

At the Frontier of Molecular Biology, Genes and Learning

By BARBARA KAPLAN LANE

DR. TIM TULLY, a senior staff investigator at the Cold Spring Harbor Laboratory, is no one's stereotype of a scientist. Dressed like a beach bum, looking very much like a shaggier incarnation of the actor John Ritter and speaking with a hint of a drawl, Dr. Tully, who just turned 40, could still pass for the good old boy he said he once was.

For six hours — make that for 24 numbing hours over four consecutive days — Dr. Tully sat hunched over a microscope in a windowless white room, painstakingly sucking fruit fly larvae into a needlelike tube with an aspirator. Bluegrass music blasted from a boom box as he deftly picked off the insects. "You can see, with something this horrible, music is our friend," he said.

As stultifying as the procedure seemed, it was part of an experiment whose larger purpose was to help demonstrate what, and how, fruit flies are genetically capable of learning and remembering. Dr. Tully's work may well represent the first steps toward understanding human learning and memory on a molecular genetic level. Dr. Tully's two latest research papers are to be featured on the cover of the Oct. 7 issue of *Cell*, the leading microbiology journal.

To be a fly — or a fruit fly — on Dr. Tully's wall is to learn about more than just biology. He is, in his way, an embodiment of the conflicts and contradictions inherent in his field.

"I'm a geneticist with an almost antithetical view to the prevalent view of genetics," he said. "The popular view is 'if you have the gene you've got the disease or whatever-it-is,'" he said. "The mass media have completely bought genetic determinism."

"Behavior is far more complex than can be explained simply by molecular biology, which is the study of how a gene makes a protein, how a DNA sequence makes an amino acid sequence. The next step is to study the function of that protein in isolation. That's as far as molecular biology goes."

"You have to understand the limits of what you're doing. Many genes underlie any particular behavior. They deliberately miss the complexity that underlies how genes affect behavior."

Clearly there are more things on heaven and earth than can be explained by molecular biology. It is irresponsible to assume that a par-



Michael Shavel for The New York Times

Dr. Tim Tully examines a vial of fruit flies at the Cold Spring Harbor Laboratory.

ticular gene is responsible for a corresponding behavior without taking into account the role that environment plays, Dr. Tully said, adding: "You cannot define a basketball game by one player. You can't define what Michael Jordan did in the absence of everyone else. It's the swath of interaction that defines the game."

"The 'nature versus nurture' issue is a pseudoquestion, because they cannot exist separately. It shouldn't even be asked but it is because of the absence of education." Having set forth his arguments, Dr. Tully made his point with numbers.

"The human genome is estimated to carry 100,000 genes," he said. "Each gene has an average of five alleles, or versions of the gene, of which we all carry two copies, resulting in 10 different two-way combinations. Therefore, with 100,000 genes, the number of unique combinations in human populations would be 10 to the 100,000 power, a number far greater than all the humans who ever existed."

"Each of us is genetically unique. Even identical twins are not identical. That is the fundamental reason why genetic determinism is a fallacious idea. My understanding of how genes and behavior interact created my point of view."

Dr. Tully's work in molecular genetics is a reason that he now finds himself at odds with his former men-

tor, Jerry Hirsch of the University of Illinois, a major proponent of behavior genetics.

"He thinks it inappropriate to study single genes," Dr. Tully said. Which is what the National Institutes of Health pays Dr. Tully to do, and what is making his name as a scientist.

"Molecular genetics has given us a new tool to identify some of the variables but we should not underestimate our ignorance," Dr. Tully said. "Our current understanding of the genetic basis of learning and memory is like a map of North America as drawn by Columbus: correct in outline and wrong in every detail."

He chooses not to indulge in fantasies about the broader ramifications of his work. "All of this kind of science is very slow, boring stuff," he said. "The exciting part is when you accumulate enough data to gain some insight. I like what I'm doing, and it's important. But it's a drop in the bucket. I really see my own little life involved in studying learning in a fruit fly."

In the course of that "little life" Dr. Tully averages 11 hours a day in the lab, with a break for dinner at home with his wife and two young sons, followed by a few more hours' work at home or back in the lab. He works every weekend, although shorter hours than during the week.

"I'm a rat on a running wheel all

day long," he said. His outlets include annual camping vacations with his family, study of Native American history and culture and a hobby making furniture.

He described his job as 10 percent hands-on and 90 percent the paper pushing that he hates. He said that he wrote grant proposals "constantly" and that found that he was writing them more frequently.

