



# NAVIGATING THE REACTIONARY WORLD OF MOLECULES

ONE MAN TAKES THE LEAD

*By Peta Owens-Liston*

**T**wo Aztec gods watch over Dale Poulter's desk as he taps away on his keyboard. Their names, Coyolxauhqui and Tlaloc, are as syllable-ridden and mysterious as the words that describe Poulter's research in isoprenoid biosynthetic pathways. Next to the Aztec moon and rain gods are two more powerful figures from the Mayan civilization—original rubbings from Mayan stone reliefs. Poulter describes how archeologists not long ago decoded the whole Mayan “language”—hieroglyphic inscriptions—providing insight into the Maya's powerful reign.



Decoding is what Poulter does, albeit the “hieroglyphics” he deciphers are the molecular structures circulating within us and all living things. A distinguished professor of chemistry,

South America, Australia. As an expert in his field, he is often a guest professor or lecturer at universities around the world. As the editor-in-chief of the premier journal in

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Poulter has homed in on a massive family of molecules known as isoprenoids, which ultimately can provide insight into how to develop drugs to lower cholesterol, curb cancer, and treat malaria—to name a few ways lives may be improved.

“Dale’s work opens up discovery for other people to understand and design drugs. He is most likely the leading researcher in the country in the study of isoprenoids,” says medicinal chemistry Professor Art Broom, who has known Poulter since he arrived at the University in 1969.

“His research is the cutting edge of interdisciplinary research at the interface between biology and chemistry,” adds chemist Peter Stang, who attended graduate school with Poulter and was hired by the U in the same year.

Organized and neat, Poulter’s office is dotted with evidence of the travels his work has taken him on: Spain, South Korea, China,

his field, the *Journal of Organic Chemistry*, Poulter treads even more ground, attending editors’ meetings worldwide. “I’ve enjoyed watching the journal grow in terms of author participation, quality, and diversity as new areas of organic chemistry develop,” reflects Poulter, who processes almost 3,000 manuscripts a year with help from nine associate editors.

“He’s an adventurer, who loves to travel and loves the outdoors,” says Stang. “And he is just as fearless in his science and in attacking new areas—he’s not afraid to try new things.”

Unrushed and soft spoken, Poulter doesn’t limit his discoveries to just the world beneath the microscope or in a test tube. Fine black sand fills an antique apothecary jar in his office, reminding him of a particular beach in Hawaii—one of the many places he and his wife, Susan, have scuba dived. (An occasional encounter with a bull shark has not deterred him from exploring this underwater world.) He also frequently helicopter skis in Canada.



A sabbatical in Australia was a chance to mix bird watching, wildlife sightings, and diving with work.

“Dale is extremely committed and dedicated to his work, which is most often what takes us on our many travels,” says Susan, who earned her Ph.D. in chemistry as well and has traveled the same path with Dale from high school on through Berkeley and to the U, where she then earned a law degree. “He loves to travel, enjoying the people and culture, but mostly he loves exploring the scenery of someplace new,” adds Susan, who points out that family is important too, and they both relish the time they get to spend with their children and grandchildren.

Poulter’s calm demeanor fuses well with the motivated and curious students who work in

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his lab—a series of rooms that run the length of a hallway. He explains to his students that if his office door is open, then he is available to them. “I haven’t seen that door closed once in six months,” says his administrative assistant, Tracy Oulman.

“Dale is interested not only in your lab work but in helping you find a career path that is right for you, so he really gets to know us and our interests,” says Rochelle Bohaty, a graduate student in her fourth year working in Poulter’s lab.

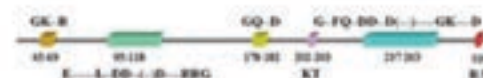
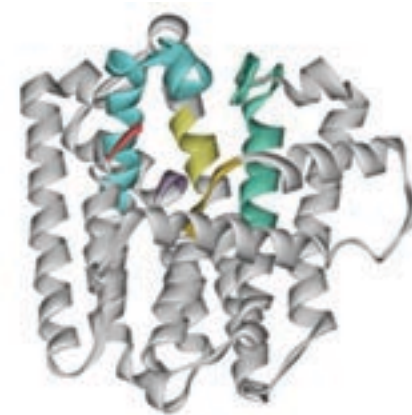
“He allows you to have freedom in the lab so you can learn on your own—he wants you to develop as a scientist so you can be successful on your own one day.”

