

Welcome to CONNECT: Helicon Therapeutics and Dart Neuroscience LLC

By Moya Gollaher, EVP CONNECT



Dr. Tim Tully bounds into the lobby of his sleek Sorrento Mesa facility, greets me and charges off to one of his two offices; one he occupies as Chief Science Officer of Helicon, the other as CSO of Dart Neuroscience LLC. We settle into the second space, looking out over the hills and scrub to a distant view of the ocean, and Tully begins the Helicon story. It is the story of a quest and how this company, recently transplanted from Farmingdale New York, is searching for a scientific Holy Grail: the biological basis of memory and the creation of drugs that will enhance cognition.

Tully had his “ah ha” moment in college when, working on separate B.S. degrees in psychology and biology at the University of Illinois, he became fascinated with the genetic basis of learning and memory. That was in 1974 and his early passion led him to a Ph.D. in genetics at the University of Illinois, postdoctoral training in NeuroGenetics at Princeton University and Molecular Genetics at M.I.T., and an Assistant Professorship at Brandeis. It was there in 1991 that he picked up the phone one day to find James D. Watson on the line. Watson was the director of Cold Spring Harbor Laboratory and starting year-round neuroscience research into the genetics of learning and memory. He knew that Dr. Tully was doing pioneering work to identify memory mutants in *Drosophila* and Watson wanted Tully on board.

At this point in the story I glanced over to Tully’s wall, chock-a-block with fly-fishing pictures, mountain ranges, and dogs. Lots of dogs. With Russian names. Tully explained: we all remember Pavlov’s elegant experiment involving the repetitive association of a bell, a hungry dog and the dog’s learned response to salivate upon hearing the bell. Tully, who in 1992 was planning a large-scale behavioral screen, needed publishable names for his newly identified fly memory mutants. A confirmed dog lover, Tully thought to honor Pavlov’s early research in associative learning by christening his *Drosophila* mutants after those long-forgotten Russian canines. The photos I am looking at, of Milkah, Ikar, Ruslan, Toi and dozens of other huskies, retrievers, shepherds and mutts, were unearthed in the tiny village north of St. Petersburg where Pavlov had last worked. Today Pavlov’s dogs lend their names to 60 pieces of scientific history in the biochemistry of memory.

The *Drosophila* research that Tully led at Cold Spring Harbor yielded several ground breaking discoveries. In 1995, Dr. Tully was the first to publish findings that a gene called CREB (cAMP Response Element Binding Protein) plays an

important role in regulating the conversion of short-term memory to long-term memory in fruit flies. At this point, reading an abstract published in Holland about mentally retarded patients with Rubenstein-Taybi Syndrome, where DNA sequencing of CREBBP demonstrated mutations in 56% of people with RTS, Tully was struck with the thought that perhaps the CREB protein that regulates memory in fruit flies could do the same in mammals.

In 2003 Tully's lab licensed Japanese mice carrying the "RTS mutation" in the CREBBP homolog and established the CREB-memory connection using a drug (phosphodiesterase inhibitor). This finding suggested that small molecule modulators of the CREB pathway might enhance memory and, therefore, would be useful in treating memory-related disorders such as Alzheimer's disease and mental retardation.

"In June of 2007 I stepped off the cliff. I quit my job at Cold Spring Harbor to devote full time to drug development. I believe in this. I'd be crazy to have done this if I didn't believe." Ten years after forming Helicon while at Cold Spring Harbor, Tully left the world of academic research, left his fruit flies and left the East Coast.

It was the State of New York that got Tully and his staff thinking about relocating the company. Onerous regulatory constraints within the state forced Helicon to move their offices and labs, but upon realizing that employees would be uprooted regardless of where they moved they began to think outside the snow zone.

The search for a new home for Helicon was typical Tully: part dispassionate analysis, part emotion. Tully weighed the pros and cons of other research centers, academic hubs and entrepreneurial hot beds-Boston, the Bay Area, and the New York metropolitan area. Then, like many before him, he looked west and found San Diego. The Helicon team discovered a world-class scientific community that supports therapeutic research and drug commercialization in the Torrey Mesa science complex, a place where he could relocate his core team of nine Ph.D.s and hire the 30 additional staff scientists. As for the emotion. Back in 1973, as a college freshman from the Midwest, Tully had stood on the same beach his office now overlooks to first glimpse the Pacific Ocean. Sold.

Backed entirely with private funds, Helicon now operates as the commercialization company seeking to develop and market new drugs while Dart Neuroscience LLC (DNS) acts as a research entity devoted to drug discovery. Helicon currently has three drugs in clinical studies, one in the IND-enabling stage of preclinical development and two drugs in early stages of discovery. The company currently employs 27 scientists and staff, occupies 45,000 square feet of lab and office space and plans to hire 15 more employees in the next 12 months.

Still ahead of Tully and his team is the very daunting challenge of proving his concept in humans. “To show that a small molecule could treat *any* type of mental retardation changes *everything*” he states emphatically. But it is hard and laborious work with no guarantee of success. Still, Tully is optimistic that he will have progressed to a point in the next 12-18 months where we may achieve “some seminal discovery that will make a difference in our society.”

Then this neurobiologist that his academic colleagues dub “a renegade” laughs; “We will succeed wildly-or we will blow up!”

Dr. Tim Tully is a neurobiologist and is the scientific founder, Vice President and CSO of Helicon. He received his Ph.D. in Genetics at the University of Illinois in 1981. Dr. Tully is an internationally recognized authority in research on learning and memory. Dr. Tully is the recipient of numerous honors and awards for his research and more recently has become CSO of Dart Neuroscience LLC.