

Reawakening the telomeres

The gradual erosion of the ends of chromosomes (telomeres) during successive cell divisions has long been associated with aging, but possible mechanisms linking the two processes have eluded scientists, until now. Bits of DNA are lost from telomeres during each cell division. When their telomeres become too short, cells stop dividing. Some cells, including 90% of cancerous cells, possess the enzyme telomerase that maintains their telomeres, allowing them to continue growing. Most cells, however, lack telomerase.

Now, Baur *et al.* have discovered an interesting phenomenon in some human cell lines: telomere position effect (TPE), whereby gene expression is turned off in the regions near telomeres. This TPE silencing is stronger in cells with longer telomeres. The researchers speculate that TPE can act as an age-sensing mechanism. As telomeres become shorter, some genes that were previously silent will become expressed again. Could this reactivation allow the cell to change its behavior before becoming senescent? [Baur, J.A. *et al.* (2001) *Science* 292, 2075–2077] NJ

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Letter

An ancient cluster of Wnt paralogues

The recently completed sequences of the human and *Drosophila* genomes reveal an interesting conserved arrangement of a group of Wnt genes¹. There are seven Wnt family members in *Drosophila* and 19 in the human genome. I aligned their protein sequences using the ClustalW program (shown on <http://www.stanford.edu/~rnuisse/genealigns/wntalign.html>). The alignment confirmed an earlier phylogenetic analysis² of vertebrate and *Drosophila* Wnt proteins that indicated an orthologous relationship between WNT1 and *Drosophila* Wingless³ (Wg); between WNT7 and DWnt2; and between WNT5 and DWnt5. Three recently identified *Drosophila* Wnt proteins also have orthologs in the human genome and are therefore called DWnt6, DWnt8 and DWnt10.

In the *Drosophila* genome, the paralogous genes *wg*, *DWnt6* and *DWnt10*

are immediately adjacent to each other at position 27F on the second chromosome, transcribed in the same orientation and with no recognizable gene in between them. This order is conserved in the human genome. Human chromosome 12q13 contains WNT1 and WNT10B immediately adjacent to one another, although they are transcribed in the opposite orientation. Human chromosome 2q35 has WNT6 next to WNT10A, expressed from the same strand with no gene in between. WNT10A and WNT10B are closely related to each other, and the result of recent duplications occurred during the evolution of the jawed vertebrate lineage². It seems probable, therefore, that there was a common ancestral cluster of Wnt genes containing WNT1, WNT6 and WNT10 pre-dating the last common ancestor of arthropods and deuterostomes. This cluster has been preserved during arthropod evolution. In the lineage leading to vertebrates, the cluster was duplicated, leading to the WNT1–WNT6–WNT10A and

WNT1–WNT6–WNT10B groups now on human chromosomes 12 and 2 (Fig. 1). After this duplication, WNT1 was lost from one cluster and WNT6 from the other.

This conservation of gene order is reminiscent of the evolutionary conservation of the Hox complex⁴ and could be similarly ancient (500 Myr old). None of the remaining Wnt genes in either the fly or the human are organized in a similar way. Although the *Drosophila* *Wnt4* gene is close to *wg*, there is one gene (CG13785) in between. The *DWnt2*, *DWnt8* and *DWnt5* genes are at separate locations. In the human genome, there are some additional examples of closely linked Wnt genes (*WNT3A–WNT14* on 1q42; *WNT2–WNT16* on 7q31; and *WNT3–WNT15* on 17q21), but there are intervening genes in each case. The conservation of the WNT1–WNT6–WNT10 cluster might imply that these genes are, like Hox gene clusters, coordinately regulated.

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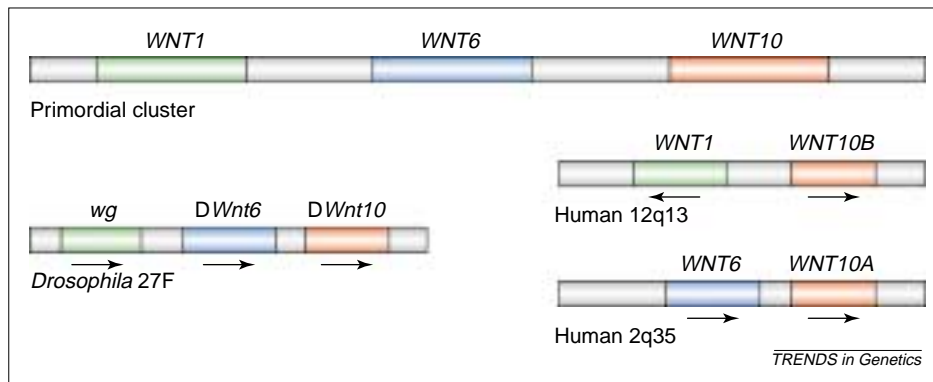


Fig. 1. A primordial cluster of three Wnt genes is present in the Arthropod lineage and in *Drosophila*. The human genome contains duplicated copies of the same cluster but WNT6 is deleted from 12q13 and WNT1 is deleted from 2q35. Because the common ancestral cluster pre-dates the last common ancestor of arthropods and deuterostomes, it is ~500 Myr old.