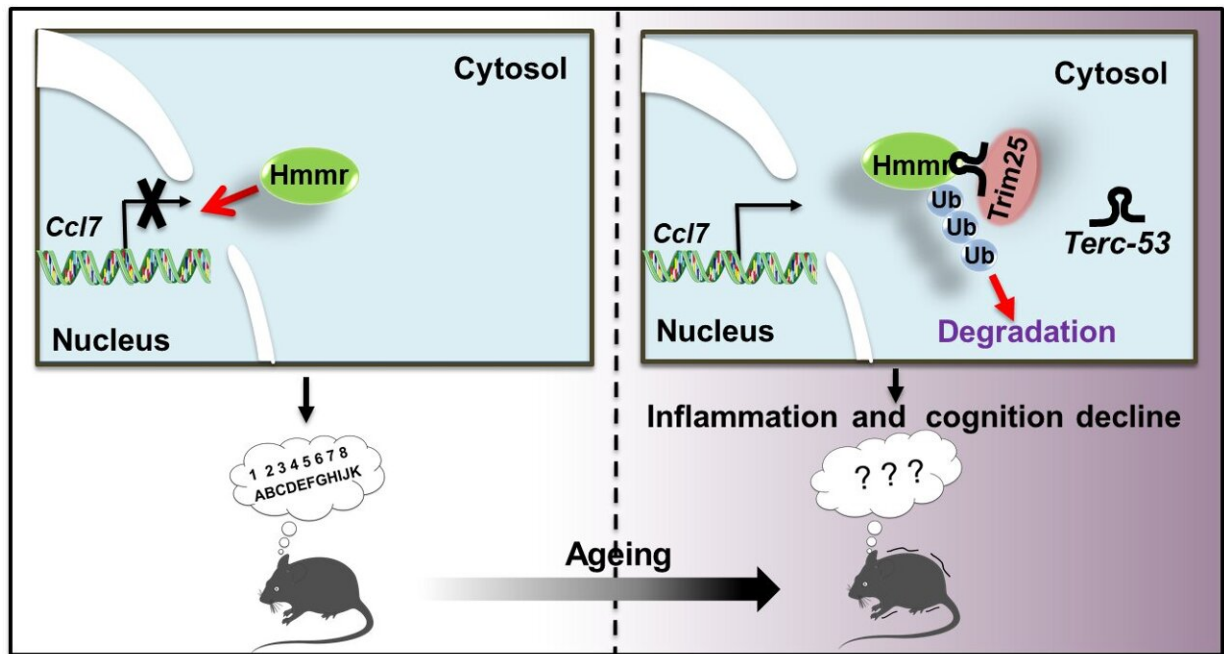# Noncoding RNA Terc-53 and hyaluronan receptor Hmmr regulate aging in mice

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Terc-53 functions as a molecular scaffold bringing together Hmmr and Trim25, accelerating Hmmr's ubiquitination-mediated degradation, which consequently leads to neuroinflammation and cognition decline. Credit: Sipeng Wu, Yiqi Cai, Lixiao Zhang, Xiang Li, Xu Liu, Guangkeng Zhou, Hongdi Luo, Renjian Li, Yujia Huo, Zhirong Zhang, Siyi Chen, Jinliang Huang, Jiahao Shi, Shanwei Ding, Zhe Sun, Zizhuo Zhou, Pengcheng Wang, Geng Wang

In a study appearing in *Protein & Cell* researchers investigated the physiological functions of Terc-53 by creating transgenic mice that

overexpress this noncoding RNA. They observe that Terc-53 overexpression affects normal aging in mammals, contributing to cognitive decline and shortened lifespan.

The work is titled " Noncoding RNA Terc-53 and hyaluronan receptor Hmmr regulate aging in mice"

Mechanistically, they find that Terc-53 binds to and promotes the degradation of Hmmr, leading to enhanced inflammation in tissues and accelerated aging. They also note that Hmmr levels decrease with age in certain brain regions, similar to Terc-53's pattern, and that restoring Hmmr levels can improve cognitive abilities and reduce neuroinflammation markers.

Key findings from the study include:

1. Terc-53's Role in Aging: Terc-53 overexpression in mice leads to age-related cognitive decline and a shorter lifespan, indicating its involvement in normal mammalian aging processes.
2. Hmmr as Effector of Terc-53: Hmmr is identified as a target of Terc-53, with Terc-53 mediating its degradation. This degradation increases inflammation, contributing to accelerated aging.
3. Restoration of Hmmr Improves Cognition: Supplementing Hmmr in the hippocampus of aging Terc-53 transgenic mice reverses cognitive decline, suggesting a potential therapeutic strategy for age-related cognitive issues.
4. Tissue-Specific Aging Patterns of Hmmr: Hmmr's involvement in aging appears to be tissue-specific, with varying expression patterns across different organs.

The study highlights the complexity of aging in mammals and the significance of noncoding RNAs and proteins that emerged late in

evolution. It demonstrates that Terc-53 regulates organismal aging through the stability of Hmmr and the modulation of neuroinflammation.

The findings open new avenues for understanding and potentially treating age-related physical disabilities and improving health span. By identifying Hmmr as a critical mediator of Terc-53's effects on aging, the research suggests that strategies aimed at stabilizing Hmmr could mitigate age-related cognitive decline and inflammation.

More information: Sipeng Wu et al, Noncoding RNA Terc-53 and hyaluronan receptor Hmmr regulate aging in mice, *Protein & Cell* (2024). DOI: 10.1093/procel/pwae023

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