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Jonathan B Weitzman
Email: jonathanweitzman@hotmail.com

The mammalian Hox gene clusters display remarkable 'quantitative colinearity', meaning not only does the temporal and spatial expression during development reflect the order of genes on the chromosome, but genes at the 5' end of the cluster are expressed at the highest levels. In the November 14 Nature, Kmita *et al.* describe analysis of a series of deletion mutations within the mouse *Hoxd* locus designed to investigate the mechanisms underlying quantitative colinearity in limbs (*Nature* 2002, **420:**145-150). Deletion and duplications of the *Hoxd13*, *Hoxd12* and *Hox11* genes were generated using targeted meiotic recombination (TAMERE) technology. Disruption or deletion of the *Hoxd13* gene results in very different digit phenotypes, and deletion affects the expression of neighbouring genes. The location within the gene cluster is critical, and *Hoxd* genes are functionally upregulated when they are shifted to replace their upstream neighbours. Duplications of *Hoxd* genes and their promoter regions result in down-regulation of downstream genes. These observations led Kmita *et al.* to develop a promoter-competition model to explain the targeted effects of a distant enhancer element. They propose that enhancer preference for the 5' extremity of the cluster explains the observed 'quantitative colinearity'.

References

1. Vertebrate *hox* gene regulation: clustering and/or colinearity?

2. *Nature*, [http://www.nature.com]

3. Engineering chromosomes in mice through targeted meiotic recombination (TAMERE).