

# ***FROM THE KITCHEN TO THE BENCH:***

## **How Yeast Helps Us Understand Neurodegeneration**

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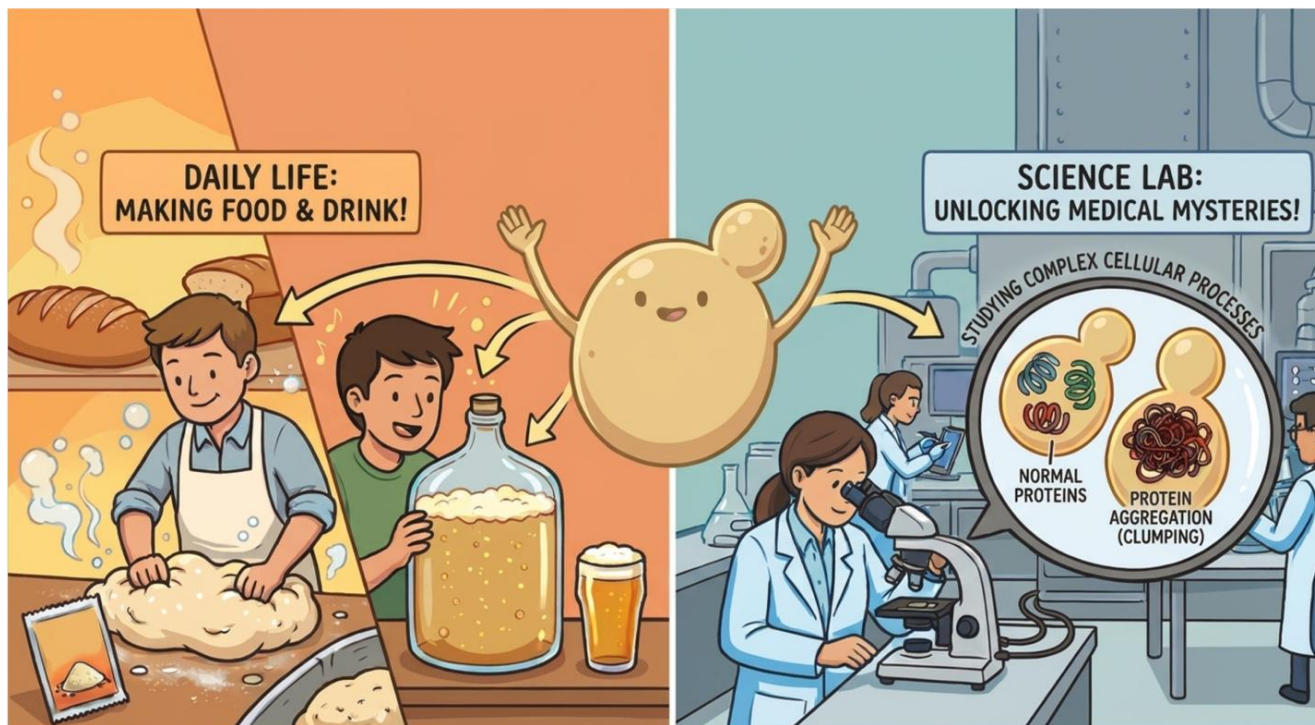
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Source: [Pastry Chef Online](#)

Proteins are the workers that carry out all the processes that our cells require to stay alive. To do this, a protein must first fold into a precise three-dimensional shape. Sometimes, however, the folding process goes awry, and misfolded proteins may begin to stick together in a process that happens in stages. First, they form small, soluble clumps called oligomers which grow and condense into bigger, insoluble deposits we call aggregates. These aggregates are a hallmark feature of many neurodegenerative diseases, usually found in the

neurons that die. For a long time, scientists have interpreted their presence in neurons as causative of cell death. Aggregates are at the scene of the crime, becoming prime suspects. However, a growing body of evidence suggests that the opposite might be the case. Aggregates could be the cell's containment method, a way of protecting itself from toxic, soluble oligomers. This [protective property of aggregates](#) is what Dr. Donovan McDonald and his colleagues studied, using yeast.



