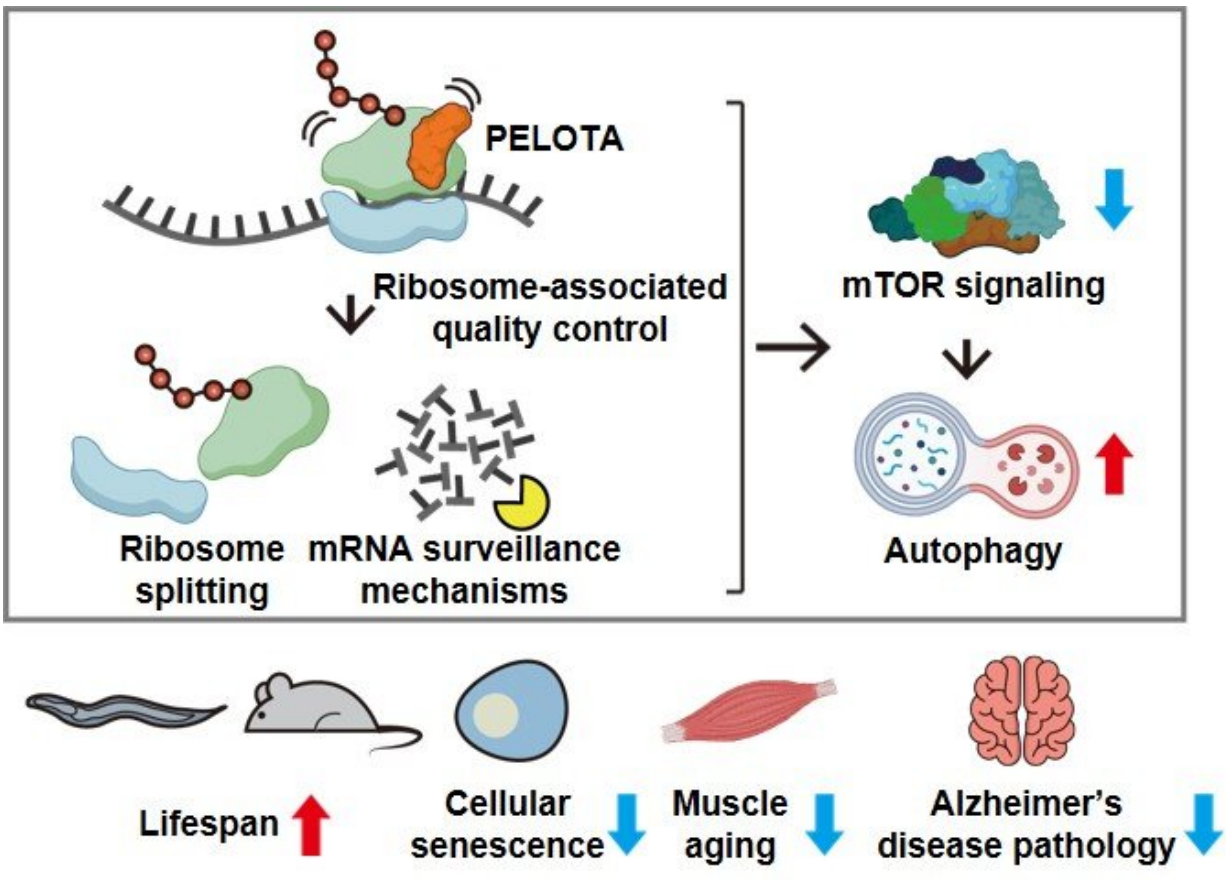
Unlocking a mechanism for longevity: Study identifies key to slowing aging via RNA regulation

August 18 2025



Credit: *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2505217122

As aging progresses, the quality of DNA and proteins inside cells declines, which is known to be the cause of various degenerative diseases. However, the connection between aging and RNA has remained largely unexplored.

Now, a Korean research team has discovered that a ribosome-associated quality control factor—PELOTA, a protein essential for eliminating abnormal mRNA—plays a central role in slowing aging and promoting longevity. This breakthrough, published in the *Proceedings of the National Academy of Sciences*, is expected to provide a new direction for future therapeutic strategies targeting human aging and neurodegenerative diseases.

The joint research team was led by Professor Seung-Jae V. Lee of the Department of Biological Sciences at KAIST and the Research Center for RNA-mediated Healthy Longevity, Professor Jinsoo Seo of Yonsei University, and Professor Kwang-Pyo Lee of the Korea Research Institute of Bioscience and Biotechnology under the National Research Council of Science & Technology.

Until now, RNA—particularly mRNA—has generally been regarded as a transient intermediary in protein synthesis. Its instability made it difficult to study quantitatively or track over time, leaving its physiological and functional roles relatively understudied compared to DNA.

Using C. elegans (a nematode widely used in aging research due to its short lifespan), the researchers first discovered that the ribosome-associated quality control factor PELOTA is essential for longevity. In particular, when PELOTA was overexpressed in normal nematodes, their lifespan was extended, suggesting that ribosome-associated quality control mechanisms involved in removing abnormal mRNA are necessary for promoting longevity.

The study also revealed that the ribosome-associated quality control system simultaneously regulates both the mTOR signaling pathway—which senses nutrient status or growth signals to control cell growth, protein synthesis, and autophagy, and plays a key role in aging and energy metabolism—and the autophagy pathway, the cellular cleanup and recycling system through which cells break down and reuse unnecessary or damaged components.

When PELOTA was deficient, the mTOR pathway became abnormally activated, and autophagy was suppressed—accelerating aging. Conversely, activation of PELOTA inhibited mTOR and induced autophagy, thereby maintaining cellular homeostasis and extending lifespan.

Notably, this mechanism was found to be conserved in both mice and humans. The study also showed that the loss of PELOTA could contribute to muscle aging and Alzheimer's disease, suggesting its relevance to age-related disorders.

These findings indicate that the study of PELOTA and ribosome-associated quality control could play an important role in developing therapeutic strategies for human aging and neurodegenerative diseases.

Professor Seung-Jae V. Lee of KAIST, who led the research, stated, "While the connection between quality control and aging has been well established at the DNA and protein levels, molecular evidence showing that RNA quality control also functionally contributes to lifespan regulation has been very limited." He emphasized that the "study provides strong evidence that the removal of abnormal RNA is a central axis in the aging regulatory network."

More information: Jongsun Lee et al, Pelota-mediated ribosome-associated quality control counteracts aging and age-associated

pathologies across species, *Proceedings of the National Academy of Sciences* (2025). DOI: 10.1073/pnas.2505217122