

CAGE TRIALS USING AN ENDOGENOUS MEIOTIC DRIVE GENE IN THE MOSQUITO *Aedes aegypti* TO PROMOTE POPULATION REPLACEMENT

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Abstract. Control of arthropod-borne diseases based on population replacement with genetically modified non-competent vectors has been proposed as a promising alternative to conventional control strategies. Due to likely fitness costs associated with vectors manipulated to carry anti-pathogen effector genes, the effector genes will need to be coupled with a strong drive system to rapidly sweep them into natural populations. Endogenous meiotic drive systems have strong and stable population replacement potential, and have previously been reported in two mosquito species: *Aedes aegypti* and *Culex pipiens*. To investigate the influence of an endogenous meiotic drive gene on *Ae. aegypti* population dynamics, we established three experimental population types that were initiated with 100%, 10%, and 1% male mosquitoes carrying a strong meiotic driver (T37 strain) and 100% sensitive females (RED strain), respectively. Among the 100% and 10% populations, early generations were highly male biased, which reflected the effects of the meiotic driver, and remained more than 60% male by the F_{15} . A genetic marker tightly linked with the meiotic driver on chromosome 1 showed strong selection for the T37 strain-specific allele. Similar but reduced effects of the meiotic driver were also observed in the 1% populations. These results suggest that release of *Ae. aegypti* males carrying a strong meiotic driver into drive sensitive populations can be an effective tool for population replacement, and provide a foundation for additional studies including both experimental populations and simulations by mathematical modeling.

INTRODUCTION

Mosquito-borne disease control has¹ relied heavily on the use of chemical insecticides to eradicate mosquito populations. However, this resulted in strong selection pressure for insecticide resistance. Rapid emergence and dissemination of resistant insects encouraged the consideration of genetic control strategies, such as the sterile insect technique.^{1–4} Conventional genetic control strategies are based on the massive release of genetically modified insects to introduce sterility in natural populations. A major drawback in these strategies was reduced fitness of released insects compared with natural populations.^{5–8} Large-scale releases of reproductively less competitive insects were prone to be lost in natural populations because of their failure in mating competition with native populations as well as immigrants. Consequently, population replacement strategies using genetic manipulation techniques have been proposed as a promising substitute for conventional genetic control strategies.^{9–11} Under this concept, instead of sterility induction and population eradication, mosquito populations are manipulated to carry anti-pathogen effector genes, which results in non-competent mosquitoes, thereby preventing disease transmission. Because genetic manipulation usually carries a large fitness cost,^{12–14} the effector gene will need to be coupled with a strong gene drive system to rapidly sweep it into natural populations.¹⁵ Gene drive systems are genetic cheaters that violate independent segregation, which favors their propagation in naive populations and, therefore, have a strong potential to facilitate population replacement.

Meiotic drive, an example of a common gene drive system, subverts meiosis in favor of a particular gamete, and has been reported in a wide variety of organisms including, plants, fungi, insects, and mammals.^{16,17} During meiosis, the meiotic

driver product blocks maturation of gametes bearing a sensitive responder locus. The driver gene and responder locus are located on opposite members of homologous chromosomes, respectively. Because driver-carrying chromosomes selectively destroy their homolog, they have the potential for increasing in frequency in natural populations despite possible deleterious effects on fitness. The best characterized meiotic drive system is Segregation Distorter (*SD*), discovered in 1956 in *Drosophila melanogaster*.¹⁸ The major components of *SD* are the driver gene (*Sd*), an enhancer (*E(SD)*), and the responder (*rsp*). These reflect strong linkage disequilibrium due to suppression of recombination across the pericentromeric region of chromosome 2, near the eye color genes *bw* and *cn*.¹⁹ During spermatogenesis, the *Sd* gene causes a failure in chromatin condensation of sensitive responder-bearing chromosomes. Thus, the phenotype of the driver can be detected by biased eye color ratios among the progeny.

The existence of an endogenous meiotic drive system has been reported in two mosquito species, *Aedes aegypti* and *Culex pipiens*.^{20,21} Meiotic drive in these mosquitoes is tightly linked to the sex determining locus on chromosome 1 and, therefore, it is a sex linked meiotic drive system rather than an autosomal one as in *D. melanogaster*. The driver gene (*D*) of *Ae. aegypti* is tightly linked to the male determining allele (*M*), and the responder locus is tightly linked to the female determining allele (*m*) on the homologous chromosome. Neither the driver gene linked to a female determining allele nor the responder linked to the male determining allele function properly to produce the drive phenotype.²² In males heterozygous for the driver (M^D) and a sensitive responder (m^s), the products of the M^D gene cause fragmentation of m^s -bearing gametes during spermatogenesis. Therefore, the observed phenotype of the meiotic drive system in *Ae. aegypti* is a highly male-biased sex ratio.

