

# Restoring "Proteostasis": New Approach to Preventing Disease and Aging

*Selectively inhibiting protein misfolding and aggregation might slow aging.*

Proteins inside any cell are packed together as tightly as passengers on the Tokyo subway at rush hour. Cell stressors can cause proteins to misfold, which in turn can cause them to aggregate and trigger disease. However, each cell also has stress sensors that attempt to restore "proteostasis": proper protein folding. In two new reports, researchers provide hope that restoring proteostasis could help inhibit disease and aging some day.

A team from England created a small molecule, guanabenz, that prevented protein misfolding and promoted cell survival. Unlike some previous attempts to restore proteostasis chemically, this approach was very precise and caused no destructive side effects.

An international team focused on small molecules that are traditionally used to stain amyloid (misfolded, aggregated proteins) in pathology specimens. These small molecules slowed the aggregation of misfolded proteins in vitro. One of these molecules, thioflavin T, lengthened life span and slowed age-related decline in spontaneous movement (a marker for loss of vitality) in worms (*Caenorhabditis elegans*). Thioflavin T also prevented aggregation of a type of amyloid- $\beta$  molecule,  $A\beta_{3-42}$ , which is important in the pathology of Alzheimer disease, and of proteins that have been implicated in several human neurodegenerative diseases.

**Comment:** These studies will not provide any near-term benefits for treating human disease. But they indicate that selectively inhibiting protein misfolding and aggregation is feasible, might be effective in certain diseases, and might slow aging.

— [Anthony L. Komaroff, MD](#)

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