DOCTORAL THESIS

Identification of asymmetric hybrid incompatibility loci in F1 generation between Caenorhabditis briggsae and C. nigoni

Bi, Yu

Date of Award:
2019

Abstract

Hybrid incompatibility (HI) is frequently manifested as lethality or sterility in hybrid progeny between related species, and plays a key role in speciation. The genetic basis of HI has been intensively studied in model organisms such as yeast and fruit fly over decades, and "*Two rules of speciation"* have been observed across species. *C. elegans* as a nematode model organism contributes little to speciation research mainly due to lack of a close relative with which it can mate and produce viable progeny. Such limitation has recently been alleviated by identification of *C. nigoni*, a close relative, also termed as sister species, of *C. briggsae*. The two can make and produce a handful of viable hybrids. Both species are members of *Elegans* supergroup. Hybrid cross between the two species uncovered asymmetric hybrid incompatibilities, i.e. crossing direction-dependent hybrid male sterility and inviability. Asymmetry was also observed in F1 hybrids from reciprocal crosses exclusively in male but not female (Woodruff, Eke, Baird, Félix, & Haag, 2010). Asymmetry was also observed in backcrosses between the F1 female hybrids and the parental species. For example, F2 progeny fathered by *C. briggsae* suffered almost 100% embryonic lethality for both males and females, whereas those fathered by *C. nigoni* were partially viable and fertile.

Further study of HI between these two species was initiated by investigating how *C. briggsae* chromosomal fragments in an otherwise pure *C. nigoni* genome affect fitness of hybrid worms. The hybrid worms were generated by repeatedly backcrossing *C. briggsae* genomic fragments each bearing a visible chromosomal-integrated marker to *C. nigoni* to produce introgression lines. Characterization of the introgression lines provided a detailed HI landscape of between the two

species. Multiple intervals on the *C. briggsae* X chromosome were responsible for hybrid male inviability or sterility while most of the *C. briggsae* autosomes were not involved in these male phenotypes (Bi et al., 2015). RNA sequencing was performed in sterile male worms bearing independent introgressions, revealing a down-regulated gene expression pattern (Li et al., 2016).

To uncover the HI mechanism underlying the asymmetric HI phenotypes exhibited in hybrids in F1 generation, I performed a genome-wide screening to identify HI loci that are responsible for the hybrid male inviability and sterility in F1 as well as hybrid breakdown in F2. By crossing between *C. briggsae* and *C. nigoni* introgression lines bearing a known *C. briggsae* fragment, I was able to construct hybrid animals homozygous or heterozygous for *C. briggsae* alleles on the introgression while those on counterpart of *C. nigoni* were absent. Contrasting the HI phenotypes here and those between two wild-type parents allows mapping of the loci responsible for the hybrid asymmetric phenotypes. The aggregated introgressions cover 94.6% of the *C. briggsae* genome, including 100% of the X chromosome. Surprisingly, I identified another two *C. briggsae* genomic intervals on chromosomes II and IV that can rescue the hybrid male inviability but not the male sterility in F1 fathered by *C. nigoni*, suggesting the involvement of differential epistatic interactions in the asymmetric hybrid male fertility and inviability. What's more, I observed that two independent *C. briggsae* X fragments that produce male sterility in *C. nigoni* as an introgression rescued hybrid male sterility in F1 fathered by *C. briggsae*. Backcrossing of the rescued sterile F1 male to its parental species showed that they can alleviate the F2 hybrid breakdown by a handful of viable F2 mothered by *C. briggsae*. Subsequent backcrossing of the rescued sterile males with *C. nigoni* led to the isolation of a 1.1-Mb genomic interval that specifically interacts with an X-linked introgression, which is essential for hybrid male fertility. In

addition, I further identified three *C. briggsae* genomic intervals on chromosome I, II, and IV that produced inviability in all F1 progeny, dependent on or independent of the parent-of-origin. Taken together, I identified multiple independent interacting loci that are responsible for asymmetric HI phenotypes especially hybrid male sterility and inviability, which lays a foundation for their molecular characterization.

Table of Contents