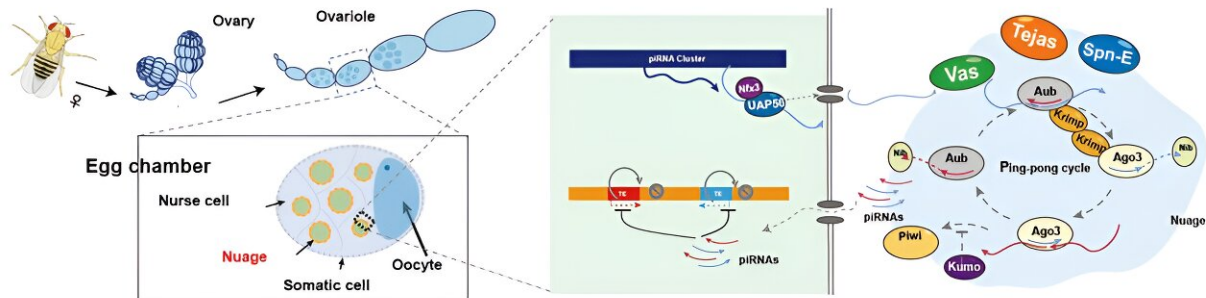


How certain proteins contribute to the formation of a class of RNA critical to protecting the genome investigated

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piRNA biogenesis pathway in the *Drosophila* germline. The *Drosophila* ovary has 16–20 ovarioles containing 14 different developmental stages of egg chambers. The piRNA precursors transcribed in the nucleus are transported to the nuage, which is located on the cytoplasmic side of the nuclear membrane. At the nuage, Tej, Vas, Spn-E, Krimp, and other proteins accumulate, and Aub and Ago3 cleave piRNA precursors and complementary-sequenced transposons. In the nuage, Tudor domain proteins cooperate with PIWI family proteins, and piRNAs are generated via the ping-pong amplification pathway, which is conjugated with the degradation of transposon transcripts. Credit: 2023, Toshie Kai, Tejas functions as a core component in nuage and precursor processing in *Drosophila* piRNA biogenesis, *Journal of Cell Biology*

You're likely familiar with RNA, the molecule that plays an important

role in protein production and gene expression control. Perhaps you're less familiar, however, with PIWI-interacting RNA (piRNA), a special type of RNA that protects the genome from mutations. Now, researchers in Japan have shed light on how these critical molecules are formed by the dynamics of several associated proteins in the germline of the fruit fly, *Drosophila melanogaster*.

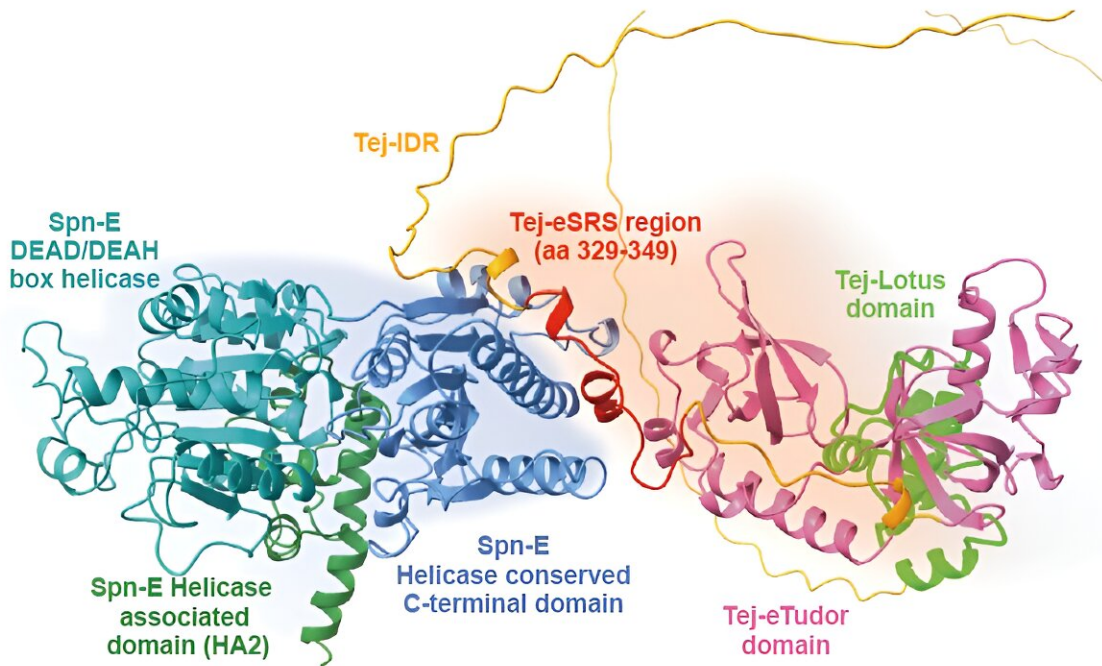
In a new study researchers from Osaka University have clarified how the proteins Tejas (Tej), Vasa (Vas), and Spindle-E (Spn-E) contribute to the creation of piRNAs, which are found in the gonads and help protect the genome from mutations or deletions caused by transposons that may be passed on through reproductive cells. The article, "Tejas functions as a core component in nuage assembly and precursor processing in *Drosophila* piRNA biogenesis," was published in *Journal of Cell Biology*.

