accustomed to drifting in a sea of anonymity. Unlike students from small campuses who had enjoyed peer-like relationships with their professors, those coming from big schools "feel bad when they ask for your attention. They're apologetic about having to meet with you," says Bertozzi, whose group joined Stanford ChEM-H (Chemistry, Engineering & Medicine for Human Health) in August 2015.

The first time Kamariza set foot in Bertozzi's office, "I thought she was going to quiz me about chemistry," Kamariza says. Instead, "we ended up talking about life, what it means to be a woman in science, where the future was going. She was very approachable."

That conversation took place before the school year began. When it started, though, Kamariza felt unsettled. "The lab was big. I'm a minority. People didn't click with me right away," she says. And Bertozzi often wasn't around, traveling frequently to speak at conferences.

Kamariza initially learned of Bertozzi when the professor gave the keynote lecture at the 2012 American Chemical Society meeting in San Diego. In the aftermath of her Open Doors efforts, Kamariza had received a fellowship to spend winter quarter of her senior year working at ACS headquarters. "My boss asked me to do a piece on Carolyn," Kamariza says. "As I researched her, I realized she did TB work."

Mycobacterium tuberculosis resists many antibiotics because of its dense, meshy cell wall. "Drugs don't typically get in," Kamariza says. As mycobacteria remodel their cell wall, they metabolize a sugar called trehalose. Trehalose is found in many animals, plants and microbes—but is uniquely used by TB and related bacteria as a scaffold for building more complex molecules. This distinct property is the secret behind the new chemical tool, DMN-Tre (4-*N*,*N*-dimethylaminonaphthalimide-trehalose), that lit up mycobacteria as green squiggles in that 2015 experiment that worked on the first try.

The idea for DMN-Tre came just a few months earlier, right after Bertozzi's group moved to Stanford. At the time, Kamariza was on a different TB project—a tricky biochemical endeavor that wasn't working and stalled further with the move. She brainstormed with Peyton Shieh, a former lab mate who now works at Illumina, a biotech company in San Diego. Shieh was about to graduate. He had created various fluorescent dyes for microscopy. But those dyes required stringent washes and thus wouldn't work in the clinic. "I wanted something easy to use for labs without a centrifuge," Kamariza says.

A week later, tinkering in the lab as a welcome break from his thesis writing, Shieh came up with DMN-Tre—a dye that glows only when incorporated into the cell wall of mycobacteria. It doesn't light up dead bugs. And it doesn't react with other kinds of bacteria. Since the reaction is so specific, it doesn't require the tedious washes typical of existing TB detection methods. That it worked the first time is a "good sign if the goal of a project is to develop a technology that is simple and robust," Bertozzi says.

BERTOZZI AND KAMARIZA presented the work at several meetings last year and submitted a paper for publication. They have filed for a patent and gotten funding from the Bill & Melinda Gates Foundation to test their diagnostic on TB-infected patient samples in places with a high disease burden. The assay isn't yet ready for prime time, but odds are Kamariza will find a way. ■

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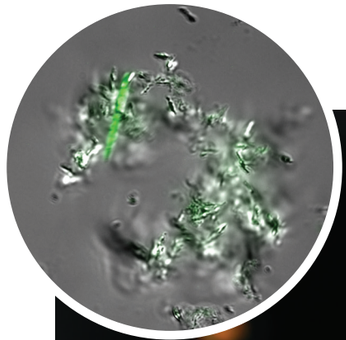

GREEN LIGHT: Kamariza's work with the new dye could help her home country, Burundi, battle TB.

COURTESY MIRIELLE KAMARIZA (TOP); GLENN MATSUMURA

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