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# Transvection

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## What is transvection?

There is something magical about transvection. It conveys the power and elegance of classical *Drosophila* genetics, and has attracted and perplexed many distinguished scientists since its discovery by Ed Lewis in 1954. Transvection refers to a special class of genetic complementation of mutant alleles on homologous chromosomes. The prevailing view is that regulatory DNAs located on one homolog can regulate the transcription unit on the other homolog in *trans*. In some cases, enhancers appear to *trans*-activate genes located on the other homolog, but transvection can also lead to *trans*-repression of gene expression across homologous chromosomes.

## What is the evidence for transvection?

Lewis described genetic complementation between mutant alleles of the *Hox* gene *Ultrabithorax* (*Ubx*) in *Drosophila*. Both $bx^{34e}$ and $Ubx^{1}$ mutants exhibit abnormalities in the patterning of the thorax, including partial transformations of halteres into wings: however, $bx^{34e}/Ubx^{1}$ trans-heterozygotes display less severe transformations than predicted from the phenotypes produced by the individual alleles. Only after the molecular cloning and mapping of *Ubx* mutant alleles did the mechanistic basis for this *trans*-complementation process come into focus.

*Ubx* is regulated by multiple enhancers, including the intronic enhancers abx and BRE (Figure 1A). The $bx^{34e}$ mutant allele is caused by the insertion of a *gypsy* transposable element between these intronic enhancers and the *Ubx* promoter. The *gypsy* element contains twelve binding sites for the Zn-finger protein Su(Hw), which functions as an insulator to block enhancer–promoter interactions. $Ubx^{1}$ is a protein transposable element within the 5′ untranslated region (UTR) of the first exon. The favored interpretation of this partial genetic complementation is that the intronic abx and BRE enhancers in the $Ubx^{1}$ allele are able to activate transcription from the $bx^{34e}$ allele in *trans* to produce functional *Ubx* transcripts (Figure 1A). Chromosome rearrangements disrupt this transvection effect, suggesting that *trans* enhancer–promoter interactions require physical association of the two alleles. Indeed, visualization of the endogenous *Ubx* locus by DNA fluorescence *in situ* hybridization (FISH) revealed substantial allele pairing during *Drosophila* development.

## How common is transvection?

Since the discovery of transvection at the *Ubx* locus, there have been numerous reports of *trans*-homolog interactions in *Drosophila*. For example, a mutant allele of *yellow* lacking 5′ enhancers can be complemented by a null mutation lacking the promoter region (Figure 1C). Synthetic promoter-less/enhancer-less *yellow* mutant alleles were integrated into different locations of the genome and found to recapitulate transvection. These results suggest that somatic pairing of homologous chromosomes may be pervasive in the *Drosophila* genome. Supporting this view, transvection has been observed at many different endogenous loci, including *Abd-B, Scr*, *dpp*, *w*, *ap*, *eya* and *vg*. DNA FISH assays have revealed frequent pairing events at many chromosomal locations. In mammalian systems, *trans*-homolog enhancer–promoter interactions have not been so clearly demonstrated, but homolog pairing is thought to take place during X-chromosome inactivation, B-cell maturation and ES cell differentiation.

## What is promoter competition?

Transvection is often attenuated by the presence of a linked promoter in *cis*. The first evidence for such promoter competition came from studies of the *yellow* locus. Similar results have been reported at other loci, including *Ubx*. The promoter-less mutant $Ubx^{Mx6}$ produces more efficient suppression of the haltere-to-wing transformation than the promoter-containing $Ubx^{1}$ mutant when placed in *trans* to the $bx^{34e}$ allele (Figure 1B). This observation suggests that the intronic enhancers located on the $Ubx^{Mx6}$ allele are now able to effectively *trans*-activate the functional *Ubx* transcription unit located on the $bx^{34e}$ allele. Promoter competition has also been documented for the *Hox* gene *Scr*, suggesting that *cis*-preference may be a general property of transvection. This phenomenon might be related to prototypic examples of promoter competition seen at the *β-globin* locus, whereby the closest promoter displays preferential activation by a shared enhancer in *cis*.

## What is the mechanism of transvection?

Insulator DNAs appear to be at the heart of *trans*-homolog enhancer–promoter interactions. As discussed above, enhancers preferentially activate neighboring promoters in *cis. Trans*-interactions are augmented by the loss of *cis*-promoters (Figure 1B and C). They are also augmented by insulator DNAs (Figure 1D). The analysis of the transvection mediating region of the *Hox* gene *Abd-B* suggests that insulators foster pairing of homologous chromosomes. Stable pairing might increase the opportunities for *trans* enhancer–promoter interactions. Importantly, insulators facilitate transvection even in the presence of a *cis*-linked promoter.

## And future prospects?

Insulator DNAs are thought to be important agents of genome organization in vertebrates, leading to the formation of chromosomal loop domains, or TADs (topologically associating domains). It has been suggested that insulators also produce loop domains in *Drosophila*. For example, the depletion of CAP-H2, a key component of Condensin II, augments

transvection at *Ubx* and *yellow*, possibly by antagonizing Cohesin. A major future goal is to determine the nature of putative chromosomal loop domains at transvecting loci. Do they serve as transcription 'hubs' for regulating homologous genes in *cis* and *trans*? With the advent of genome editing methods and quantitative live-imaging technologies, it won't be long before these and other mysteries of transvection are revealed.

## Where can I find out more?


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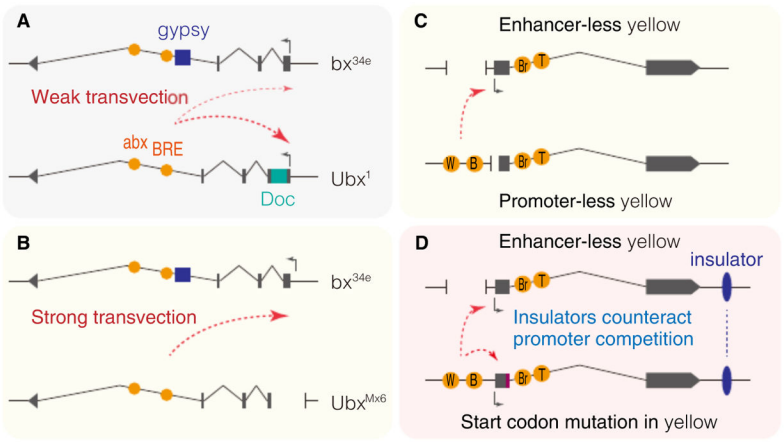


**Figure 1. Transvection in *Drosophila***

(A) Transvection in $bx^{34e}/Ubx^{1}$ trans-heterozygotes. Intronic abx and BRE enhancers on the $Ubx^{1}$al-lele activate transcription from the $bx^{34e}$ allele in *trans*. (B) Loss of *cis*-linked promoter augments transvection. $Ubx^{Mx6}$ mutation consists of a 3.4 kb deletion including the *Ubx* promoter. (C) 5′ wing and body enhancers on the promoter-less allele activate transcription from the enhancer-less allele in *trans*. W, wing enhancer; B, body enhancer; Br, bristle enhancer; T, tarsal claw enhancer. (D) Insulator DNAs facilitate transvection at *yellow*.