In *Drosophila*, piRNAs first appear as long sequences, known as precursor transcripts, which are processed in membrane-less cellular compartments called "nuage" and turned into their shorter forms as functional piRNAs. These nuage are composed by the interactions of RNA-processing proteins, PIWI family proteins, and a group of proteins known as the Tudor-domain-containing (Tdrd) proteins.

Of those, Tej, a Tdrd [protein](#), has been previously shown to play a key role in the piRNA pathway, with a major reduction in piRNAs observed in the absence of Tej. However, the role that Tej plays in the generation of piRNA is not fully understood. The research team set out to investigate the molecular function of Tej during piRNA biogenesis.

"We first evaluated the detailed function of Tej in the *Drosophila* ovary and confirmed that Tej is involved in processing precursor transcripts with two RNA-processing helicases: Vas and Spn-E in the nuage," explains lead author of the study Lin Yuxuan. "In the mutant germ cells that lack Tej, we observed that Vas and Spn-E are not properly

assembled in the nuage, indicating that Tej plays a critical role in recruiting Vas and Spn-E to the nuage."

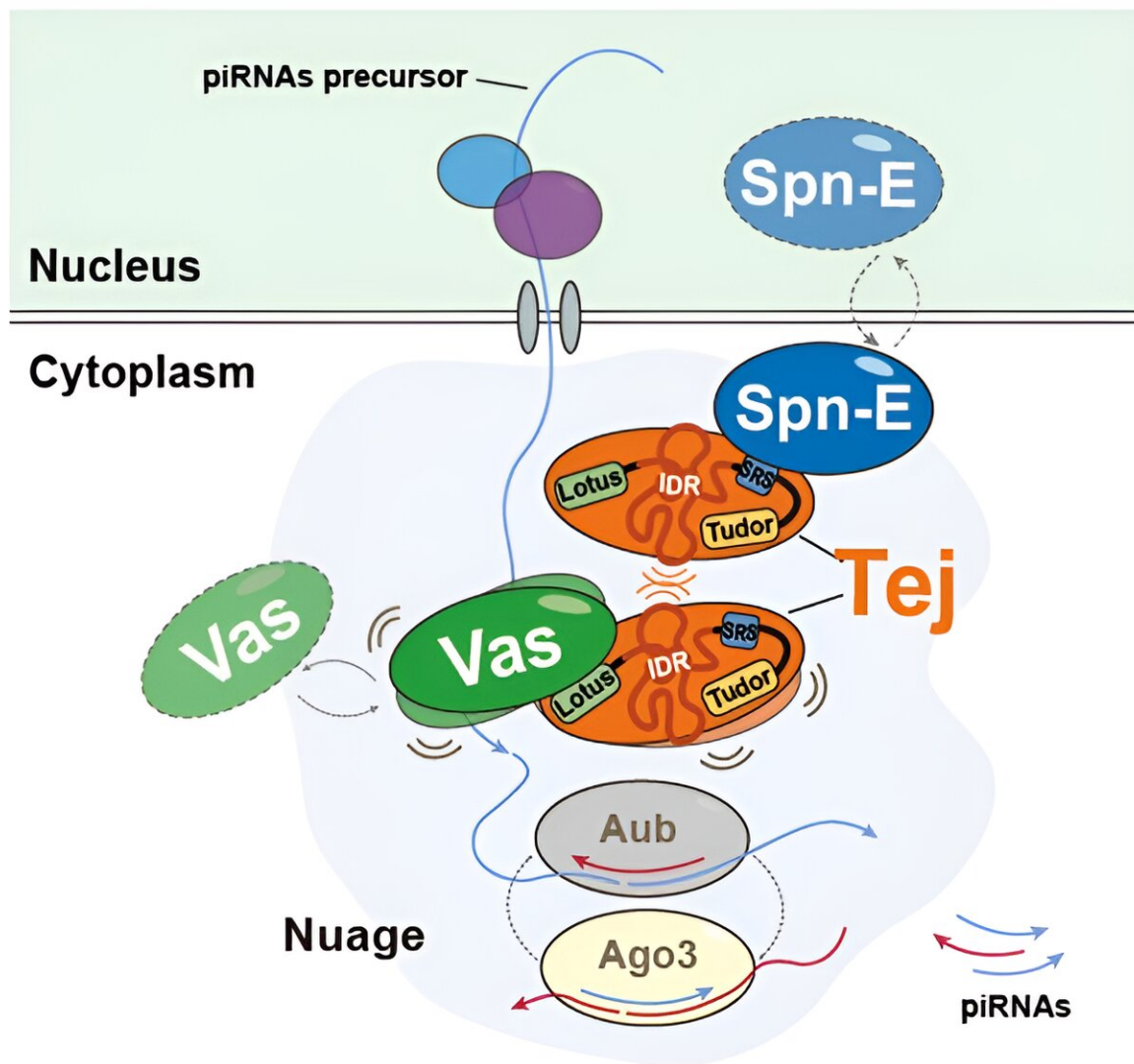


AlphaFold prediction of the interaction regions for Tej–Spn-E proteins. Heterodimeric structures of Tej (right, red) and Spn-E (left, blue) are predicted using AlphaFold v2.2. The C-terminal conserved region of Spn-E (blue) predicted to interact with Tej-eSRS (red) was experimentally proven in the *Drosophila* ovary. Credit: 2023, Toshie Kai, Tejas functions as a core component in nuage and precursor processing in *Drosophila* piRNA biogenesis, *Journal of Cell Biology*

By generating variants of Tej that lack specific regions of the protein, the investigators could identify which areas of Tej are crucial for interacting with Spn-E and modulating the mobility of Vas. They found that one distinct region, termed the "Spn-E recruit site," contributes to

