Letters to the Editor

Is *Stellate* a Relict Meiotic Driver?

XO males of *Drosophila melanogaster* are sterile. Associated with this sterility is the presence of crystals in the sperm. Crystal production is determined by the *Stellate* (*Ste*) locus which maps to position 45.7 on the *X* chromosome (HARDY *et al.* 1984). Expression of stellate is repressed in normal males by *Suppressor of Stellate Su(Ste)* on the *Y* chromosome just proximal to the fertility factor *kl-2* (LIVAK 1984, 1990). In *D. simulans* and *D. mauritiana* the *Stellate* sequence has been identified on the *Y* chromosome whereas in *D. erecta*, *D. teissieri* and *D. yakuba* it is not found at all. This is taken as an indication that the gene is possibly not necessary for normal spermatogenesis (LIVAK 1990). How could a gene which is possibly not required for spermatogenesis, and which can render the host sterile unless suppressed ever have evolved? Below I attempt to answer this question by proposing that *Stellate* was originally a meiotic drive gene.

Consider a Drosophilid with "normal" meiosis in the male. The meiotic process involves accurate packing and winding of DNA. Consider now a mutant gene on the *X* which interferes with DNA packing in such a manner that the *Y* chromosome is more profoundly affected than the *X*. This might be simply due to the fact that the large *Y* has more DNA or heterochromatin requiring packing than the *X* or because the *Y* has more sites of interaction with the mutant protein. In consequence the gene will be present in more than 50% of the viable sperm. So long as the fertility of this fly is not reduced too dramatically this gene can invade. In contrast, a comparable gene on the *Y* would not be successful. Formally the gene is a *X vs. Y* meiotic driver. Interference with the packing of heterochromatin is believed to underlie the mechanism of drive in the *Segregation Distorter* system in Drosophila (WU 1991).

As the driver invades so it imposes a cost in both reducing male fertility and biasing the sex ratio. Thus a suppressor of this condition on the *Y* chromosome can also invade and go to a stable equilibrium (HURST and POMIANKOWSKI 1991). If this suppressor acts in a dose dependent fashion then a duplication of the driver locus can once again act as a driver by evading suppression. This driver can in turn however be suppressed by an increase in the copy number of the suppressor and so on. At an equilibrium if there is a cost to attempting to drive then a deletion of some of the copies of the driver can also be selected for. Hence the copy number of the driver can be selected to go both up and down.

Depending on the copy number of the driver, complete removal of the *Y* suppressors will have a drastic effect on meiosis. If the drivers were in high copy number the meiotic process will be saturated with proteins interfering with DNA packing and hence the whole process is likely to break down. Saturation of chromosomes with driver products has been implicated in the sterility of mice homologous for driving *t* alleles (LYON 1991). If driver copy number is low the gametes with more DNA/heterochromatin are more likely to be disrupted hence a biased recovery of meiotic products with fewer chromosomes is to be expected.

I contest that in the above model *Ste* can be understood as the driver and *Su(Ste)* the *Y* chromosome suppressor. The *Stellate* locus contains a repeated gene whose transcription is known only in the testes. Copy number of the repeat varies among strains, up to about 200 in the Oregon R strain. Low copy number corresponds to the Ste^{+} allele which in the $Ste^{+}/0$ condition is associated with the production of needle like crystals and meiotic disturbance associated with preferential recovery of the gametes with fewer chromosomes (HARDY *et al.* 1984). In contrast high copy number *Ste* in the *Ste/0* configuration is associated with the star form of the crystals and sterility.

The predicted *Stellate* protein is homologous to the β subunit of casein kinase II of Drosophila and cow (LIVAK 1990). The α unit of this protein is known to be implicated in the phosphorylation of DNA topoisomerase II in Drosophila Kc cells (ACKERMAN, GLOVER and OSHEROFF 1988), a protein known to be involved in DNA packing and organization. The β subunit is believed to have a regulatory role (TAKIO *et al.* 1987). It is not unreasonable to suppose that involvement of DNA topoisomerase alterations might also be implicated in the *Segregation Distorter* meiotic drive system.

The mechanism by which *Su(Ste)* inhibits the production of *Ste* product is unknown. LIVAK (1990) has proposed that *Su(Ste)* and *Ste* genes might compete for transcription at a limited number of sites at a transcription complex centre with *Su(Ste)* gaining preference. DANILEVSKAYA *et al.* (1991) have proposed that the competitive interaction might be mediated through sense/antisense RNA binding. *Su(Ste)* is known to be homologous to *Ste*. It is also known that

Su(Ste) hinders the correct splicing of *Ste* mRNA and competition for some splicing factor might also explain the mechanism of inhibition assuming unspliced *Ste* mRNA was unstable (LIVAK 1990). Whatever the mechanism, in *XO* testes the *Ste* mRNA has no competition and hence is translated.

The hypothesis that *Ste* is a relict driver can be tested by deleting a number of copies of *Su(Ste)* but without removing the *Y* chromosome. Removal of an excess number of *Su(Ste)* will result in meiotic disturbance of the type described for *XO* individuals. Removal of too few copies will probably have no effect. However at some position between these two the model presented here predicts that drive should be seen. Without knowing the mechanism and dynamics of the functioning of *Su(Ste)* it is impossible to predict at what copy number drive is to be expected. An initial experiment of this variety has been performed (LYCKEGAARD and CLARK 1989). Using two different *X* chromosomes of unknown *Ste* copy number the authors found a three fold difference in copy number of *Su(Ste)* on the 34 different *Y* chromosomes. They did not, however, find any correlation between copy number and segregation effects. This however neither proves nor disproves the hypothesis that *Ste* is a relict meiotic driver as the experiments never went through the threshold copy number of *Su(Ste)* which is known to result in meiotic disturbance.

If *Ste* is indeed a driver suppressed by *Su(Ste)* then the observed sterility of *Ste/0* males has significant bearing on recent theories of unisexual hybrid sterility. FRANK (1991) and HURST and POMIANKOWSKI (1991) have independently conjectured that the sterility of the heterogametic sex in the F_1 of a species cross might be the result of an imbalance between diverged drivers and suppressors. The sterility of *Ste/0* conforms to the pattern which FRANK (1991) and HURST AND POMIANKOWSKI (1991) propose and demonstrates the validity of the notion that an unrepressed driver might result in sterility rather than drive. This lends support to the conclusion that Haldane's rule is brought about by meiotic drivers (FRANK 1991, HURST and POMIANKOWSKI 1991). What would happen in the reciprocal cross is unknown as the effect of an excess of *Su(Ste)* mRNA is unknown.

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