GENETICS

Understanding hybrid incompatibility in mice

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Usually, different species don't mate. But when they do, their offspring, called hybrids, may not be viable or fertile. Reduced fertility or viability of hybrid offspring are known as hybrid incompatibilities that prevent interbreeding between two distinct species. Hybrid incompatibilities are important evolutionarily because they act as reproductive barriers that can both promote speciation and maintain the integrity of the species. A study published in *Nature* provides new insights into the mechanisms underlying hybrid incompatibility in mice.

The authors of the study, Warif El Yakoubi and Takashi Akera (NIH, National Heart, Lung, and Blood Institute), decided to focus on hybrid female sterility, a phenomenon contributing to hybrid incompatibility but less studied than hybrid lethality and hybrid male sterility. Previous work had shown that female hybrid mice between *Mus musculus domesticus* and *Mus spretus* are subfertile due to chromosome segregation errors during meiosis I, but the molecular basis underlying this process remained unclear.

To understand the cell biological mechanism underlying reduced fertility in *domesticus* × *spretus* hybrid female mice, the researchers live-imaged chromosome dynamics in their oocytes. They confirmed the existence of chromosome segregation errors in hybrid oocytes and showed that these errors were mainly due to *domesticus* chromosomes lagging in anaphase I. The investigators linked chromosome segregation errors in hybrid oocytes to chromosome condensation defects, especially those impacting the *domesticus* centromere structure. Further imaging revealed that centromere stretching was always observed on major satellites, repetitive DNA sequences that are enriched in *domesticus* versus *spretus* pericentromeres.

The experiments also revealed that condensin II, a protein complex having a critical role in chromosome condensation, was reduced on hybrid oocyte chromosomes compared with pure *domesticus* oocyte chromosomes. Altogether, these results suggest that hybrid oocytes inherited the low condensin II trait from *spretus* and the high major satellite copy number from *domesticus*; and that this combination led to *domesticus* centromere stretching in hybrid oocytes, causing meiotic failures and leading to egg aneuploidy.

Therefore, this new study provides cell biological insights into hybrid incompatibility by revealing that species divergence in centromere organization and condensin regulation, which drives meiotic failures in hybrid oocytes, creates a reproductive isolating barrier between *M. m. domesticus* and *M. spretus*.

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