Dr. Tully's projects are financed by the National Institutes of Health, by far the most significant single source of money in biology research. Although N.I.H. funds for research continue to rise, they have not kept pace with the demand. In 1992, 30 percent of applications were approved. The agency is projecting a decline to 22 percent by the end of this year.

"I never thought it would be so hard," Dr. Tully said. "In this field we live or die on our ideas. Maybe I have 20 years' work left in me."

Dr. Tully called financial insecurity and the lack of pension benefits "the hidden side of science today," saying, "We're going to be paupers."

In science circles "publish or perish" is more than a maxim, it is a fact of life. "Cold Spring Harbor Lab lives or dies by the good placement of research in respectable journals," Dr. Tully said. "It motivates scientists to choose the experiments which are most meaningful to do.

But it doesn't account for all the basic groundwork that doesn't necessarily result in 'big' results. I live on the knife edge. There are no guarantees if I'm not renewed here."

Dr. Tully's salary is paid by the grants that he attracts. No grant, no job. His current grant expires in August 1996. As he sees it his publication in *Cell* "just bought us a couple more revolutions around the drain."

One of the things that help keep him going around the drain as opposed to slipping down it is his sense of humor. An admirer of Ivan Pavlov, the early 20th-century physiologist and psychologist, Dr. Tully names the genes that he discovers after Pavlov's dogs. Because Pavlov had more than 50 dogs, Dr. Tully reasoned, he would not run out of names soon.

Dr. Tully's personal odyssey to the cutting edge of molecular biology has taken him a long way from his roots in Washington, Ill. "Southern Illinois is Southern," he said. "Rural and agricultural and very conservative. I was your typical small-town redneck."

He grew up in a traditional large Irish-American family. Dr. Tully said growing up with five brothers and sisters and observing the ways in which each displayed different characteristics of their parents planted an irresistible need to understand the biological reasons behind those differences.

"My whole professional life has been to justify the differences between me and my brothers and sisters and give my own kids the same understanding of it so they don't have the same contentious views of themselves," he said.

Dr. Tully took pre-med courses as an undergraduate at the University of Illinois. Taking Dr. Hirsch's course in behavior genetics in his junior year caused him to change his plans. "It literally was the light coming on," Dr. Tully recalled. Despite the insecurity of his present vocation, he said he never regretted his decision not to become a physician, calling himself "too much of an optimist and a romantic" for the healing profession.

It was his predoctoral work, an interdisciplinary study of scientific and institutional racism, that he credits with reversing the cultural biases that he grew up with. "These values and attitudes are transmitted down family lines," he realized.

"It was an absolute eye-opener," Dr. Tully said, adding that his education in genetics reinforced its effects. "It made me liberal. I believe in a

system maximizing civil liberties, a system that supports our individualism because we are individuals."

With all the competition for research positions, Dr. Tully said, his background qualified him for his post at Cold Spring Harbor. With a B.A. in biology and psychology, he earned a Ph.D. in genetics at Illinois and switched to neurogenetics for postdoctoral work at Princeton, and later to molecular genetics at the Massachusetts Institute of Technology.

"I occupied a niche that wasn't filled," he explained. "I was the behavior expert to the biologists and I was in their world. I recognized two completely separate disciplines and I set out to bridge the gap. I am at heart a geneticist and someone who has seriously set out to learn all levels of genetics as it pertains to behavior. I'm historically unique to the problem."

After giving an irreverent talk on learning and memory at an international meeting sponsored by Cold Spring Harbor in 1989, he was approached by Dr. James D. Watson, the director of the laboratory. Less than two years later Dr. Watson, who shared the 1962 Nobel Prize in Medicine and Physiology with Dr. Francis Crick for discovering DNA, asked Dr. Tully to join him at the newly established Center for Learning and Memory at Cold Spring Harbor. Dr. Tully has been there since.

He has flourished, with 34 publications to his credit and nine in progress, and with hopes for bigger discoveries, he said, by the end of the year. Science has been good to Dr. Tully, but he characteristically tempered his enthusiasm.

"If I was independently wealthy I'd love this place," he said. "This job is a plum, doing cutting-edge work. Most grad students won't be as lucky as this. They're in a dogfight for their first job. A lot of people behind me gave up and went into industry or teaching."

"I'm not interested in any other part of science. I would be a woodworker in Sedona, Ariz., if I didn't have this job. I'm always on call and I hate it. My idea of a good time is sleeping on the ground. I romanticize a simple life, that all I do is wake up, catch a fish and eat it. I'm sure that when I do burn out I'll go back to woodworking and live happily ever after."