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LETTER TO THE EDITOR

Sex bias in gene expression is not the same as dosage compensation

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Melamed *et al*. (2009) raise criticism of our recent demonstration (Mank and Ellegren, 2009) of how male and female expression levels vary along the chicken Z chromosome, a study that arrived at a slightly different conclusion when it comes to the interpretation of dosage compensation (DC) in a male hypermethylated region than that in a previous report by Melamed and Arnold (2007). In their criticism, they state 'a major issue is that the two studies differ in their view of the process of DC' and we can do nothing but agree. They judged that 'genes with low (female-biased) M:F ratios were compensated'. Clearly, this is contrary to how we think DC should be understood.

Organisms have evolved intricate regulatory mechanisms for controlling gene expression in order to reach phenotypic optima under varying environmental conditions. As a special case, gene expression differs between males and females for many genes, and this is a major explanation for how two such discrete phenotypes can be obtained from essentially the same genome (Mank, 2009a). Expression differences between sexes can be in the form of female bias or male bias. However, even if there were no intrinsic differences in gene expression between sexes, genes on the sex chromosomes would still be expected to show expression differences due to a difference in gene dose, as the homogametic sex possesses a second copy of the sex chromosome, which presents an extra target for transcriptional machinery. However, in several diverse organisms, including nematodes, flies and mammals, most sex-linked genes show similar expression levels in males and females, a phenomenon generally referred to as DC (Mank, 2009b).

Birds seem to lack a general mechanism for DC, as most sex-linked genes show higher expression levels in males (ZZ) than in females (ZW). It remains to be understood how they can cope with the overall imbalance in sex-linked gene expression. However, just as selection at individual loci across the genome has led to differences in expression levels between the sexes, there might of course also be loci on the Z chromosome at which the optimal sex-specific expression levels differ from the levels given by the absence of chromosome-wide DC. In fact, there are several dominance scenarios in which evolutionary theory predicts an over- or under-representation of genes important to one of the sexes on the sex chromosomes (Ellegren and Parsch, 2007).

This leads us to disagree with the assertion of Melamed and Arnold that female-biased Z-linked genes in chicken are dosage compensated. They state that 'genes with low M:F ratios are compensated with respect to the inequality of Z chromosome number, but that other gene-specific forces act to reduce the ratio below 1'. However, it would seem quite difficult to demonstrate that a female-biased gene is both dosage compensated (to reach similar levels in males and females) and female-biased. A more parsimonious explanation seems to be that these genes are simply female-biased, rather than dosage compensated and female-biased.

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