Introducing strong driver males into a sensitive mosquito population has been proposed as a mechanism to reduce population size. However, the use of meiotic drivers to suppress *Ae. aegypti* populations has been investigated with labo-

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ratory cage studies with limited success. Hickey and Craig observed quick reversion of the sex ratio after introducing driving males into sensitive female cage populations.²³ After reversion of distorted sex ratio, driver alleles were still present and active in the population. They suggested accumulation of a suppressor reducing the sensitivity of the responder, which was identified as the *tolerance* gene on chromosome 1 by Wood and Ouda.²⁴ Therefore, the meiotic drive gene may impart strong selective pressure for driver suppressors, thereby desensitizing females to meiotic drive. For a successful application of the M^D system, two alternative ways of using the mosquito meiotic drive system were suggested and tested successfully. Wood and others tested population replacement potential in the M^D system using an eye color marker gene.²⁵ Curtis and others²⁶ and Suguna and others²⁷ combined the meiotic drive system with the double translocation homozygote technique and tested for population suppression potential. Although both cases were successful in cage experiments, there were no field trials. These studies showed that M^D has a strong potential for population replacement and suppression in spite of its strong negative selection potential against drive sensitivity.

Release of an *Ae. aegypti* strain carrying a strong meiotic driver and an insensitive responder ($M^D m^i$) into a sensitive population should have strong selection potential for both the driving chromosome and its insensitive homolog. The potential use of the M^D system for population replacement could include strategies that couple a desired transgene with either a drive insensitive m^i allele or with the M^D gene itself.²⁸ In this study, we investigated the population replacement potential of the M^D system in laboratory cage populations. We used the *Ae. aegypti* T37 strain that carries a strong meiotic driver and insensitive responder, and the drive-sensitive RED strain to maintain three population types.^{23,28,29} The first population type consisted of 100% driving males and 100% sensitive females, and the second and third population types were initiated with 10% and 1% driver males, respectively. With the latter two populations, we subsequently added 10% and 1% driver males to them every other generation. We also selected one strain diagnostic restriction fragment length polymorphism (RFLP) marker on each chromosome, including one marker on chromosome 1 that is tightly linked to the M^D system as a proxy for examining replacement potential. Our results suggest that the strong negative selection potential of the M^D gene can be used as a strong population replacement strategy.

MATERIALS AND METHODS

Cage populations: initiation and maintenance. Mosquitoes were reared in an environmental chamber at a temperature of 26°C, a relative humidity of 84%, and 16-hour light/8-hour dark cycles with a 1-hour crepuscular period at the beginning and end of each light cycle in large mesh cages (volume = 15,390 cm³). Larvae were reared on a bovine liver powder suspension. Adults were maintained on a 5% sugar solution. Adult female mosquitoes were blood fed on anesthetized rats. Our protocol for maintenance and care of experimental animals was reviewed and approved by the Institutional Animal Care and Use Committee at the University of Notre Dame. Animals are maintained and cared for in the Freimann Life Science Center, an Association for Assessment and Accredi-

tation of Laboratory Animal Care International (Rockville, MD)-accredited facility. Two *Ae. aegypti* genetic stocks were used for this experiment: 1) the T37 strain that carries a strong M^D gene and is largely fixed for an insensitive m^i allele, and 2) the RED strain that was previously shown to be highly sensitive to meiotic drive.^{23,28,29}

The effect of the M^D gene on *A. aegypti* population dynamics was evaluated across three experimental population types designed to examine the effects of the meiotic driver on sex ratio distortion and allele replacement potential, and maintained until the F_{15} generation. We established three experimental population types that were initiated with 100% (500), 10% (50), and 1% (5) male mosquitoes carrying a strong meiotic driver ($M^D m^i$: T37 strain) and 500 sensitive females ($m^s m^s$: RED strain). Thus, the 10% cages and 1% cages were initiated with 10% and 1% driving males and 90% (450) and 99% (495) non-driving males ($M^d m^s$: RED strain), respectively. At every even numbered generation (F_2 , F_4 , F_6 ,... F_{14}), we added 10% (50) and 1% (5) T37 males to the 10% and 1% cage populations respectively, which simulates repeated introductions of a meiotic driver into natural populations. Each population type was replicated three times. At each generation, 1,000–1,500 eggs per cage were hatched to determine sex ratios and initiate the next generation. Observed sex ratios were tested for a 1:1 sex ratio using chi-square analysis.

