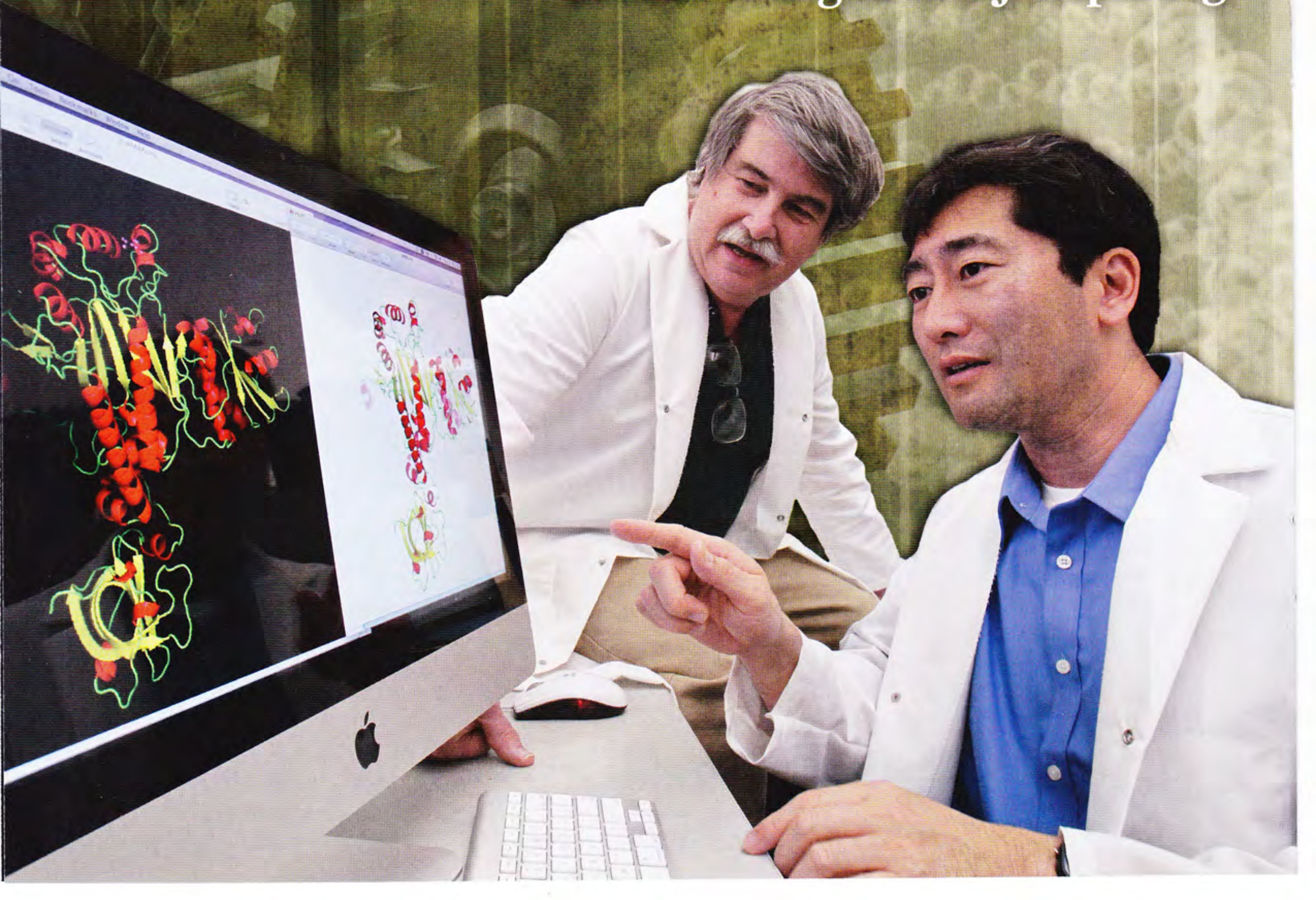
Designer genes

Novel ways to use nature's building blocks intrigue Dr. Joseph Ng



By Diana LaChance

A man infected with a deadly virus boards a plane heading for the United States. He knows he will die, but he is not afraid. He is on a mission: to infect as many people as he can before he succumbs. Who is this man? He is the new face of bioterrorism.

This may sound like a doomsday scenario, but it's one that we must be prepared for, says Dr. Joseph Ng, founder of iXpressGenes and associate professor and director of the University of Alabama in Huntsville's biotechnology program. "The next bioterrorism event won't be a bomb or explosion; it will be a suicidal person carrying a deadly disease," says Ng. And that's where synthetic biology comes in. "A lot of synthetic biology, in terms of defense, deals with addressing those kinds of threats."

