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The Molecular Mechanisms and Evolution of Natural Gene Drives in Different Organisms

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DESCRIPTION

Gene drives are selfish genetic elements that are transmitted to progeny at super-mendelian (>50%) frequencies. They can bias the inheritance of particular alleles or genetic traits, allowing them to spread rapidly and persistently throughout a population. Gene drives can be engineered using CRISPR-Cas9 technology, but they also occur naturally in various organisms, such as insects, plants, fungi and viruses. Understanding the molecular mechanisms and evolution of natural gene drives can provide insights into their diversity, function, regulation and potential applications.

Natural gene drives can be classified into two main types: meiotic drives and post-meiotic drives. Meiotic drives act during gametogenesis to increase the transmission of a drive allele over its counterpart. Post-meiotic drives act after gametogenesis to increase the fitness or fecundity of individuals carrying a drive allele. Both types of drives can use different molecular strategies to achieve their transmission bias.

Meiotic drives can be further divided into three subtypes: segregation distorters, chromosome rearrangements and gamete killers. Segregation distorters interfere with the normal segregation of chromosomes during meiosis, resulting in an unequal distribution of drive alleles among gametes. For example, in Drosophila melanogaster, the Sex Ratio (SR) system consists of a drive X chromosome that encodes a nuclease that cleaves the Y chromosome during spermatogenesis, causing male-biased progeny. Chromosome rearrangements involve inversions, translocations or fusions that suppress recombination between homologous chromosomes, preventing the loss of drive alleles by crossing over. For example, in Anopheles gambiae, the 2La inversion is a large chromosomal inversion that confers resistance to malaria and drought, and is maintained at high frequencies by suppressing recombination with the standard arrangement. Gamete killers induce the death or dysfunction of gametes that do not carry a drive allele, reducing their chance of fertilization. For example, in mice, the t haplotype is a large chromosomal region that encodes a toxin–antidote system that kills sperm that do not carry the t allele.

Post-meiotic drives can be further divided into two subtypes-endosymbionts and homing endonucleases. Endosymbionts are intracellular bacteria or fungi that manipulate the reproduction or development of their hosts to favor their own transmission. For example, Wolbachia is a widespread endosymbiont that infects many insects and can cause cytoplasmic incompatibility (reduced viability or fertility of offspring from uninfected females and infected males), feminization (conversion of genetic males into females), male killing (death of male offspring) or parthenogenesis (asexual reproduction of females). Homing endonucleases are enzymes that recognize and cleave specific DNA sequences in the genome, creating double-strand breaks that are repaired by copying the drive allele from the homologous chromosome. For example, in yeast, *VDE* is a homing endonuclease that targets an intron in the *VMA1* gene and induces its own copying during meiosis.

The evolution of natural gene drives is influenced by several factors, such as mutation rate, fitness cost, resistance allele frequency, population structure and environmental variation. Natural gene drives can arise by mutation or horizontal gene transfer from other species. They can also be lost or suppressed by counteracting mutations or epigenetic modifications in the host genome or by coevolution with other selfish elements. Natural gene drives can have various evolutionary consequences for their hosts, such as reduced genetic diversity, increased reproductive isolation, altered sex ratio or phenotypic adaptation.

Natural gene drives are fascinating examples of molecular evolution and genetic conflict. They can also serve as models or sources for synthetic gene drives that aim to modify or control target populations for various purposes, such as pest management, disease prevention or conservation. However, natural gene drives also pose challenges and risks for synthetic gene drive design and deployment, such as genetic variability, resistance evolution, ecological interactions and ethical

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implications. Therefore, studying natural gene drives can help to improve our understanding and application of this powerful technology.