Genotyping and allele frequencies. One strain diagnostic RFLP marker was identified on each chromosome to track the change of allele frequencies associated with the meiotic drive system using our standard Southern blotting procedures.^{30,31} An RFLP marker closely linked to the sex determining locus on chromosome 1 was identified as a proxy to track the M^D and m^i alleles, respectively. Bulked genomic DNA mixtures from 30 mosquitoes from each strain were digested with *EcoRI* at 37°C for three hours, separated by electrophoresis on a 0.9% agarose gel, and transferred onto Hybond N⁺ filters (Amersham Biosciences, Piscataway, NJ). Radiolabeled probe was synthesized using α -P³² dCTP and polymerase chain reaction amplicons of previously mapped RFLP markers as templates.³⁰ The RFLP markers, which showed no common alleles between the two strains, were selected and used for genotyping the cage populations over multiple generations.

We extracted genomic DNA from 72 males and 72 females per cage for selected generations. Genomic DNA extractions were digested with *EcoRI* at 37°C for two hours, separated by electrophoresis on a 0.9% agarose gel, and transferred onto Hybond N⁺ filters. We genotyped and calculated allele frequencies using strain diagnostic RFLP markers as radio labeled probes up to the F_{15} generation using our standard protocol.³¹ To test for the effect and frequency of the *tolerance* gene, which is known to be linked to the *red-eye* locus, we also determined the eye color of 200 F_{15} males from the 100% cage populations.²⁴

RESULTS

Influence of initial meiotic drive gene frequencies on observed sex ratios. The changes in the observed male frequencies in each cage population are shown in Table 1. The P values for the chi-square test for an expected 1:1 sex ratio are

TABLE 1
Observed sex ratios in *Aedes aegypti* shown as percent males with 1:1 chi-square test in each cage*

	100%			10%			1%		
	1†	2	3	1	2	3	1	2	3
F ₁	57.1 175 (0.059)	54.5 304 (0.073)	55.9 374 (0.023)	52.3 275 (0.433)	50.5 440 (0.849)	48.2 274 (0.546)	51.6 243 (0.653)	57.4 385 (0.004)	51.3 300 (0.644)
F ₂	83.7 367 (0)	85.5 449 (0)	85.3 421 (0)	61.3 388 (0)	53.4 382 (0.183)	54 491 (0.078)	54.7 234 (0.150)	55.1 396 (0.044)	51.4 514 (0.537)
F ₃	80.8 672 (0)	75.2 274 (0)	72.4 359 (0)	67.1 705 (0)	61.1 257 (0)	58.6 515 (0)	54.7 757 (0)	51.1 624 (0.575)	47.8 609 (0.274)
F ₄	79.7 390 (0)	75.3 384 (0)	76.4 522 (0)	74.9 487 (0)	75.5 257 (0)	62.4 338 (0)	55.4 312 (0.054)	50.0 324 (1.000)	52.9 522 (0.189)
F ₅	72.7 297 (0)	73.7 506 (0)	66.6 305 (0)	69.6 385 (0)	78.7 413 (0)	63.9 441 (0)	58.7 339 (0.001)	53 713 (0.107)	51.1 278 (0.719)
F ₆	74.1 791 (0)	73.3 749 (0)	73.5 490 (0)	76.5 391 (0)	79.2 562 (0)	69.7 458 (0)	64.3 610 (0)	56.8 315 (0.015)	54.2 826 (0.015)
F ₇	72.3 282 (0)	66.4 430 (0)	75.8 447 (0)	72.2 496 (0)	73.1 424 (0)	70.3 367 (0)	65.5 611 (0)	48.1 547 (0.369)	52.1 445 (0.367)
F ₈	75.0 507 (0)	77.7 426 (0)	70.2 410 (0)	69.1 301 (0)	77.4 421 (0)	68.3 369 (0)	60.5 443 (0)	48.6 397 (0.581)	57.6 342 (0.005)
F ₉	70.9 589 (0)	71.1 589 (0)	63.7 588 (0)	71.1 446 (0)	76.4 449 (0)	68.4 450 (0)	75.7 614 (0)	48.8 613 (0.545)	58 612 (0)
F ₁₀	66.7 454 (0)	70.0 760 (0)	61.0 983 (0)	71.9 270 (0)	74.7 989 (0)	72.6 846 (0)	70.8 439 (0)	49.4 796 (0.723)	57.8 806 (0)
F ₁₁	71.9 793 (0)	70.8 730 (0)	60.9 744 (0)	76.8 790 (0)	74.1 1,098 (0)	70.5 555 (0)	70.5 773 (0)	48.1 726 (0.299)	56.6 458 (0.005)
F ₁₂	67.9 1,117 (0)	67.7 878 (0)	57.7 605 (0)	74.5 640 (0)	71.6 879 (0)	72.1 1,331 (0)	71.6 756 (0)	52.1 1,061 (0.167)	58.9 1,471 (0)
F ₁₃	66.7 729 (0)	60.1 401 (0)	59.1 629 (0)	74.3 778 (0)	66.6 740 (0)	70.0 714 (0)	66.6 668 (0)	51.7 603 (0.92)	64.0 738 (0)
F ₁₄	65.8 1,234 (0)	61.3 675 (0)	55.0 707 (0.008)	67.2 1,358 (0)	66.4 1,261 (0)	61.1 700 (0)	64.0 1,269 (0)	54.4 1,095 (0.003)	65.5 733 (0)
F ₁₅	60.4 1,594 (0)	61.9 1,283 (0)	61.3 1,011 (0)	67.5 1,363 (0)	68.0 900 (0)	64.2 491 (0)	66.0 1,009 (0)	57.2 881 (0)	72.8 624 (0)

