Iron man

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NEW REGENTS PROFESSOR LAWRENCE QUE STUDIES IRON-CONTAINING ENZYMES THAT SCIENTISTS WOULD LOVE TO MIMIC TO SAVE ENERGY AND EVEN LIVES

Lawrence Que, the new Regents Professor of Chemistry, is one of the world's foremost experts on iron-containing enzymes.

Photo: Patrick O'Leary

By Deane Morrison

Growing up in the Philippines, University of Minnesota chemistry professor Lawrence Que found his calling early. "I was interested in magic," he explains. "That proceeded to chemical magic like smoke and fire and color changes. A high school teacher would give me chemicals even though I wasn't in high school yet. I took them and did experiments." Que ("Kay") has since become a world leader in the chemistry of a large class of medically and commercially important enzymes. This June he and two other professors were named Regents Professors, the University's highest faculty rank. The enzymes Que studies contain iron, but hold it in place with structures quite unlike the one found in hemoglobin. Known as "nonheme iron" enzymes, they capture oxygen and use it to build chemical messengers in the nervous system like adrenaline, L-dopa (used to treat Parkinson's disease), and serotonin; to make antibiotics; or to repair damaged DNA in cells. Understanding how these enzymes work could lead to better treatments for maladies like Parkinson's or even cancer. But nonheme iron enzymes also perform the crucial first step in the production of industrial chemical feedstocks from methane gas. That talent, if harnessed, could mean enormous energy savings for industry.

Swamp gas and diamonds After graduating from college in Manila, Que came to the University of Minnesota for doctoral work with chemistry professor Louis Pignolet. Que left for other positions but returned to the University's chemistry department for good in 1983. Working with University of Minnesota biochemistry professors John Lipscomb and Eckard Münck (now at Carnegie Mellon), he became intrigued by how nonheme iron enzymes use iron to put oxygen to work.

If a chemist can be said to have a pet enzyme, Que's is one that turns swamp gas—methane—into methanol, a major feedstock for all kinds of industrially important chemicals. The enzyme is found in lake bacteria living in the zone where methane rising from the ooze meets oxygen diffusing from the surface.

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Methane is a simple molecule: one carbon atom and four hydrogen atoms. To make methanol, a hydrogen atom must be pulled away from the carbon to make room for an atom of oxygen. But the carbon doesn't let go easily; thus, making methanol commercially requires very high temperature and pressure. "But bacteria in the middle of [Minnesota's] Lake Minnetonka [do this] at or near 35° F," says Que. "We'd like to understand how that works because soon we'll have to think about methane as a replacement for petroleum to make all sorts of things, like plastics and drugs. Plastic now comes from crude oil, and we'll probably run out of that before methane." In a major discovery, Que and his colleagues found that the lake bacteria's enzyme generates a key, diamond-shaped structure—the "diamond core"—comprising two iron atoms and two oxygen atoms. The diamond core efficiently catalyzes the conversion of methane to methanol, a feat that, if reproduced on an industrial scale, would mean big savings of money and energy in the commercial production of chemicals. By discovering the diamond core mechanism, Que, Lipscomb, and Münck knocked out a major obstacle to understanding how nonheme iron enzymes work. "Realizing that the diamond core was a possible explanation for how [the bacterial enzyme] works was a major highlight for me," Que remarks. Que is best known for producing simplified chemical models of what makes nonheme iron enzymes work their magic. The environment of an iron atom within such an enzyme is complex, and "it would be impossible to fully understand how the chemical reactions occur without the aid of the simpler [models]" that Que synthesizes, says Lipscomb, who remains one of Que's closest research colleagues. "Larry is right at the pinnacle of this field worldwide," he adds, calling Que's synthesized models "his masterworks."

Personal chemistry A sought-after teacher and adviser, Que has shepherded 32 doctoral students (with 10 more currently in his lab) and around 70 postdoctoral fellows. Often, they learn about more than chemistry. "One reason I like the Twin Cities is the abundance of accessible theater," Que says. "I've been known to get my students to go." Que has a way of bringing out the most in them—and his colleagues. "He gets things done, and he not too subtly encourages the rest of us to keep moving forward," Lipscomb says. "Somehow [people find themselves] volunteering for projects that they might never take on when left to their own devices. Almost always it works out for the best, but you end up shaking your head and wondering how he talked you into it. "We need people like Larry."