Prion discovery gives clue to control of mass gene expression

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The discovery in common brewer's yeast of a new, infectious, misfolded protein -- or prion -- by University of Illinois at Chicago molecular biologists raises new questions about the roles played by these curious molecules, often associated with degenerative brain diseases like "mad cow" and its human counterpart, Creutzfeldt-Jakob.

Susan Liebman, distinguished university professor of biological sciences, and postdoctoral research associate Basant Patel propagated the new prion from a normal yeast protein called Cyc8. They note that like the Cyc8 protein, the prion of Cyc8 can affect the expression of a large number of yeast genes.

"We know this prion turns on the expression of genes but we don't know if the prion forms naturally," said Liebman. "If it were to form, it would have this effect. But whether it happens out in the wild all the time, we don't know."

Liebman and her coworkers discovered that Cyc8 was a prion candidate using a genetic screen that looks for proteins that when overproduced can spur formation of new prions. To date, scientists have discovered only seven prions, six of which are only in fungi, including yeast. The latest two discovered, Cyc8 and another, identified as Swi1, came from genes screened in Liebman's lab. The Cyc8 prion was characterized by the UIC scientists, while the Swi1 prion was found by Northwestern University researchers.

The normal Cyc8 protein shuts down expression of more than 300 genes in yeast, says Patel, including some genes that are involved in stress tolerance.

"Once Cyc8 is converted to a prion, it loses that function," he said. "This might provide some advantages under stressful conditions. Since the protein represses more than 300 genes, it's possible the prion form can activate the genes on a mass level." If an organism wanted to activate all the genes in a cell that the protein repressed, he said, "converting the protein into a prion would be an easy way to do it."

Patel and others in Liebman's lab are testing the protein to see if this molecular mechanism does in fact take place naturally. They're also studying the interaction of prions to determine if pre-existing prions facilitate or destabilize new prions.

Whether the actions of prions in yeast are analogous to mammalian models is not yet fully known, but the possibility certainly is on the minds of Liebman and her associates.

"There could be prions in humans that are not causing disease but have important effects on the cell or organism," said Liebman. "They may even be related to the ones we find in yeast. The more prions we learn about and study, the more information we learn from them -- how they arrive, what proteins are needed to maintain them. As we study other models, we have a better idea."

Jackie Gavin-Smyth, a former research specialist in Liebman's lab now at the University of Chicago, was another co-author of the letter in the March issue of *Nature Cell Biology* describing the new prion.

Source: University of Illinois at Chicago (news : web)