Erroneous ribosomal RNAs promote the generation of antisense ribosomal siRNA

With the support by the National Natural Science Foundation of China, the research team directed by Prof. Guang ShouHong (光寿红) at the University of Science and Technology of China recently reported that erroneous rRNAs can trigger antisense ribosomal siRNA (risiRNA) generation and subsequently turn on the nuclear RNAi-mediated gene silencing pathway to inhibit pre-rRNA expression, which was published in *PNAS* (2018, 115 (40): 10082—10087).

Ribosome biogenesis is a multistep process during which mistakes can occur at any step of pre-rRNA processing, modification, and ribosome assembly. Misprocessed rRNAs are usually detected and degraded by surveillance machineries. In 2017, the Guang lab firstly reported in *Nature Structural & Molecular Biology* that a new subset of 22G-RNAs termed as risiRNAs regulate pre-rRNA expression and maintain rRNA homeostasis.

To further understand the biological roles and generation mechanism of risiRNAs, the Guang lab isolated a series of mutants in which risiRNAs were accumulated by forward and reverse genetic screens and CRISPR/Cas9-mediated gene knockout technology. Many of the isolated genes are highly conserved from yeast to humans and are involved in rRNA modification and pre-rRNA processing. Thus, this work suggests that the deficiency in the modification and processing of rRNAs may promote the generation of risiRNAs, which further act in a feedback loop to maintain cellular rRNA homeostasis via the nuclear RNAi pathway.

For a long time, small ribosomal RNA sequences have been widely treated as non-specific degradation products and neglected as garbage sequences. The Guang lab's work suggests that these sequences may play important regulatory functions and should be carefully investigated.

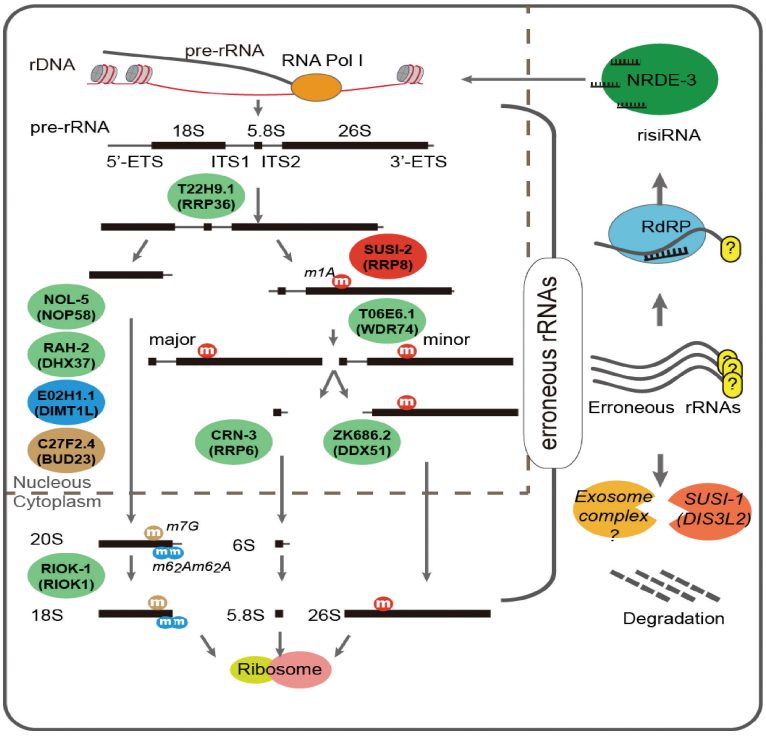

Figure A working model of risiRNA generation. Misprocessed rRNAs or defects in rRNA modifications can trigger risiRNA generation and subsequently turn on the nuclear RNAi-mediated gene silencing pathway to inhibit pre-rRNA expression.