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LEADERS & SUCCESS

Bruce Ames Pulls It Together

Innovate: Scientist uses an interdisciplinary approach in the fight against disease

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Dr. Bruce Ames isn't afraid to stir up controversy. He relishes it.

Ames has made a career out of challenging prevailing views in the scientific community.

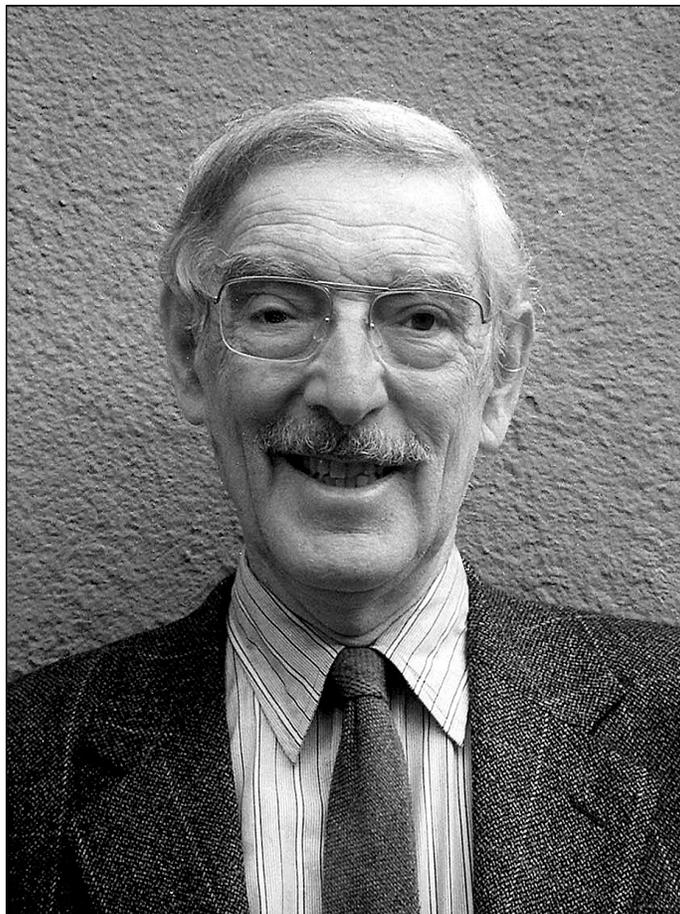
Most notably, Ames raised the ire of environmentalists and fellow scientists about 25 years ago when he challenged the procedures used to determine which chemicals cause cancer in humans.

The standard procedure at the time was to subject rodents to high doses of chemicals. But Ames concluded that the tests were of little benefit in establishing whether those same chemicals would cause cancer in low doses — levels people were actually exposed to in the real world.

His research also showed that the possible cancer risk from traces of synthetic chemicals such as pesticide residues was tiny compared with that from natural chemicals in people's diets.

Ames argued that the focus on cancer from minor hypothetical risks, rather than major risks like cigarette smoking and unbalanced diets, was hurting public health.

"He's not afraid to go out on a limb with notions that he thinks are important," said Dr. Tory Hagen, a principal investigator at the



Geneticist/biochemist Bruce Ames created a test used by labs and drug and chemical firms to detect harmful mutagens in products coming to market.

Linus Pauling Institute and an associate professor of biochemistry and biophysics at Oregon State University. "He's been a lightning rod for a lot of things. And he's willing to take on that kind of role, saying things very provocatively, very much in a challenging way, that gets other scientists to think."

Some critics labeled Ames

a "tool of industry" after he discounted the impact of trace amounts of synthetic chemicals on the environment. But Ames has a policy not to accept money from industry, or to testify in lawsuits, or to consult.

"I'm not afraid to overturn conventional wisdom," Ames said in a recent interview.

Debate in the scientific community is good for vetting research and for raising awareness, he says. Even in his own lab, Ames likes to surround himself with smart, tough-minded associates who'll challenge his assumptions and data.

