iCeMS News Release

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Protecting the Genome: New Transposon-Silencing Protein Discovered

In discovering a new protein that protects the germline genome by silencing transposable genes, researchers have successfully identified host defense mechanisms. These findings, appearing in the latest issue of the journal *Developmental Cell*, can potentially aid in analyzing a cause of male sterility as well as expand the boundaries of epigenetic regulation.

This work has included contributions from Kyoto University, the University of Tokyo, the National Institute of Genetics (Japan), the Mitsubishi Kagaku Institute of Life Sciences, the National Research Institute for Child Health and Development (Japan), the University of Colorado School of Medicine, the European Molecular Biology Laboratory (EMBL), and the Research Institute of Molecular Pathology (IMP, Austria).

A Preview of this paper appeared in the same issue of *Developmental Cell*, in recognition of the influential nature of this finding.

Prof. **Norio Nakatsuji** (left) and Asst. Prof. **Shinichiro Chuma** presenting their findings at a press conference (Dec. 15, 2009)

Publication Information

The TDRD9-MIWI2 Complex Is Essential for piRNA-Mediated Retrotransposon Silencing in the Mouse Male Germline

Masanobu Shoji, Takashi Tanaka, Mihoko Hosokawa, Michael Reuter, Alexander Stark, Yuzuru Kato, Gen Kondoh, Katsuya Okawa, Takeshi Chujo, Tsutomu Suzuki, Kenichiro Hata, Sandra L. Martin, Toshiaki Noce, Satomi Kuramochi-Miyagawa, Toru Nakano, Hiroyuki Sasaki, Ramesh S. Pillai, Norio Nakatsuji and Shinichiro Chuma

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[Abstract]

Host-defense mechanisms against transposable elements are critical to protect the genome information. Here we show that tudor-domain containing 9 (*Tdrd9*) is essential for silencing *Line-1* retrotransposon in the mouse male germline. *Tdrd9* encodes an ATPase/DExH-type helicase, and its mutation causes male sterility showing meiotic failure. In *Tdrd9* mutants, *Line-1* was highly activated and piwi-interacting small RNAs (piRNAs) corresponding to *Line-1* were increased, suggesting that feedforward amplification operates in the mutant. In fetal testes, *Tdrd9* mutation causes *Line-1* desilencing and an aberrant piRNA profile in prospermatogonia, followed by cognate DNA demethylation. TDRD9 complexes with MIWI2 with distinct compartmentalization in processing bodies, and this TDRD9-MIWI2 localization is regulated by MILI and TDRD1 residing at intermitochondrial cement. Our results identify TDRD9 as a functional partner of MIWI2 and indicate that the tudor-piwi association is a conserved feature, while two separate axes, TDRD9-MIWI2 and TDRD1-MILI, cooperate nonredundantly in the piwi-small RNA pathway in the mouse male germline.

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Preview

Defending the Genome in Tudor Style

Godfried W. van der Heijden and Alex Bortvin

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Contact

Yutaka Iijima | pr@icems.kyoto-u.ac.jp

Manager, International Public Relations

Institute for Integrated Cell-Material Sciences (iCeMS), Kyoto University