Neurodegenerative diseases kill cells by disrupting basic biological processes shared by species as diverse as humans and yeast. The conservation of cellular structures and functions across eukaryotes allows researchers to study the genetic and molecular underpinnings of neurodegenerative diseases in various model organisms. Yeast cells are a particularly valuable system, as the fungi grow rapidly, are inexpensive to maintain, and can be genetically modified more readily than any other eukaryote. By introducing mutations linked to certain brain diseases, researchers can investigate the genetic and molecular mechanisms underlying neurodegenerative diseases in various model organisms. Yeast cells are a particularly valuable system, as the fungi grow rapidly, are inexpensive to maintain, and can be genetically modified more readily than any other eukaryote. By introducing mutations linked to certain brain diseases, researchers can investigate the genetic and molecular mechanisms underlying neurodegenerative diseases in various model organisms. Yeast models created through genome engineering methods unavailable in other model systems became critical tools in this endeavor. For disease-linked genes with a yeast homolog, researchers could remove the native yeast gene and replace it with wildtype or mutant forms of its human counterpart. This approach became an important platform for identifying mutations that cause disease in humans, as such as the FK5 mutations that impair mitochondrial function in Friedrich's ataxia and the NPC1 mutations that impair lipid metabolism in Niemann-Pick disease.

Other neurodegenerative disease–causing mutations occur in human genes with no yeast homolog. Nevertheless, researchers found that when such genes are expressed in yeast, they often function as they do in human cells. These “humanized yeast” models supported neurodegenerative disease research in the 1990s and early 2000s, particularly for studying a phenomenon termed “toxic gain of function,” in which a mutation converts a gene’s product into a form that negatively affects cellular viability. By building humanized yeast strains expressing various mutant forms of disease-linked genes, researchers discovered that many mutations exert a toxic gain of function by causing the associated protein to misfold and aggregate into inclusions that disrupt a number of essential cellular functions.