Source: Created using [BioRender.com](#), Daniel Sanchez Fonseca.

One of the main hurdles in studying neurodegenerative diseases is that we cannot get an accurate picture of what happens as the disease progresses. While imaging and other medical tests might give us insight into what is generally happening with patients, we are unable to observe what happens to the cells that these diseases are directly affecting. That is, we are unable to take a brain biopsy to visualize and study its cells without causing permanent damage to the patient, since this tissue does not regenerate. What we can do is take the brains of diseased patients and run tests attempting to guess what happened that led cells directly affected by disease to die prematurely.

Think of it this way: you just saw the aftermath of a car crash as you were walking down the street. Try imagining how it happened. Was one of the drivers distracted? Or could it be the traffic light malfunctioned and that led to the crash? You can probably come up with a few other plausible explanations. Nonetheless, without being able to see what happened as the crash occurred, you cannot be certain of how it could have been prevented. This is where cell models of disease, like yeast, come into play.

You might be wondering, how can an organism as simple as yeast be used to study a phenomenon as complicated as neurodegeneration? Historically, the tiny organism we use to bake bread and make beer has been used to study intricate cellular processes, like protein aggregation or even cancer. While it might seem more intuitive to use human cells or mice as model systems, yeast offers a set of advantages that make it very useful in the study of these complex cellular processes. The ageing process and responses to different environmental stressors (e.g., how cells respond to toxins or exposure to extreme heat) in human cells are quite similar, even identical in some cases, to how they occur in yeast. Furthermore, yeast serves as a 'living test tube': a system that we can genetically manipulate in days rather than months, with a level of control that is hard to achieve in human

cells. Also, since they grow very quickly in laboratory settings, we can test many different things at once, substantially increasing how many questions we can address in shorter time frames.

In their study, Dr. McDonald and his colleagues aimed to *uncover how two proteins that aggregate in neurodegenerative disease, TDP-43 and FUS, change as cells age*. The group reasoned that since ageing is a prominent risk factor for the development of neurodegenerative diseases, it might play a role in how proteins aggregate, whether increasing or decreasing their aggregation. Thus, the study of how TDP-43 and FUS behave as cells age might help uncover the underlying mechanism by which clumps of these proteins contribute to disease. With this in mind, the group genetically manipulated yeast to produce TDP-43 and FUS inside them and aged the cells. Interestingly, Dr. McDonald and his colleagues saw that as cells got older, the number of aggregates of these two proteins decreased. Even more surprisingly, the group also observed an increase in cell death as aggregation decreased.

So, if the clumps aren't the ones causing damage, what is? Dr. McDonald's findings indicate that because aggregation is decreasing as a result of ageing, it is likely that there are specific cellular processes in charge of keeping the clumps together that break down as cells age. As a result, it is possible that oligomers are being released from aggregates that are falling apart in older cells. Since a decrease in the formation of the big 'sticky' clumps coincided with an increase in cell death, the group hypothesized that these more soluble oligomers might actually be the culprit we have been looking for.

Thanks to their yeast model, Dr. McDonald and his colleagues showed that *aggregates might not be the main suspect for the death of brain cells* in patients living with neurodegenerative diseases. But the story does not end there; yeast can help answer countless scientific questions that advance our understanding of diseases like cancer and metabolic diseases. So, next time you are about to eat some French toast, remember that the same microorganism that allows you to enjoy it is also saving lives by helping us understand the diseases that take them.

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**Original Article:** McDonald, D. W., Chugh, N., Sava, R., & Duennwald, M. L. (2026). FUS and TDP-43 aggregation are uncoupled from toxicity in ageing yeast models. *BMC biology*, 24(1), 66. <https://doi.org/10.1186/s12915-026-02537-3>