* Values are sex ratio in **bold**, sample size (*P* value of 1:1 chi-square test). *P* values < 0.01 are shown in **bold**.

† Replication number.

indicated in parentheses. Mean sex ratios for the three replications were calculated and are shown in Figure 1 with standard deviations (error bars).

100% cage populations. The 100% T37 male cage populations showed slightly male-biased sex ratio at the F₁ generation, then reached the highest peak at the F₂ generation with 84.8 ± 0.97% (mean ± SD) males. Thereafter, with minor

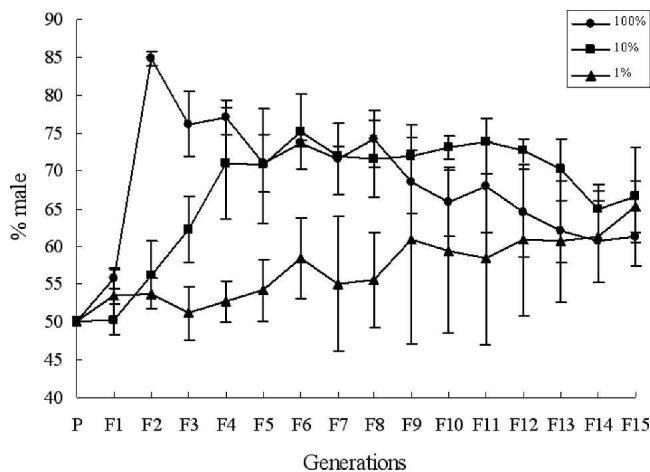


FIGURE 1. Changes in observed male frequencies in each cage population. The mean sex ratios for three replications were calculated and plotted as percent males with standard deviations (error bars).

fluctuations, the male-biased sex ratios of the 100% cage populations gradually decreased to 62 ± 0.75% at the F₁₅ generation. At the F₁₅ generation, the frequency of the red-eye phenotype among males was 0.025. Assuming Hardy-Weinberg equilibrium, the red-eye allele frequency was 0.158 (square root (0.025)), which represents a 3.16-fold reduction compared with the initial red-eye allele frequency of 0.5.

10% cage populations. The 10% T37 male cage populations showed a consistent increase in male frequencies until peaking at 75.13 ± 4.9% at the F₆ generation. Male frequencies remained at fairly constant levels from the F₇ to F₁₃ generations, then decreased to less than 70% males after the F₁₃ generation.

1% cage populations. The 1% cage populations remained relatively constant at approximately 54% males until the F₅ generation. However, beginning about the F₆ generation, male frequencies slowly but constantly increased, and exceeded 65% by the F₁₅ generation.

Effect of M^D and mⁱ on RFLP allele frequencies. Selected strain-diagnostic RFLP markers were LF284 (chromosome 1), LF355 (chromosome 2), also known as *RpL17A*, and LF323 (chromosome 3) (Figure 2). LF284 is tightly linked with the sex determining locus, and the other two markers are autosomal. Therefore, the frequency of the T37-LF284 allele in the male population is highly correlated with frequency of M^D and mⁱ, respectively, while in the female population, the T37-LF284 allele represents the mⁱ allele frequency. The RED-LF284 allele in the male population is highly correlated with frequency of M^d and m^s, and the RED-LF284 allele in

