論文の内容の要旨

Piwi nuclear localization and its regulatory mechanism in *Drosophila* ovarian somatic cells

(ショウジョウバエ Piwi-piRNA 複合体の核局在制御機構の解析)

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In *Drosophila* ovarian somatic cells (OSCs), Piwi represses transposons transcriptionally to maintain genome integrity. Piwi nuclear localization requires the N-terminal region and piRNA loading of Piwi. However, the nuclear import machinery and the mechanism underlying the piRNA loading-dependency remain unknown. Here we showed that Importinα (Impα) plays a pivotal role in Piwi nuclear localization and that Piwi has a classical bipartite nuclear localization signal (NLS) at the N-terminal end. Impα2 and Impα3 were fairly highly expressed in OSCs, whereas the last member Impα1 was the least expressed. Loss of Impα2 or Impα3 in OSCs caused mislocalization of Piwi, but not of SV40-NLS-cargo, to the cytoplasm. The overexpression of Impα1, Impα2, or Impα3 rectified Piwi nuclear localization in the OSCs.

Extension of Piwi-NLS by fusing an additional Piwi-NLS led Piwi to be imported to the nucleus in a piRNA-independent manner, whereas replacement of Piwi-NLS with SV40-NLS failed to do so. Limited proteolysis analysis suggested that the N-terminal approximately 200 residues of Piwi were hidden when not loaded with piRNAs, but piRNA loading triggered conformational change in Piwi, exposing the N-terminus to the environment. These results suggest that Piwi autoregulates its nuclear localization by exposing the NLS to Impα exclusively upon piRNA loading.