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LETTER TO THE EDITOR

Could interallelic interactions be a key to the epigenetic aspects of fitness-trait inbreeding depression?

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Inbreeding depression is currently thought to result mainly from the expression of recessive deleterious alleles combined with 'inbreeding × environment' interactions (Charlesworth and Willis, 2009). Recent experiments and discussion have, however, revitalized the old idea that epigenetic processes also impact on the phenotypic variation of complex traits and embryo development in inbred individuals (Biémont, 2010; Cheptou and Donohue, 2012; Vergeer *et al.*, 2012; Schmitz *et al.*, 2013; Liebl *et al.*, 2013). However, further experiments are required if we are to decipher the precise mechanisms that underly the inbreeding/epigenetic relationship. Recent findings suggest that in addition to DNA methylation, histone modification and chromatin changes, paternal–maternal chromosomal complement interactions, and differential effects of transposable element (TE) expression on host gene regulation and developmental processes may impact on inbreeding depression during the development of eukaryotic organisms. We therefore suggest as a first approach that crosses involving sibs, father–daughter or mother–son could be used, as these have been shown in *Drosophila* to lead to different effects during the development, even though they theoretically result in the same inbreeding coefficient (Biémont, 1972, 1974, 1991). Whereas father–daughter crosses affected larvo-pupal viability, mother–son crosses increased only embryonic mortality, and brother–sister crosses increased both embryonic and larvo-pupal mortality rates. Because all these three kinds of crosses involve parental chromosomal sets of various different origins (a father, a mother or a brother/sister), it has been postulated that the maternal and paternal sets of chromosomes might differ as a result of some epigenetic process, so that their interactions during embryo development lead to distinct inbreeding effects (Biémont, 1974).

Some regions of the imprinted loci (the expression of imprinted genes depends on their parent-of-origin) are methylated differently in maternal and paternal alleles (Miyazaki *et al.*, 2009). These differentially methylated regions (DMRs) are involved in the paternal or maternal control of the regulation of specific genes, and consequently they lead to allelic differences between individuals who may subsequently be transmitted down the generations. It is now well known that in many organisms both maternal and paternal genomes, which exhibit different epigenetic compositions, contribute to the formation of a viable zygote and its subsequent development (Meehan *et al.*, 2005).

The parent-of-origin expression of the imprinting genes is regulated by specific regions known as imprinting control regions (ICRs). These ICRs acquire their DNA methylation pattern in the male germ line, and the paternal imprint is protected from demethylation in the paternal genome of the zygote. The methylated imprint is thus maintained throughout the development (Kacem and Feil, 2009) in the somatic cell lineage. One important characteristic of these ICRs is that the maternally methylated ICRs can either exert promoter activity on the paternal allele or silence it (Haun *et al.*, 2009). This kind of interallelic talk resembles the paramutations that have been reported in plants and in the mouse, and more recently in *Drosophila* (de Vanssay *et al.*, 2012). In these paramutations the two parent-of-origin alleles can influence one another's expression; these epigenetic modifications are known to be transmitted to the offspring, and have been shown to be triggered by changing epigenetic states of TEs in maize (Goettel and Messing, 2013). In addition to interallelic talk, paternal and maternal effects that influence the phenotype of the offspring have been reported in both *Drosophila* and mammals. These effects also involve epigenetic information that is inherited across generations (Chong *et al.*, 2007).

Imprinted genes often contain repeated sequences that include TEs or their remnants (Park *et al.*, 2012). These sequences recruit the epigenetic machinery, and mark the DMRs and ICRs, thus determining the epigenetic status of the affected alleles. Because TEs are known to be able to modulate gene expression, and regulate host genes differentially during the embryonic development (Peaston *et al.*, 2004), many changes in individual phenotypes are to be expected. This is consistent with the report that epigenetic processes, which involve chromatin remodeling proteins that control TE expression, may contribute to the loss of fitness due to inbreeding in Arabidopsis (Kakutani *et al.*, 1996). There is also evidence that some imprinting genes are acquired from retrotransposons and that retrotransposon silencing by DNA methylation can drive genomic imprinting in mammals and in plants (see Gifford *et al.* (2013) for a review).

The possibility that TE RNAs could contribute to various cell processes has recently been suggested by the observation that some retrotransposons produce differential regulation of host genes, and affect development processes in mouse oocytes and preimplantation embryos (Peaston *et al.*, 2004). This observation suggests that TEs may have an important role in genome remodeling during the early embryo cleavage stage. Some TEs display different patterns of expression in the maternal and paternal genomes (Josefsson *et al.*, 2006), which implies that TEs must have an important role in deciding the fate of the two parental sets of chromosomes during the early stages of development, and that RNA derived from TEs could be involved in controlling embryo development (Simonelig, 2011). Josefsson *et al.* (2006) have proposed a model of the activation of silent genes in hybrid crosses in Arabidopsis, in which the two parents contribute differing amounts of repressive factors and of the target sites required for fertility. The TE, ATHILA, has been shown to be involved in this phenomenon.

We propose that interallelic interactions could explain the differential effects reported above, which are seen in the various inbred

crosses observed during the early and late stages of development in *Drosophila*. Brother–sister, father–daughter and mother–son crosses, and other kind of inbred crosses, could therefore be used in various organisms to investigate the early processes involved during embryogenesis, and to decipher the precise roles of the two chromosomal complements, the interactions between them and their links with TE silencing and RNA-directed DNA methylation in the context of inbreeding.

DATA ARCHIVING

There were no data to deposit.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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