Letter to the Editor

Further Evidence Consistent With Stellate's Involvement in Meiotic Drive

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STELLATE is an X-linked multicopy gene found in Drosophila melanogaster and is one of the most bizarre gene arrays yet described (for details see HARDY et al. 1984; LIVAK 1984, 1990; DANILEVSKAYA et al. 1991; BALAKIREVA et al. 1992; SHEVELYOV 1992; PALUMBO et al. 1994). The activity of Stellate is restricted to spermatogenesis. However, the transcription and translation of Stellate is inhibited in most males by a Y-linked multicopy gene, Suppressor of Stellate (Su(Ste)) alias crystal (cry). If Stellate is not suppressed, then the protein product (homologous to the beta subunit of casein kinase 11) is produced at levels dependent upon the copy number of Stellate. If Stellate copy number is relatively low, then linear crystals form and the males are of reduced, but nonzero, fertility. In high copy number (up to 200), however, the protein forms a star-shaped crystal in sperm, and the males are typically sterile. An understanding of this system is hence potentially of importance for the study of both intra- and inter-specific sterility and hence of HARDANE'S Rule.

In D. simulans and D. mauritiana a Stellate-like sequence has been identified on the Y chromosome, whereas in D. erecta, D. tessieri 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). This latter possibility has yet to be proven, however, as, despite extensive effort (PALUMBO et al. 1994), an X chromosome without Stellate has yet to be generated.

How could a gene array that is possibly not necessary for spermatogenesis, but that causes sterility unless suppressed, have evolved? I presented an hypothesis for the evolution of this system that proposed that Stellate is an X vs. Y meiotic drive gene (HURST 1992). The model supposed that an X chromosome with one or a few copies of Stellate would invade a population (initially lacking Su(Ste)) through its ability to drive, i.e., by interfering with the Y-bearing sperm so as to ensure that more than 50% of the progeny of that male have the Stellate-bearing X chromosome. The spread of this X chromosome created, it was supposed, the conditions for the spread of a Y-linked suppressor, i.e., Su(Ste). The high copy numbers of Stellate found in many flies were envisaged as the product of an “arms race” between X and Y chromosomes: invasion of a new X chromosome with yet more copies of Ste to escape the suppression by Su(Ste), would be followed by the invasion of a new Y chromosome with yet more copies of Su(Ste) to suppress the new X chromosome, which would be followed by the invasion of an X chromosome with yet more copies of Stellate, etc.

The release from suppression of the multicopy array in Su(Ste) flies would generate a level of transcription never previously witnessed in the lineage of any extant fly. The excessive over-expression of a gene whose function is the interference with meiosis would, it was suggested, cause sterility.

Since the initial presentation of this model, it has further been shown that some copies of Stellate are tightly linked to the centromere on the X chromosome (and in heterochromatin) (SHEVELYOV 1992), features typical of many meiotic drive genes (LYTLE 1991) and two locus distorters in general (HURST 1993). Further, the model predicted that Su(Ste) should have been derived after Stellate and this appears to be the case (BALAKIREVA et al. 1992).

For the model to be correct, it is necessary (but not sufficient) that, at relatively low copy number, a Stellate-bearing X chromosome should, on the average, be recovered in more than 50% of progeny when the Y chromosome lacks Su(Ste). From the recent study by Palumbo et al. (1994) it is possible to investigate this and other predictions of the model. These authors provide a detailed and elegant report of segregation data from males with few/no copies of Su(Ste), but that varied in the copy number of X-linked Stellate (PALUMBO et al. 1994).

As required by the drive model, from the data presented by PALUMBO et al. (Table 2) it can be concluded that when copy number of Stellate is low, more than 50% of sperm contain the X chromosome (rather than Y, O or XY). Meiotic drive is occurring.

This, however, as Palumbo et al. note, does not prove that Stellate is a meiotic drive gene, as a linked gene could in principle account for this segregation distortion. Indeed, it is this “linked gene” model that these
authors tentatively prefer. They are disinclined to the notion that \textit{Stellate} is the drive gene for, among other reasons, in males with a Y chromosome with no copies of Su(Ste), their measure of drive was only weakly correlated with the copy number of \textit{Stellate} and what correlation there was was negative.

Here I show that the data presented by \textsc{Palumbo et al.} is, however, consistent with the hypothesis that \textit{Stellate} is a meiotic drive gene and that the weak correlation that they found is the result of two antagonistic forces, one of which is \textit{X} vs. \textit{Y} meiotic drive. In addition, the detailed nature of \textsc{Palumbo et al.}’s analysis allows some conclusions to be drawn as to the mechanism of drive. These too are in agreement with the previously presented model (Hurst 1992).