'LIFE FROM SCRATCH'

Synthetic biology is a relatively new field that combines science and engineering to create or redesign biological systems for specific purposes. In essence, says Ng, it's "creating life from scratch" by synthesizing genes at the molecular and structural level to create microorganisms that have beneficial value. Take a bioterrorism threat as an example. Sensitive detection systems already exist in nature, says Ng, referring to those found in bees or sharks. "So we can take those known proteins, or enzymes, and put them into a microorganism to detect, say, heavy metals or fertilizer or a virus," he says. But those proteins don't have the capability of alerting authorities to the threat.

"What if you then instructed the microorganism to change color when it detects a pathogen?" asks Ng. Like detection systems, this color-changing ability is already seen in nature; consider fireflies or jelly fish. All that needs to be done is to add those known color-changing proteins to the detection proteins. "The result would be a microorganism that you could then paint on a wall, and if it turns a certain color, you know the toxin is there," says Ng. Again, this new microorganism, now considered a super enzyme, can't be found in nature but is made up of naturally occurring biological systems that have been combined and repurposed for a particular application.

It may sound like science fiction but, says Ng, "this is entirely engineering. We're not building airplanes and missiles and tanks, but we're building things at an atomic scale." To help explain the process, he likens it to a molecular Lego project in which he and his team use the same building blocks found in nature. "Nature is not infinitely diversified. There are only about 1,000 pieces," he says. "We have the same pieces; we just have to figure out how to put them in a useful shape or form so that it can be used for benefit, whether it's defense or health or energy."

Bioremediation is another perfect example. "Say you wanted to break down oil, as in the Gulf spill," says Ng. "There are already microorganisms in nature that eat oil, but their byproducts may be more dangerous than the oil itself." The goal is to create a new microorganism that can metabolize oil but break it down into something that's inert. To do that, he says, "we're taking enzymes from different organisms and putting them together in the best way possible so that they will rely on each other to complete a biochemical task." In the case of Ng's microorganism, however, "it works in the grasslands, not just the water." After all, he points out, there is still a lot of oil in the marshes of Louisiana. "So if you had a grass that you could plant, it could suck it up."

Ng says that bioremediation and biodefense tend to go hand in hand, but the bigger challenge is biofuel. "Biofuel, and specifically cellulosic energy conversion, is a big problem. We need something that can break down grass, for example, and turn it into fuel," he says. "So you have to put in proteins that can work together in a pathway to take the grass and digest the cell wall to give out a metabolite that can be used for ethanol production or any other combustible product." That doesn't exist in nature, and efforts made thus far to create such a microbe have been unsuccessful. "The problem is you're not getting enough ethanol for the amount of energy you're putting in, so it needs to be more efficient," says Ng, who says he considers biofuel more of a long-term goal. "It will take two more years before we can get a first prototype organism."

Health also falls into that category. "For health uses like drugs, you have to get FDA approval," says Ng. "That's a long and expensive path, so partly because of that, we didn't go that route." There's also the accompanying issue of public perception. "With every new technology, there is always this Armageddon type of thinking," he says. "But for most people, it's just a question of not knowing about it and watching too many Hollywood movies!" Jurassic Park is just one of many that come to mind. "But everything can be dangerous; it just has to be overseen," says Ng. "It's not only understanding the science but being responsible for it."

SAFETY PRECAUTIONS

That's why he and his team take precautions above and beyond what is already mandated by the federal government. "There is government oversight and there are policies in place for synthetic biology. And even as we speak, there is legislation going through," says Ng. "But right now, we are self-regulated. We have a committee overlooking us and to make sure things don't run amok." He also incorporates other safety measures. "We don't make things that can replicate themselves, for example. We put in a suicidal gene, so it can grow up and then die in case of the Armageddon scenario." And he adds that he and his team also use specific hosts that are not able to contaminate people or animals. "As the people closest to the technology," Ng says, "we have every reason to be safe."

Ng has many years of experience in the field of biochemistry and in synthetic biology specifically. His early work in the field focused on extremophiles, organisms that live in physically extreme conditions. In his case, it was deep-sea hydrothermal vents known as black smokers. "We wanted to know what it is about the molecular architecture of black smokers that renders them resilient to the high heat and pressure, so we made trips to the Mid-Atlantic Ridge, got cultures, isolated the organisms, sequenced the genome," says Ng. Funding for that project eventually ran out, but he says "after five years, we picked up a lot of technology used for cloning and synthesizing genes to make unique recombinant proteins. When we realized these enzymes may have commercial uses, we looked at trying to commercialize them." ■

Glenn Baeske

Dr. Joseph Ng, right, and his partner Dr. Marc Pusey, left, look at a computer image of a model of a protein showing its structural elements.