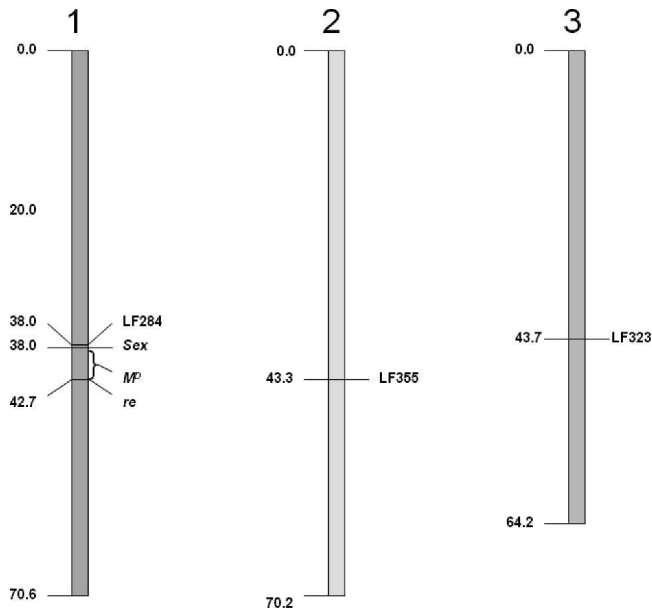


FIGURE 2. Strain-diagnostic restriction fragment length polymorphism markers on each chromosome: LF284 on chromosome 1, LF355 on chromosome 2, and LF323 on chromosome 3. Map distances are indicated in Kosambi centiMorgans (cM).³⁰ M^D is located between *sex* and *re* (*red-eye*), as indicated by the bracket on chromosome 1.²⁴

the female population represents the m^s allele frequency, respectively. The observed changes in allele frequencies for each marker in each cage are shown in Figure 3.

100% cage populations. In the 100% cage populations, the T37-LF284 allele frequencies of male populations consistently increased, while the T37 allele frequencies at the chromosome 2 and chromosome 3 markers consistently decreased (Figure 3A). After the F_{10} generation, the T37-LF284 allele frequencies remained at approximately 0.8. Female populations showed similar patterns as the male populations, although the T37-LF284 allele frequencies were lower than observed in the males and decreased slightly at the F_{14} and F_{15} generations (Figure 3B).

10% cage populations. In the 10% cage populations, the T37-LF284 allele frequencies increased in both male and female populations (Figure 3C and D). However, the male population showed a quicker change and attained much higher frequencies than female populations. The T37-LF355 and T37-LF323 allele frequencies gradually increased in the early generations, and fluctuated between 0.2 and 0.3 after the F_6 generation in both male and female populations.

1% cage populations. The 1% cage populations showed similar patterns of changes in T37-LF284 allele frequencies to the 10% cage populations, although at reduced levels comparatively (Figure 3E and F). The T37-LF284 allele frequencies increased from 0.01 at the F_1 to 0.34 at the F_{15} generations in the male populations. The T37-LF284 allele frequencies increased in female populations but at lower levels than observed in male populations. The T37-LF355 and T37-LF323 allele frequencies increased slightly, but remained at frequencies less than 0.1 in both male and female populations across all generations.

Impact of M^D and m^i in cage populations. The impact of a meiotic driver on the observed sex ratio at each generation is

determined by the frequency of driving males ($M^D m^s$) in the previous generation. Furthermore, the $M^D m^s$ frequency at each generation is determined by the allele frequency of the sensitive responder (m^s) in female populations of the previous generation. Therefore, the extent of a male biased sex ratio at each generation is highly correlated with the allele frequency of sensitive responders in the population of its grandmother generation (Figure 4). This indicates that increased m^i allele frequencies in the 100% cages are responsible for the reduction in male frequencies at later generations.

To examine the population replacement potential of the *Ae. aegypti* meiotic drive system, changes in allele frequencies at the whole population level are shown in Figure 5. The consistent increase in T37-LF284 allele frequencies in all cage populations indicates that the meiotic drive system has strong population replacement potential (Figure 5A), which is clearly not observed with T37-specific alleles at chromosome 2 and chromosome 3 markers (Figure 5B and C).

DISCUSSION

In this study, we investigated the potential utility of an endogenous meiotic drive system in *Ae. aegypti* as a mechanism for moving effector genes of interest into natural populations. Because driver alleles have strong selection potential against sensitive responders, if insensitive responder alleles are introduced with strong driver alleles into sensitive populations, the driver alleles should effectively replace sensitive responders with insensitive responder alleles in these populations.

In our 100% cage populations, after mating T37 males with RED females, all F_1 males and females were heterozygotes with genotypes $M^D m^s$ and $m^i m^s$, respectively. The products of the M^D allele in the F_1 males acted on the sensitive responder, and therefore, the F_2 generation showed maximum maleness. After peaking at the F_2 generation ($84.8 \pm 0.99\%$), male frequencies decreased gradually to $61.2 \pm 0.72\%$ at the F_{15} generation. Both males and females in the 100% cage populations showed quick increases in T37-LF284 allele frequencies, which represents the increase of m^i allele frequencies. The decrease in male frequencies is highly proportional to the increase of m^i allele frequencies. That is, m^i replaced m^s at the later generations, and the male-biased sex ratios gradually reverted back to approximately 1:1.