the recruitment and maintenance of Spn-E in the nuage. Another distinct region, known as the intrinsically disordered region, affects both the ability of Vas to move within the nuage and the dynamics of other components of the nuage.

"Our study demonstrates that Tej is a key component of nuage formation and piRNA processing," says senior author Kai Toshie. "By recruiting Vas and Spn-E, Tej facilitates nuage formation, allowing the processing of piRNA precursor transcripts into their mature, functional forms."



Tej interacts with Spn-E and Vas and has a role in processing piRNA precursors. In *Drosophila* germ cells, Spn-E localizes to the nuage in the perinuclear membrane region via the eSRS motif in Tej. In contrast, the Lotus domain of Tej facilitates Vas localization to the nuage. This complex is involved in the processing of piRNA precursors, and the IDR of Tej provides mobility to the Tej–Vas complex in the nuage, contributing to its role as a component of a non-membrane organelle. Credit: 2023, Toshie Kai, Tejas functions as a core component in nuage and precursor processing in *Drosophila* piRNA biogenesis, *Journal of Cell Biology*

Disruption of piRNA formation is known to cause infertility. The research team's insight into the formation of nuage and piRNA processing mediated by Tej in *Drosophila* germline may help to uncover the mechanisms underlying reproductive disorders, including infertility, and may contribute to the development of new fertility drugs.

More information: Yuxuan Lin et al, Tejas functions as a core component in nuage and precursor processing in *Drosophila* piRNA biogenesis, *Journal of Cell Biology* (2023). [DOI: 10.1083/jcb.202303125](https://doi.org/10.1083/jcb.202303125)

Provided by Osaka University

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