Spatially clustered piRNA genes promote the transcription of piRNAs via condensate formation of the H3K27me3 reader UAD-2

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C. Zhu[I], X. Si[I], X. Feng[I], **S. guang**[II]

[I]Hefei, Anhui, Hefei, Anhui, China, [II]School of Life Sciences, University of Science and Technology of China, Hefei, China

PIWI-interacting RNAs (piRNAs) are essential for maintaining genome integrity and fertility in various organisms. In flies and nematodes, piRNA genes are encoded in heterochromatinized genomic clusters. The molecular mechanisms of piRNA transcription remain intriguing. Through unique molecular indexed-small RNA sequencing and chromosome editing, we discovered that spatial aggregation of piRNA genes enhances their transcription in nematodes. The heterochromatinized piRNA genome recruits the piRNA transcription complex USTC (including PRDE-1, SNPC-4, TOFU-4, and TOFU-5) and the H3K27me3 reader UAD-2, which phase separate into droplets to initiate piRNA transcription. We searched for factors that regulate piRNA condensate formation and isolated the SUMO E3 ligase GEI-17 as inhibiting and the SUMO protease TOFU-3 as promoting condensate formation, thereby regulating piRNA production. Our study revealed that spatial aggregation of piRNA genes, phase separation and deSUMOylation may benefit the organization of functional biomolecular condensates to direct piRNA transcription in the heterochromatinized genome.