Prion switching in response to environmental stress

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If you have had a hard day at work, you may change your eating habits, perhaps favoring comfort food, but you don't suddenly develop the ability to eat the plate and cutlery. A new paper, published in this week's issue of *PLoS Biology*, describes an evolutionary mechanism in yeast that allows cells to respond to environmental stress in novel ways, including digesting materials that they were previously unable to use – though admittedly, they aren't eating crockery just yet! The work shows that a protein-misfolding mechanism that can reveal hidden genetic variation is far more likely to be triggered when yeast is under environmental stress, and is therefore an evolutionary strategy to trigger rapid evolution.

All animal cells contain DNA that is never used, which includes old copies of genes that have become defunct during the evolutionary process, and even parasitic bits of DNA introduced by viruses that now lie dormant. It has been suggested by evolutionary theorists that difficult environmental conditions would favour organisms that have increased 'evolvability' – i.e. those that are capable of adapting rapidly to the environment. One way of having increased 'evolvability' is to utilize some of the variation encoded in this unused DNA. A new paper, by Dr. Susan Lindquist and colleagues at the Whitehead Institute for Biomedical Research and Howard Hughes Medical Institute, suggests that such a mechanism exists in yeast, a mechanism based on the presence of a prion called [PSI+].

Best known as the infectious agents in mad cow disease, prions also can play positive roles in biology, the scientists emphasize. "A prion is not necessarily detrimental; in yeast it can be a different way for a cell to code information," says Jens Tyedmers a lead author. In yeast, the [PSI+] prion is a mis-folded version of a protein that plays a key role in making other proteins. Earlier studies showed that the presence of [PSI+] in a yeast cell changes protein production such that hidden genetic variations are included in the proteins that a cell produces. Most of the resulting phenotypes (variants of the organism) have no effect on cell survival, or make things worse. "But about a quarter of the time, the phenotypes are good," says Lindquist. "Sometimes the yeast can grow on energy sources it couldn't grow on before, or withstand antibiotics it couldn't withstand."

This heightened ability to adapt to changing environments may be maintained in yeast as a way to accelerate evolutionary changes. Under stress, yeast cells can unleash a remarkable mechanism based on these misfolded proteins that give them new characteristics without a prior genetic mutation. This mechanism is triggered much more often as the cells undergo stress, suggesting that it is tailored to play exactly this role in evolution.

To test their hypothesis, the scientists first examined what genes might help to induce the prion state, plowing through the entire genome of Saccharomyces cerevisiae, the common baker's yeast that biologists have studied intensively for many years. Tyedmers tested 4700 yeast strains that each lacked one of the genes in the yeast genome, and then tested each strain's ability to create the prion. Among the strains most successful at generating prions, many had changes in regulating the response of a cell to stress.

With that encouragement, Maria Lucia Madariaga, another lead author on the paper, went on to do stress tests on the yeast. Madariaga notes,"We wanted to use some conditions you would find in nature. Yeast hanging out in a vineyard are subject to heat, salt and other stresses."

They found that the more stress experienced by the organism, the more likely it is to flip into a prion state. Otherwise, "when things are hunky-dory, only one in a million yeast cells flips into the prion state," observes Lindquist.

That finding helps to make the case that this mechanism aids in accelerating evolution. "It's always difficult to prove any argument about how a mechanism evolved, but this does offer a coherent logical story," she says.

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