Previously, Wood and Ouda reported quick selection of *tolerance* genes originating from the RED strain under driving conditions.²⁴ The *tolerance* gene is linked to the *red-eye* locus on chromosome 1 and suppresses responder sensitivity to a driver. Although the maximum distortion of the male frequency at the F_2 generation ($84.8 \pm 0.99\%$) was reduced to $61.2 \pm 0.72\%$ at the F_{15} generation, strong selection of *tolerance* genes linked to the *red-eye* locus was not observed in the 100% cages. This implies that the insensitive responder originating from T37 males may have higher fitness than the *tolerance* gene originating from the sensitive RED strain under driving conditions in 100% cage populations or that the *tolerance* gene is no longer segregating in our RED strain. Increased frequencies of the insensitive responder, which was absent in the cage populations of Wood and Ouda, at the later generations in the female populations of the 100% cages

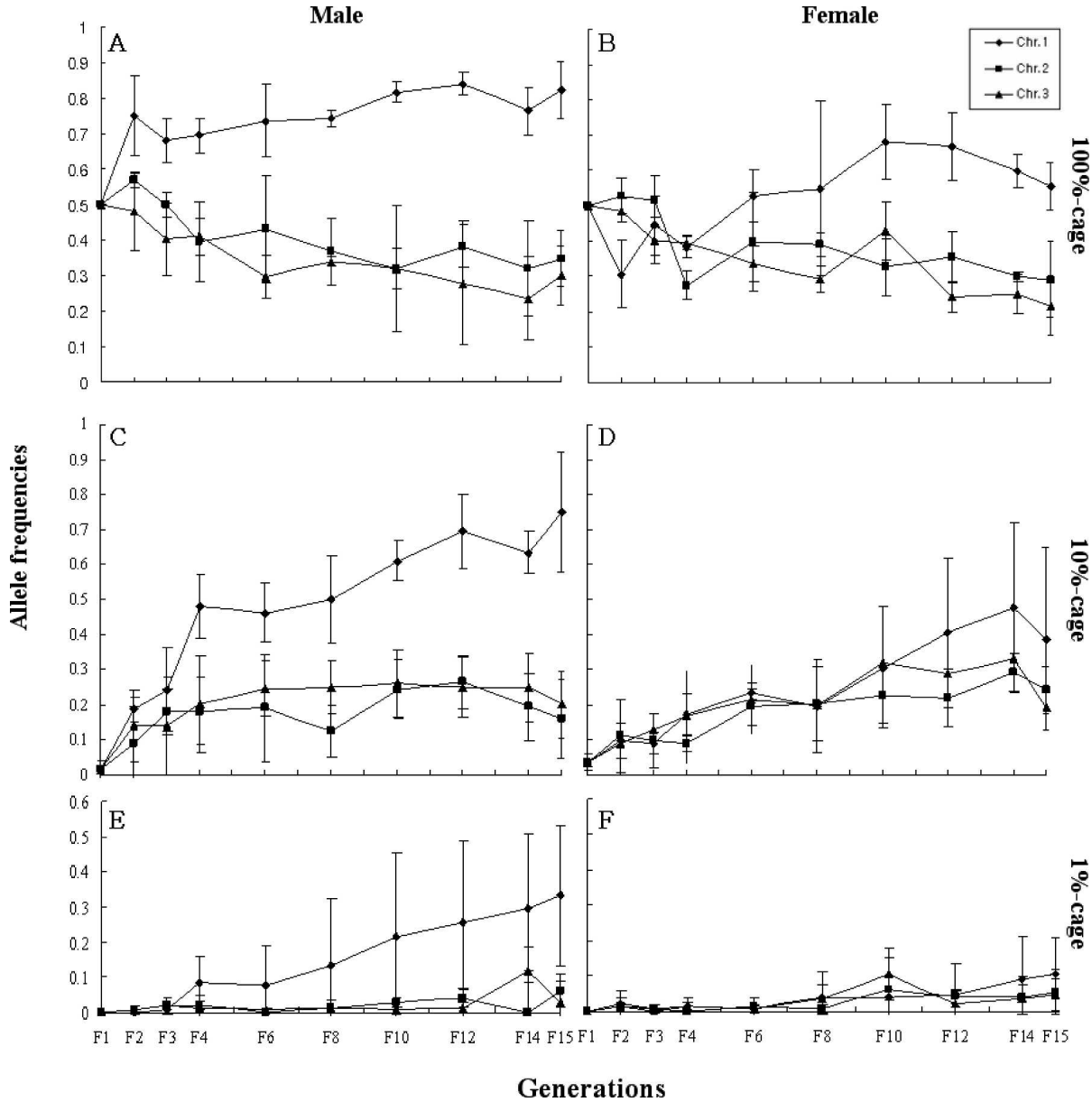


FIGURE 3. Changes in T37-specific allele frequencies for each chromosome (chr). **A**, **C**, and **E**, male population. **B**, **D**, and **F**, female population. **A** and **B**, 100% cage. **C** and **D**, 10% cage. **E** and **F**, 1% cage. Error bars show the standard deviation.

probably served as the primary reason for reversion of the male biased sex ratio back to 1:1 under driving conditions. However, the T37-LF284 frequencies in female populations decreased after the F₁₂ generation in the 100% cages. The observed decrease may be due to random sampling variance or recombination between the responder locus and our diagnostic RFLP marker. Although unlikely, it may be due to selection for driver suppressors as Wood and Ouda suggested.²⁴

Repeated introduction of 50 $M^D m^i$ males at every even numbered generation greatly influenced the increase of T37-LF284 allele frequency in the 10% cage populations. Although our 10% cage populations were initiated with only 10% $M^D m^i$ males, the allele frequency of T37-LF284 quickly increased in both male and female populations (Figure 3C and D), which implies quick increases of both M^D and m^i in

