How proteins help yeast adapt to changing conditions

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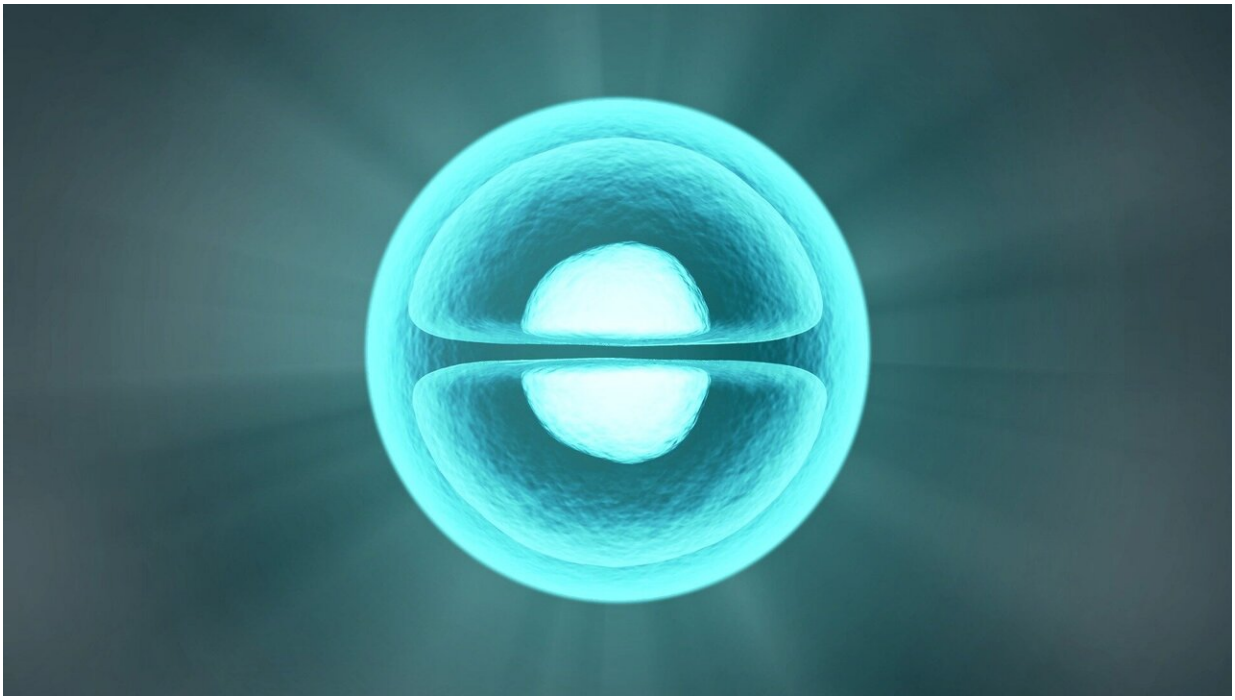

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Proteins in the brain called prions are well known for their involvement in causing disease, but a study published today in *eLife* suggests they may help yeast cope with rapidly changing environmental conditions.

The findings show that prions may be part of an important epigenetic mechanism for controlling cell growth in changing conditions. Further

insight into this role could aid our understanding of diseases that involve abnormal cell growth or cell death.

Prions are proteins that are abnormally folded into different shapes. Prions can spread or be passed on to new cells. They have famously been linked to two deadly brain diseases, Creutzfeldt-Jakob and Mad Cow disease. But some prions can be helpful. Each shape of prion may perform a different task in the cell, in a similar way to a Swiss Army knife.

"While scientists have known about prions for decades, we don't yet know what distinguishes beneficial prions from harmful ones," says co-first author David Garcia, Ph.D., who was a postdoctoral fellow at the Department of Chemical Systems Biology at Stanford University School of Medicine, California, US, and is now Assistant Professor at the Institute of Molecular Biology, University of Oregon, US.

To learn more, Garcia and colleagues studied a yeast enzyme called pseudouridine synthase that can take on two different shapes. They found that, in its alter-ego prion form, this enzyme causes yeast to multiply and grow more quickly, although these changes come at the cost of a shorter lifespan for the yeast.

Through computer modelling, the team then showed that the changes brought about by the prion are beneficial when environmental resources are abundant, but harmful when resources are scarce. By reducing a so-called protein 'chaperone', they also showed that the prion can revert to its original enzyme shape. Since protein chaperones themselves fluctuate during changing conditions, they propose that this might be a way to turn the prion on or off when desirable.

"We've identified a new role for prions in which they can transform cell growth and survival," says co-first author Edgar Campbell, a Ph.D.

student in Chemical and Systems Biology at Stanford Medicine. "These findings suggest that prions may be another form of epigenetic control of cells."

Epigenetic changes can alter the behaviour of cells without changing their DNA, can be passed on to new generations of cells, and may be turned on or off by environmental conditions. The authors suggest that learning more about the role of prions in epigenetic control may be critical to improving our understanding of prion diseases.

"These types of epigenetic changes are missed when we sequence genomes but can still have a major influence on cell growth," concludes senior author Daniel Jarosz, Ph.D., Associate Professor of Chemical and Systems Biology and Developmental Biology at Stanford Medicine. "It is critical to learn more about the consequences of prion-driven epigenetic changes in cells and find new ways to search for them in yeast and other organisms."

More information: David M Garcia et al, A prion accelerates proliferation at the expense of lifespan, *eLife* (2021). DOI: 10.7554/eLife.60917

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