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What's Nu in Prion Research?

He's quick with a pun when naming a new form of a yeast protein, but HHMI predoctoral fellow Lev Z. Osherovich knows his research is far from trivial. His findings so far have convinced him that prions—abnormal forms of cellular proteins implicated in Alzheimer's disease and other devastating neurological disorders—might also perform some important physiological function within cells. Now he's working to determine what prions' normal role might be.

One of the authors on a paper published in the Jan. 21, 2000, issue of *Cell*, Osherovich discovered and described a novel prion in a particular kind of yeast. He named it Nu, the 13th letter of the Greek alphabet, because that's what it was—new—a prion of a previously uncharacterized protein called New1p, and because it is a convention in yeast research to use Greek letters to name genetic elements that behave abnormally.

Like Susan Lindquist, a former HHMI investigator at the University of Chicago who published related findings in the January 28, 2000, issue of *Science* and the January issue of *Molecular Cell*, Osherovich and fellow graduate students working in the University of California, San Francisco, lab of Jonathan Weissman found that a variety of proteins rich in the amino acids glutamine and asparagine are capable of forming prions.

"There is something very important about this property, so important that evolution has conserved it in every yeast species that we tested," Osherovich observes. "My own contribution concerning the Nu prion indicates that even within one species of yeast, there are likely to be numerous proteins capable of forming prions. Since prions are so ubiquitous, they must have some important physiological function. They are not just aberrations or accidents."

Weissman, assistant professor of cellular and molecular pharmacology at UCSF and senior author on the *Cell* paper, calls his graduate student's findings significant. "Lev's work suggests that prions, first identified for their role in rare and devastating neurodegenerative diseases, might be far more common than suspected and might even play a beneficial role," he says. "His studies provide a framework for identifying new prions, not only in yeast but in more complex organisms, perhaps even in humans."

Science has long been a way of life in Osherovich's family. His father is an astrophysicist and his mother, a chemist. His grandfather was a pioneer in atmospheric ozone research who worked in the early Soviet space program. Born in Leningrad in the former Soviet Union, Osherovich grew up in California, where his family settled when he was a child. While working on an undergraduate degree in genetics at the University of California, Berkeley, he read an article by the scientist who discovered prions, UCSF professor and Nobel laureate Stanley Prusiner.

"I was fascinated by the idea that normal proteins inside cells could adopt an aberrant and even malignant form that could spread throughout the body and cause devastating conditions such as mad cow disease [or Creutzfeldt-Jakob disease]," Osherovich says. "At that point I decided that I wanted to study prions in graduate school." He won an HHMI predoctoral fellowship, crossed San Francisco Bay and joined Weissman's prion research team.

Osherovich plans a career in laboratory research, but he's equally committed to helping open a dialogue between practicing scientists and the public. "I think it's essential to explain what we do, to help allay the public's concerns about new biological technologies such as the production of genetically modified food and cloning animals," he says. "I'm concerned that the public's reaction to these technologies reflects a deep distrust of scientists and science."

The 24-year-old graduate student is already working to demystify science for the coming generation, by participating in UCSF's Science Education Partnership, an HHMI-supported program that pairs research scientists with teachers and students in classrooms throughout San Francisco.