“His breadth of knowledge is substantial and makes him unique as a scientist,” recalls

Hans Erickson, who spent 3 1/2 years as a post-doc in Poulter’s lab and now works as a scientist at a company in Cambridge that develops anti-cancer

drugs. “He has never been afraid to branch out into all areas of chemistry and has never stagnated—I remember him always coming up with new strategies and fresh ways of looking at old challenges.”

While Poulter doesn’t get as much one-on-one with students in his large organic chemistry and biochemistry classes, he enjoys seeing the light bulbs go on as he reveals how something as “boring” as chemistry is actually very relevant to their lives. “Their eyes start opening more when they realize that everything that goes on in their bodies has to do with chemistry,” says Poulter. “Then, they learn about the direct correlation to diseases through our



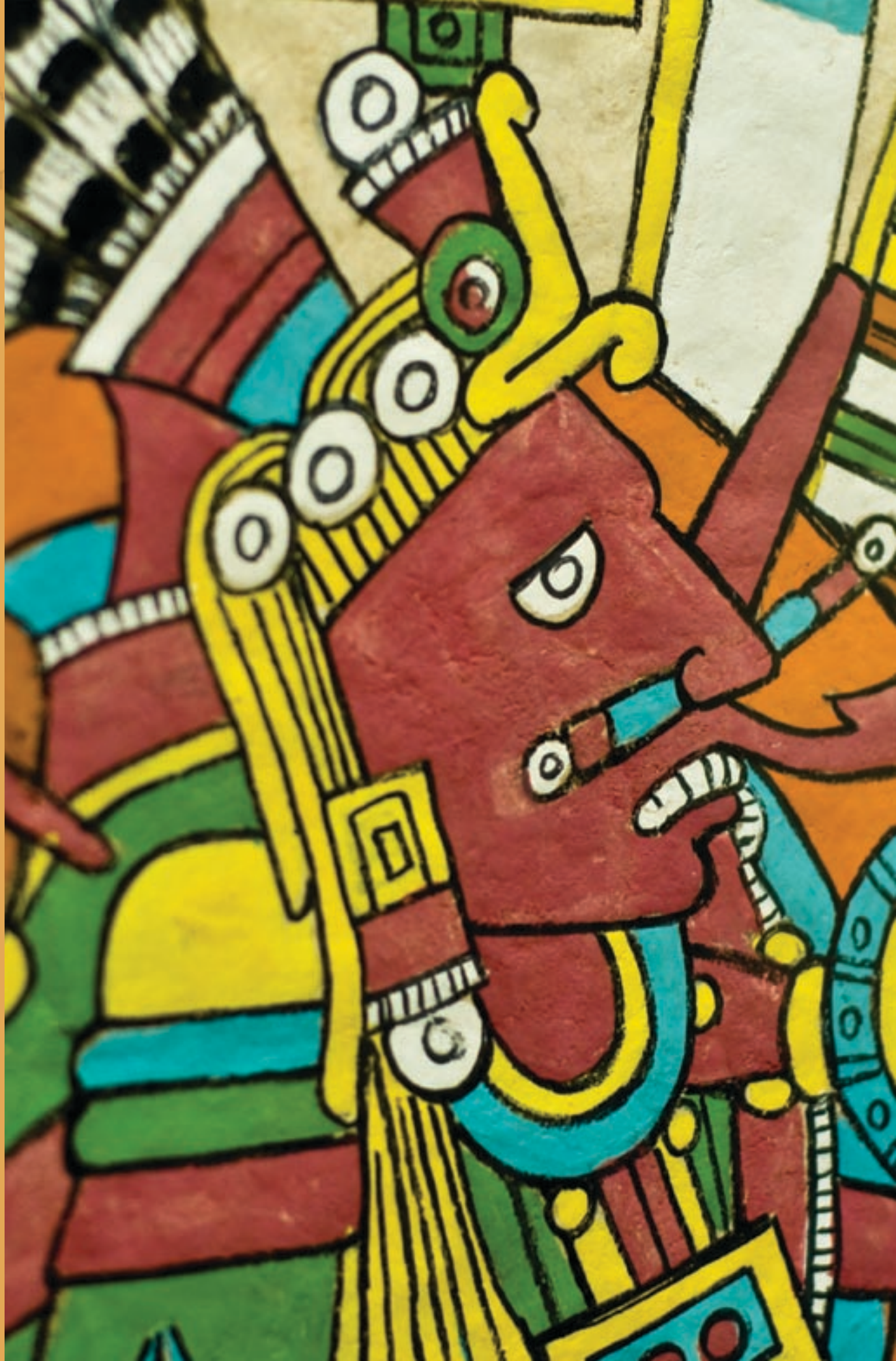
chemical make-up—that’s when they start coming up after class to tell me about a mother or uncle or grandparent that has a certain disease.”