"I like to have people around me who are very hard-nosed and say, 'Have you dotted that i and crossed that t?'" he said.

Ames, 76, is currently a professor of biochemistry and molecular biology at the University of California, Berkeley, and a senior scientist at Children's Hospital Oakland Research Institute. He's won numerous awards including the U.S. National Medal of Science in 1998.

Ames credits his success to enthusiasm for his work. "If I get excited about something, I'll dig into it," he said. He proves that you're much more likely to succeed if you love what you do.

His enthusiasm is contagious and helps him to attract the best people to work with him, Hagen says.

Ames overcame an unimpressive academic background to succeed. He admits he wasn't the best student and didn't get the best grades in high school and college. "I never liked taking courses too much," he said. "I was never terribly good at memorizing things and spewing them back on exams."

(Continued)

Ames preferred independent study. He also liked lab work because it involved problem solving, something he thrived on.

The Excitement Factor

Ames had doubts early on about whether he'd make a good scientist. He admits to having "a so-so memory" and being "easily distracted" by new interests. But when he got excited about something, he really focused on it, such as reading all of Tolstoy or learning about the Phoenicians.

Having diverse interests has helped Ames in his work. He takes a multidisciplinary approach to his research.

He considers himself half a geneticist and half a biochemist. This allows him to work in-between fields where there's less competition. He'd see all the problems geneticists turned up and didn't know how to tackle and the problems biochemists didn't know existed, he says.

"I enjoy learning new fields, and I always seem to be in the midst of learning a new one. I can often bring a fresh perspective to a new area because of my broad in-

terests in science," he wrote in an invited memoir for the "Journal of Biological Chemistry."

This was the case when he developed a new tool for detecting potential carcinogens.

In 1964, Ames was reading the list of ingredients on a box of potato chips and began to wonder whether preservatives and other chemicals could cause genetic damage to humans. He decided to develop a test for chemical mutagens.

Ames saw a link between mutagens and cancer. But when he tried to get funding for his research, the National Cancer Institute turned him down. Undeterred, he later sought and received funding from the Atomic Energy Commission.

"Having had a background in genetics as well as biochemistry, all of my intuition told me that mutagens ought to be carcinogens, though this was not the prevailing view at the time or for many years," Ames wrote.

Two major conclusions of his work were that mutation is one aspect of the mechanism of cancer causa-

tion and that a high percentage of carcinogens are detectable as mutagens.

His mutagenicity test was simple, fast and inexpensive. Before its availability, scientists used expensive and time-consuming rodent cancer tests.

The so-called "Ames test" is now in use in more than 3,000 laboratories and in all of the major drug and chemical companies, where it has had a major influence in weeding out mutagenic chemicals before they are introduced into commerce.

Making Connections

The science profession could use more people who cross disciplines, he says. Most scientists are pretty narrow in their focus and just want to stay in their own field, he says.

"There are lots of discoveries to be made by linking two areas where people don't talk to each other," Ames said. "I seem to be good at that."

When Ames explores a new research area he spends a lot of time getting an overview and looking for where "the least amount of effort will bring the maximum return," he said. He

wants to do research with the highest potential payoffs, he says.

His primary interest now is on aging, in particular the role of mitochondrial decay as a major contributor to aging and age-related degenerative diseases, such as Alzheimer's.

"I told a colleague I'm doing the best work of my career. And he looked at me and said 'Bruce, you've been telling me that for 30 years.'"

Ames is interested in finding chemicals that can revitalize mitochondria, the power plants of cells, which deteriorate as people age. He formed a company called Juvenon to develop and market cell-rejuvenating supplements based on his research at the University of California, Berkeley.

Ames chairs Juvenon's scientific advisory board but put his founder's stock in a charitable foundation and will take no remuneration from the company.

Ames says he has no plans to retire. "Who wants to play golf? I'm having too much fun," he said.

Hagen has heard the same thing. "He told me they'll have to carry him out feet first and I believe that."