\textsc{Palumbo et al.} use an index of drive that compounds the recovery of \textit{XY} sperm with \textit{X-only} sperm (\textit{X-only} here is a short hand for those \textit{X}-bearing sperm that are not \textit{XY}, it should not be read as an indicator that no autosomes were present). Were \textit{Stellate} a meiotic drive gene that acted to inhibit sperm containing the \textit{Y} chromosome, then this index should reveal a positive correlation with \textit{Stellate} copy number (\textit{X-only} sperm should survive better than \textit{Y-only} sperm and \textit{XY}-sperm better than \textit{Osperm}). That \textsc{Palumbo et al.} find only a weak negative correlation proves that this form of drive is not occurring.

\textit{Stellate} could, however, be a meiotic drive gene that acts to inhibit sperm containing the \textit{Y} chromosome. The model that I originally presented supposed this to be the case (Hurst 1992). It was argued that \textit{Stellate} interferes with the packing of the \textit{Y} chromosome and hence by implication that any sperm, disjunctive or nondisjunctive, with such an affected \textit{Y} chromosome would be less likely to survive. Were this the case, then a drive index that compounds recovery of \textit{X-only} and \textit{XY} sperm (\textit{e.g.,} \textit{R}_{\text{XY}} that employed by \textsc{Palumbo et al.}) would hide such an effect: although \textit{X-only} sperm would survive better than \textit{Y-sperm}, \textit{XY}-sperm would do worse than \textit{Osperm} and the two effects would more or less cancel out.

The key prediction then of the meiotic drive model that I proposed (Hurst 1992) is that the survival of \textit{X-only} sperm relative to that of \textit{Y-only} sperm, should go up with increasing copy number. The data of \textsc{Palumbo et al.} are detailed enough to allow this effect to be parti-
tioned out (Figure 1). It is found that, as the copy number of Stellate goes up, so this proportional survival of X-only sperm does indeed go up ($P < 0.05$). In addition, it is predicted that the proportional recovery of XY-bearing sperm relative to O sperm should go down as Stellate copy number goes up. This is also found ($P < 0.05$) (Figure 2). This is consistent with Stellate being an $X$ vs. $Y$ meiotic drive gene that acts to inhibit any sperm containing a $Y$ chromosome.

There are, however, at least four possible problems with the above analysis. First, autosomal genes interacting with the system have been described (J. Hackstein, personal communication). While the existence of such genes may be expected from the drive model (suppressors of $X$-linked drive need not be exclusively $Y$-linked), were there a covariance between the activity of these genes and Stellate copy number, this could act as a confounding variable of unknown effect. It could potentially explain some of the variance in the intensity of drive (Figure 1).

Second, the data do not prove that the effect is prezygotic, as is necessary for the meiotic drive model. Although the data of Palumbo et al. is interpreted as probabilities of sperm survival, it is unclear whether postzygotic effects can be eliminated. Such an effect would, however, have to be consistent with the fact that Stellate’s expression is restricted to spermatogenesis. This is not unreasonable. Stellate could perhaps interfere with a $Y$ chromosome lacking $Su(Ste)$, so as to inhibit early development of embryos with this altered chromosome. A similar effect (but on progeny sterility) has been postulated for the $Y$ chromosome of Heliothis sp. (Roehrdanz 1990) and is not so very different from the action of selfish elements such as Medea of Tribolium (Beeman et al. 1992). Note then, that if the death of such $Su(Ste)$ progeny enhances the increased fitness of surviving progeny, then Stellate may still be a selfish genetic element and, in principle, the argument for its evolution through a coevolutionary arms race with its $Y$-linked suppressor would still apply (except the precise invasion conditions and dynamics would be slightly altered).

That Drosophilids harbor male-killing cytoplasmic spiroplasmas (Williamson and PoulsOn 1979) is consistent with them having an ecology such that the death of sibs enhances the fitness of surviving progeny (Hurst 1991), although the nature of the fitness enhancement remains enigmatic (Ebbert 1995). Note also, however, that $D. melanogaster$ does not have a naturally occurring male-killer (Williamson and PoulsOn 1979).

Third, it may reasonably be argued that significance at the 5% level (Figures 1 and 2) is not thoroughly convincing. It is perhaps more convincing, however, when considering that the prediction was the opposite of what would have been expected from previous data (Hardy et al. 1984). It has been established that copy number of Stellate affects the degree of meiotic disturbance (Hardy et al. 1984). It was also noted that Stellate copy number appeared to be positively correlated with what was described as meiotic drive (Hardy et al. 1984). The definition of drive in this context was that sperm with few and small chromosomes were preferentially recovered. As the $X$ chromosome is larger than the $Y$ chromosome in $D. melanogaster$, were this the unique effect of Stellate, then one might expect an increase in the relative proportion of $Y$-bearing sperm as Stellate copy number goes up.

Fourth, and finally, a linked gene cannot be fully eliminated as the cause of the distortion. However, as is established here, this gene’s distorting potential must have to be positively correlated with Stellate copy number for it to be a candidate. In the absence of evidence of such a correlation, and assuming the effect to be prezygotic, it seems most reasonable to suppose that Stellate is a meiotic drive gene that acts by inhibiting sperm bearing a sensitive $Y$ chromosome.

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