the populations. However, the increase of T37-LF284 allele frequencies were greater in males than in female populations. The M^D alleles quickly spread in sensitive populations due to the higher male-biased segregation ratios than observed with normal male determining alleles. As the frequencies of the M^D allele increases in the 10% cage populations, m^i alleles have strong selection potential. Conversely, m^i alleles do not have strong selection potential under low driver frequencies. In addition, after the F₆ generation obvious increases in the T37-LF284 allele frequency are evident in the 1% cage populations, which were supplemented with only five $M^D m^i$ males at every even numbered generation (Figure 3E and F). Of note are the obvious increases in the T37-LF284 alleles among females.

Our results suggest that under the influence of a strong meiotic driver, the alleles linked with the m^i allele on chro-

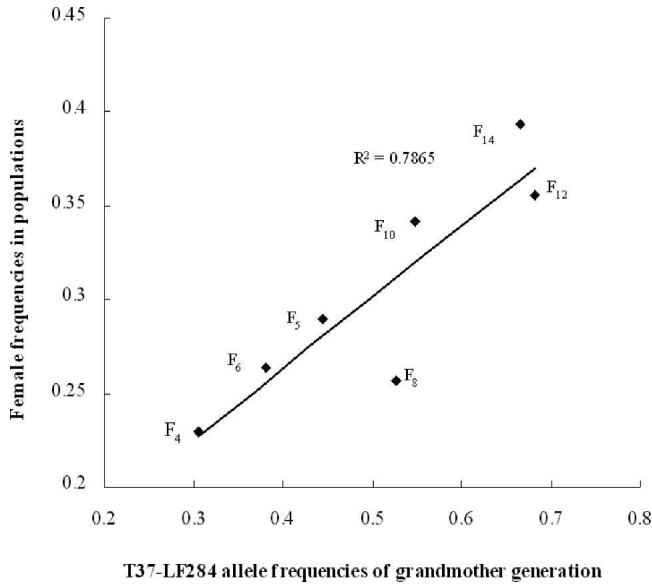


FIGURE 4. Relationship between the T37-LF284 allele frequency in the grandmother generation and the observed frequency in their granddaughter generation.

mosome 1 are effectively replacing those linked with the m^s allele. Although introducing $M^D m^i$ males into sensitive populations has proven unsuccessful as a tool for population suppression due to the strong selection potential of M^D for m^i alleles, genes linked to M^D and m^i would have strong popu-

lation replacement potential. The distribution of the meiotic driver in *Ae. aegypti* populations does not appear to be worldwide,³² which may imply a short evolutionary history. This suggests that release of $M^D m^i$ males into sensitive populations can be an effective tool for population replacement. However, Wood reported between family variation in sex ratios within the Trinidad-derived *Ae. aegypti* T-30 strain and suggested that there were at least six different alleles at the responder locus with varying sensitivities to the driver.³³ Clearly, a better understanding of the complexities of interactions among the drive system components is needed. Our present study provides important empiric data that will facilitate additional studies, including experimental population studies and simulations by mathematical modeling.

