Structural and mechanistic insights into the complexes formed by Wolbachia cytoplasmic incompatibility factors

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Wolbachia bacteria, inherited through the female germ line, infect a large fraction of arthropod species. Many Wolbachia strains manipulate host reproduction, most commonly through cytoplasmic incompatibility (CI) [1]. CI, a conditional male sterility, results when Wolbachia-infected male insects mate with uninfected females; viability is restored if the female is similarly infected (called “rescue”) [2]. CI is used to help control mosquito-borne viruses such as dengue and Zika, but its mechanisms remain unknown [3].

The coexpressed CI factors CifA and CifB form stable complexes in vitro, but the timing and function of this interaction in the insect are unresolved. CifA expression in the female germ line is sufficient for rescue. We report high-resolution structures of a CI-factor complex, CinA-CinB, which utilizes a unique binding mode between the CinA rescue factor and the CinB nuclease; the structures were validated by biochemical and yeast growth analyses. Importantly, transgenic expression in Drosophila of a nonbinding CinA mutant, designed based on the CinA-CinB structure, suggests CinA expressed in females must bind CinB imported by sperm in order to rescue embryonic viability. Binding between cognate factors is conserved in an enzymatically distinct CI system, CidA-CidB, suggesting universal features in Wolbachia CI induction and rescue.

Figure 1. Structural basis of CinA-CinB interaction. (A) CinA consists of an N-terminal domain and a carboxyl-terminal domain. (B) The overall structure of the CinA-CinB complex. (C) CinB consists of two nuclease domains (NDs), CinBND1 and CinBND2. Active site residues are shown as spheres. The interface between CinA and CinB can be divided into three regions, interfaces I (D), II (E–F), and III (G), in which interface II is further divided into interfaces IIA (E) and IIB (F).