### INNOVATION AND A FEW PINK ELEPHANTS

**A** scientist to the core, Poulter looks back on his growing-up days in Lake Charles, Louisiana and chuckles at his penchant for experiments as a youngster. There was his “secret” under-the-front-porch laboratory, where he and three of his buddies collaborated and contributed from their own chemistry sets. “Chemistry sets back then sold things they wouldn’t dare sell today, so we able to do all sorts of things. Let’s just say explosives were the *in* thing to do,” recalls Poulter with a chuckle. “Our real passion was making gunpowder, but we quickly concluded that what we made from scratch was inferior to what we could get from cherry bombs.” They also incorporated biology into their “lab” work, resulting in the kind of experiments that happen when you mix boys, fish, and frogs together. Best not to elaborate. “It’s a good thing mom and dad didn’t know what I was up to,” says Poulter, with the same smile he probably gave them when they asked.

In college at Louisiana State University, he first pursued chemical engineering for a year and then decided it was leading him down a path that would prove too regimented for him. “It made me realize that it was the hows and whys of chemistry that I was most interested in,” says Poulter.

Arriving at the University of California, Berkeley, in 1964 to earn a graduate degree in organic chemistry, he found an atmosphere churning with



passionate sit-ins and the free-speech movement. He attended some of the rallies, but often Poulter watched the action unfold from the sidelines; for a small-town southern boy, it was mind altering. Poulter recalls one rally, where the students decided there should be a huge sit-in inside the chemistry building. Several chemistry faculty and students ran

clothes,” which turned out to be ski gear.

Although the U’s chemistry department was much smaller at the time, Poulter recognized that it was rapidly transforming into a strong research-oriented department, primarily due to strong support from the state for a new building and new faculty positions, and a

with two colleagues, Bill Epstein and Hans Rilling, who had backgrounds in “natural products” chemistry and biochemistry. He received an award from the National Institutes of Health that was the catalyst into his current research today on isoprenoids. Trained in organic chemistry, the award allowed Poulter to develop a new area of expertise in biochemistry and enzymology. “With Hans’ help, I went into biochemistry labs up at the medical school and started trying to figure things out.”

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ahead and quickly posted “Danger, Radioactive Isotopes” signs all over the building.

As his friends started returning home from Vietnam, via San Francisco, Poulter started questioning in areas he never had before. “This was the first time that I started thinking about how what I was being told on the news wasn’t matching up with what my friends were telling me.”

While finishing up his post-doctorate at UCLA in 1969, his research advisor told him of a job opening at the University of Utah’s Department of Chemistry. He was invited to interview. “I didn’t know anything about Utah. I flew in when it was dark and woke up to one of those blue-sky days after a big snowfall,” recalls Poulter, noting that people were running around in some “pretty funny

recent National Science Foundation grant. He also sensed the chemistry among faculty: “I could tell there was a spirit of real support and closeness.”

Ultimately, it may have been Professor Henry Eyring’s words that won Poulter over. I remember sitting in his office and he said: “Dale, no doubt you’ll be visiting universities with a lot more resources, but you won’t find a place that allows you more creativity than here. If you go out and raise half the money for a herd of pink elephants, we’ll match it.”