Mori and others suggested two strategies for using the M^D system for introducing novel genes into natural populations.²⁸ One strategy would be to insert a desired transgene adjacent to or within an m^i allele on chromosome 1, and then use selection by a strong driver to increase the transgene frequency in naive, drive-sensitive populations. The second strategy would be to couple the transgene with a strong driver gene, and then insert this construct into an autosome. Release of males carrying the driver/transgene construct and homozygous for m^i alleles would result in selection for both, thereby effecting population replacement with the transgene. Therefore, meiotic drive seems particularly advantageous because it represents a relatively stable system that has the potential to be linked with effector genes that influence vector competence by transgenic insect techniques without significant risk for horizontal transfer in natural populations.¹⁷

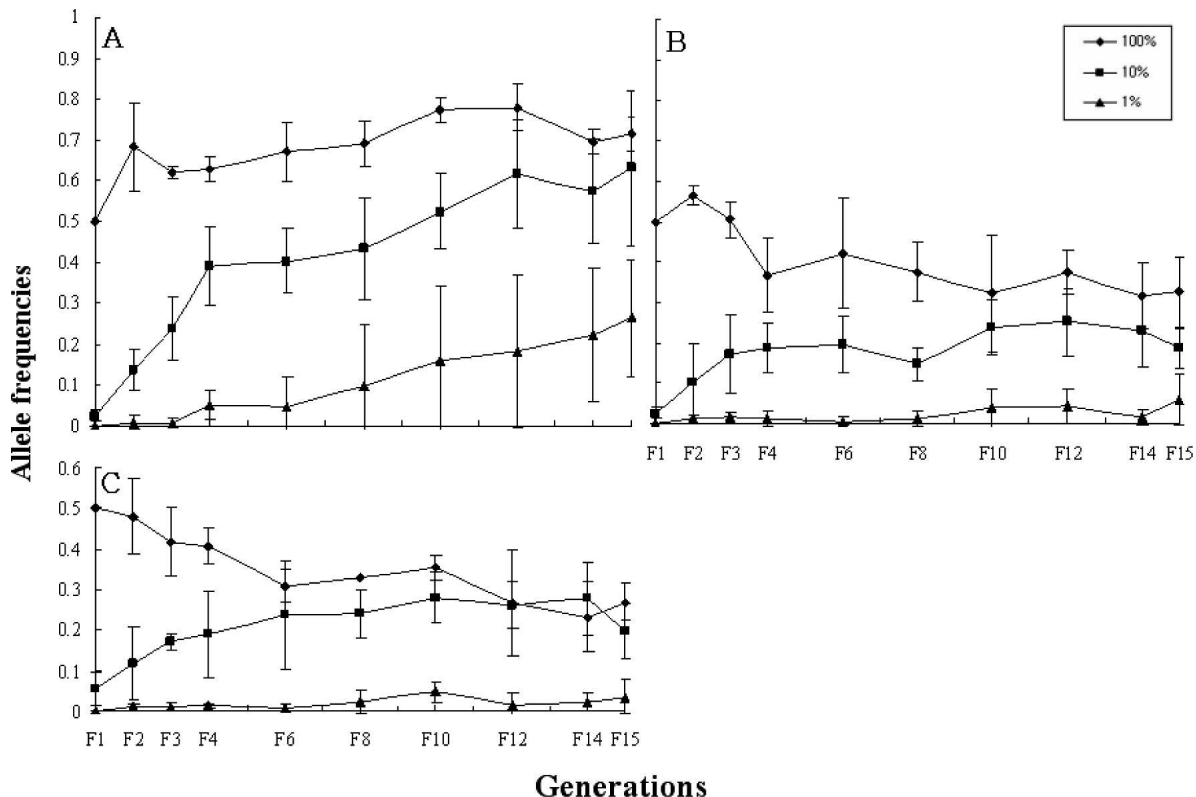


Figure 5. Changes in T37-specific allele frequencies for each chromosome at the whole population level. **A**, LF284; **B**, LF355; **C**, LF323. Error bars show the standard deviation.

Aedes aegypti is the primary vector for the yellow fever and dengue fever viruses. Efforts to test the utility of meiotic drive as a novel vector control strategy will require the molecular characterization of the M^D system. The segregation distorter (*SD*) system in *D. melanogaster* is the best characterized meiotic driver.³⁴ The *SD* gene has been determined to be the result of a 3'-truncated tandem duplication of the *RanGAP* (*Ran* GTPase activation protein) gene.³⁵ Kusano and others reported that the mislocalization of *RanGAP* was responsible for the meiotic drive phenotype.³⁴ However, additional studies are needed to test whether expression of truncated *RanGAP* will result in meiotic drive in *Ae. aegypti*. Alternatively, other genes involved in the *Ran* signaling pathway could be considered as candidates for M^D .³⁶

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