Researchers Uncover Negative Regulator of RNA Exosome Complex

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The RNA exosome complex is the most versatile RNA processing and degradation machinery. Up to date, most studies have been focused on the identification of new exosome cofactors that targets the exosome to different substrate RNAs. How the exosome is negatively regulated remains largely unknown.

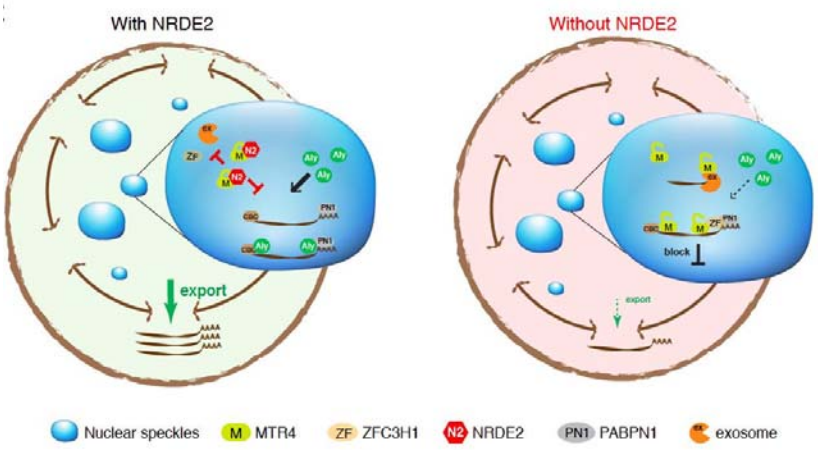
In a recent study published in *Genes & Development*, scientists from Shanghai Institute of Biochemistry and Cell Biology of Chinese Academy of Sciences, Peking University Health Science Center, and Wuhan University, uncovered NRDE2 as a negative regulator of the nuclear exosome.

They found that NRDE2 is mainly concentrated in nuclear speckles where it forms a complex with MTR4, the essential nuclear exosome cofactor determining exosome recruitment, via a conserved N terminal region (MID, MTR4-interacting domain).

RNA- and RIP-seq data revealed that NRDE2 inhibits MTR4 recruitment and exosomal degradation, and thereby ensures mRNA stability and nuclear export. Intriguingly, structural and biochemical data demonstrated that NRDE2 occupies MTR4's key residues, locks MTR4 in an unusually closed conformation, and inhibits MTR4 interaction with the exosome as well as proteins important for MTR4/exosome recruitment.

Therefore, the results showed that NRDE2-mediated exosome inhibition is required for self-renewal of mouse embryonic stem cells.

This study uncovered NRDE2 as the first negative regulator of the nuclear exosome, and demonstrated that this negative regulation is important for ensuring mRNA stability and nuclear export, and thereby maintains ESC self-renewal.



A model for NRDE2 negatively regulates MTR4/exosome. (Image by CHENG Hong)

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