“This made it clear to me that there was a real sense of innovation here and that there was a spirit here that took in the ideas of the researchers,” recalls Poulter. “It’s still true.”

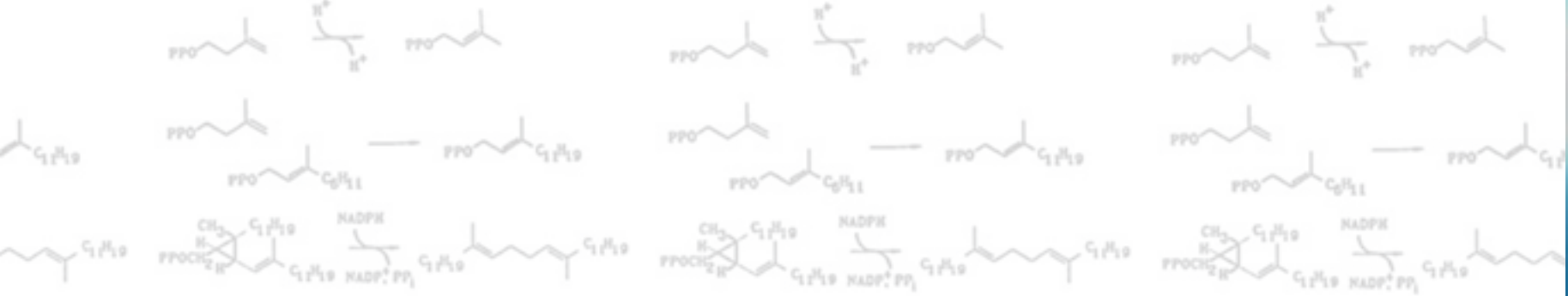
Soon after joining the U, Poulter collaborated

“Dale has always been flexible about learning new fields and he’s bright so he learns fast,” recalls a now retired Bill Epstein, who helped hire Poulter. “I remember taking him out as a young man, when he was new to Utah, to teach him how to fly fish on the Green River. He became a very good fly fisherman—and then he ended up teaching me a lot.”

#### FROM A TREE SPROUTS NEW POSSIBILITIES

Simply put, we are trying to understand how molecules are made in nature, in us. In all of nature the same kind of reactions are used to make 55,000 isoprenoid structures. With this knowledge, we can figure out how molecules are made from molecular building



