Prions serve as important source of variation in nature

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Special proteins known as prions, which are perhaps best known as the agents of mad cow and other neurodegenerative diseases, can also serve as an important source of beneficial variation in nature, confirms a new study in the April 3rd issue of the journal *Cell,* a Cell Press publication. After an extensive search through the genome of yeast for proteins with prion-like character, the researchers found two dozen prion-forming proteins, most of which had never been seen before.

"We had previously proposed prions as a means for generating phenotypic diversity," but that notion had been a subject of considerable controversy, said Susan Lindquist, a Howard Hughes Medical Institute investigator at the Whitehead Institute for Biomedical Research and the Massachusetts Institute of Technology. "With this paper, we show that it just plain happens."

Despite the fact that a handful of prions had been identified in yeast before, those had largely been considered as "odd examples," she added. Now, they show that there are in fact many prions that likely confer phenotypes with benefits under certain environmental conditions. (Phenotype refers to an organism's observable characteristics and traits, including their appearance, biochemistry and behavior.) Lindquist also said she thinks that the abundance of prions found in yeast will prove to exist in other organisms "all over biology."

Unlike most proteins, which exist in a single folded structure, prions are unique in that they can transition from a soluble, "non-prion" state to an insoluble form that clumps together by switching from one folded form to another, explained Simon Alberti, also of the Whitehead Institute. That switch also changes the proteins' function in important ways.

The transition to the aggregated state, which depends on particular modular domains, occurs relatively rarely, but once it does the protein itself acts as a template capable of transforming the structure of proteins existing in the more common, "non-prion" state. Importantly, prions can also transmit biological information from one generation to another as a protein-only mode of inheritance.

Previous studies had shown that prion-like proteins are abundant in many simple organisms, with 100 to 170 such sequences in yeast. However, the researchers said, the experimental tools needed to determine the prion properties of those proteins in a systematic manner had been lacking. As such, only five yeast proteins had ever been confirmed to harbor a domain capable of forming a prion.

In the new study, the researchers first scanned the yeast genome for prion-like proteins. They then subjected the top candidates to genetic, cell biological, and biochemical assays to determine their prion-forming capacity, ultimately finding that at least 24 yeast proteins contain a prion-forming domain. Further evaluation of one of those, called Mot3p, by study author Randal Halfmann confirmed it as a bona fide prion that alters the yeast cell wall in ways that are likely to be advantageous under certain environmental conditions.

Prions set up "a bet hedging scenario," Halfmann said. "A handful of cells can hold out in case things go bad."

The tools that the team has developed in yeast can now be applied to other organisms, he added. "We now know much more about what controls prions at the sequence level. There's no reason we can't look at the genomes of mammals or other organisms and say 'that's a prion.'"

Source: Cell Press (news : web)