RNA and longevity: Discovering the mechanisms behind aging

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The vigors of youth and the greener pastures of yesteryears. Some might refer to these and other similar clichés as nothing more than rose-tinted literations of the past; a cognitive side effect of life. Romanticizing collective memories aside, however, it would be a challenge to find anyone who could argue against the physical degradations that accompany aging. One needs only to search for 'photos of aging' to realize that such yearnings are perhaps nothing more than ourselves giving form to the personal struggle with the byproducts of life.

What if, though, human beings could harness the power to control aging? Scientists have long strived to understand the aging process in order to combat age-related diseases and attain longevity. However, a complete picture of the inherently complex underpinnings remains ever elusive.

Research conducted by Professor Seung-Jae V. Lee's team from the Department of Life Sciences at Pohang University of Science and Technology in collaboration with Professor Hong Gil Nam from the Center for Plant Aging Research at Institute for Basic Science has made great contributions to solving this mystery by showing that RNA quality control affects aging. This achievement has been published in the world-renowned *Nature Communications*.

DNA, RNA, and proteins carry the genetic instructions within all known living organisms. Existing research has collectively shown that organisms with long lifespans tend to have more stringent DNA and protein quality control. In other words, deterioration of DNA and protein quality control is centrally correlated with aging and age-related diseases. However, the role of the RNA quality control in aging remained almost unexplored.

The research team concentrated on a specific RNA quality control mechanism called nonsense-mediated mRNA decay (NMD), a key pathway which degrades both abnormal as well as some normal RNAs. The team has successfully shown that NMD is crucial for longevity in the roundworm called *C. elegans*, a popularly used animal for aging research. They first discovered that NMD activity decreases during aging. The team then discovered that enhanced NMD underlies the longevity of famous *C. elegans* strains called daf-2 mutants, which have reduced insulin hormone signaling.

Since the main role of NMD is degradation of its target mRNAs, the team focused on mRNAs that were downregulated in daf-2 mutants. Their research showed substantially decreased levels of a gene yars-2, an NMD target, are at least partially responsible for long lifespan in daf-2 mutants. In other words, research data collectively suggest that NMD-mediated RNA quality control is critical for longevity in *C. elegans*.

Professor Lee anticipates that the research team's leading discovery of the causal relationship between RNA quality control and longevity will play a significant role in shedding light on the mechanisms behind aging and eventually contribute to curing and even preventing age-related diseases.

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