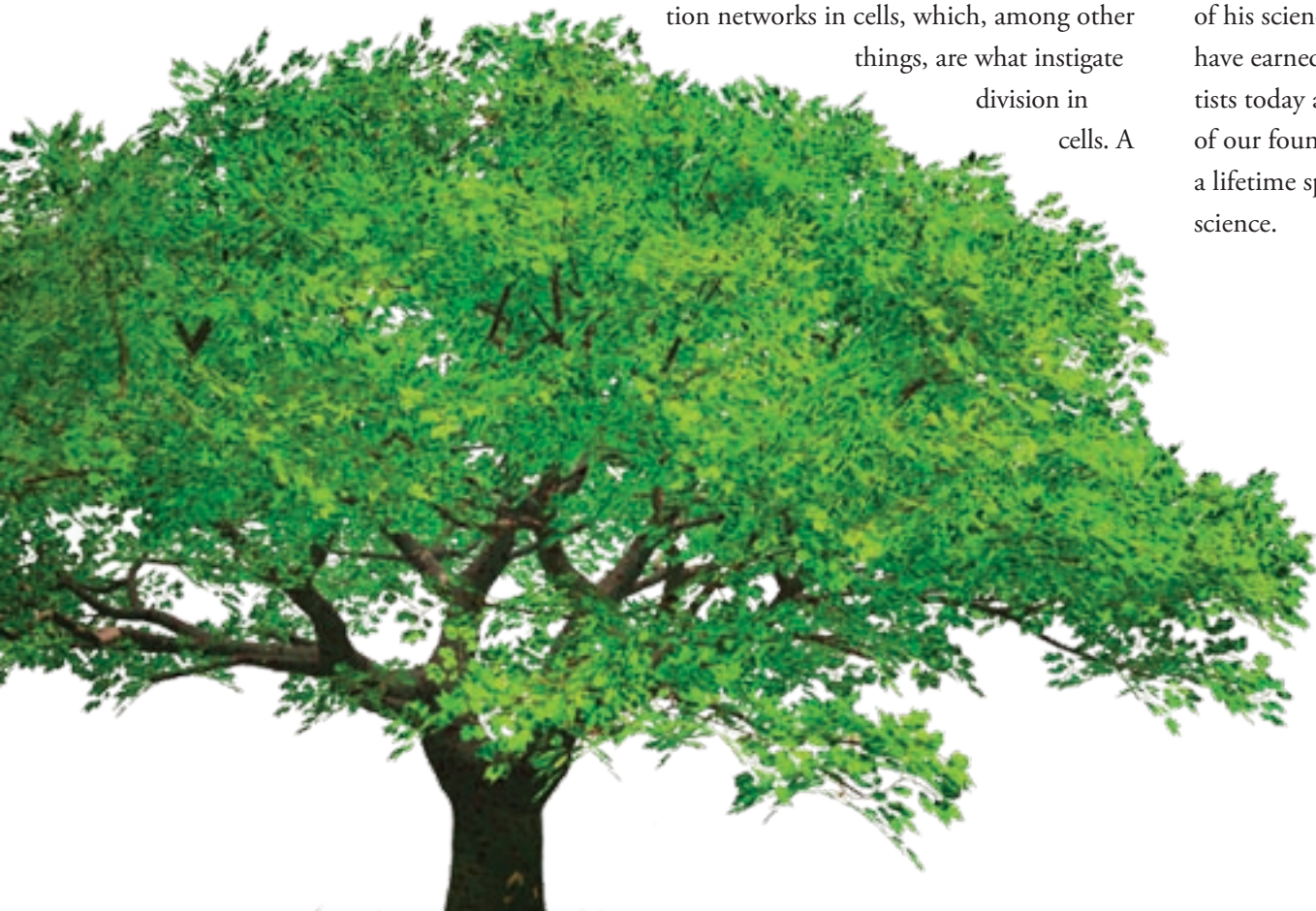


blocks,” explains Poulter, who has the ability and patience to break down complex ideas into digestible pieces.

One suspects that blank stares just make him more determined.

He goes on. “Organisms have evolved in such a way to have complete control over the chemical reactions necessary to survive. It is an amazing control system we have in our bodies that make reactions happen fast, due to catalyzing enzymes. Understanding this in combination with genetic knowledge allows scientists to understand how nature’s ability to make new isoprenoids has evolved over long periods of time.”

A tree grows on Poulter’s whiteboard, from



his marker sprouts branches. The whole tree is a swarm of molecules reacting and each branch is the resulting product from certain molecular reactions: steroids (which includes cholesterol); dolichols (necessary for cells to stick together); proteins. Poulter illustrates: “We are learning that we can regulate the amount of molecules that flow into one of these ‘branches’ or pathways that lead to, for example, the production of cholesterol.” Not only are egg-eaters thrilled with this new find, but it is sending pharmaceutical companies scrambling to develop drugs using this information.

Another area of Poulter’s research that is gaining interest outside his lab is the growing understanding of signal transduction networks in cells, which, among other things, are what instigate division in cells. A

protein called RAS controls the starting and stopping of cells dividing and is a factor in about one fourth of all cancers. “We’ve learned that if you remove a particular isoprenoid, it turns that RAS switch off in cancer cells,” explains Poulter.

A long list of honors follow Poulter’s career. However, it is his nomination as a fellow of the American Academy of Arts and Sciences that most astounds him. The academy, founded in 1780, houses letters from other fellows such as Ben Franklin, George Washington, Thomas Jefferson, and Alexander Graham Bell. “I was humbled by this honor,” says Poulter.

For such an unassuming man, the flowering of his science is not. His findings not only have earned him the respect of leading scientists today and landed him in the company of our founding fathers, they do justice to a lifetime spent in the passionate pursuit of science.

