# Save Our Sons: Exploring RNAi-mediated Intragenomic Conflict in D. sim through Genetic Assays and Testis Cytology 

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Intragenomic conflict occurs when selfish genes attempt to increase their own prospects of replication at the expense of the organism. It has clinical and ecological significance-the genes and pathways involved are often co-opted by lineages of cancer cells, and intragenomic conflict itself can have impacts on genome evolution, sex determination, and speciation. One of the most studied cases of intragenomic conflict is the Durham and Winters sex-ratio (SR) meiotic drive systems in D. simulans (D. sim). Both systems consist of distorter and repressor elements that bias and restore equal transmission of $X$ and $Y$ sperm, respectively. However, mechanisms of SR meiotic drive systems are still poorly understood, and there exist little genetic evidence of the active outputs of the distorters MDox and Dox and repressors Tmy and Nmy. This study elucidates genetic evidence for the SR-distorting activities of Dox and MDox through genetic sex-ratio assays of null and natural mutants. An examination of the interactions between Dox and MDox also showed that the distortive activities of the Winters and Durham systems may overlap and have synergistic effects. Moreover, through immunostaining and testis cytology assays, it was found that the etiology of Dox and MDox-induced SR bias lie in abnormal spermiogenesis. Altogether, the data from the study demonstrates an unanticipated complexity of intragenomic conflict pathways in D. sim, provides evidence that continuous cycles of sex ratio distortion and suppression mediate balanced sex ratio, and discusses the first case of two intragenomic conflict systems that present synergistic interactions.

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