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DISEASE GENETICS

Y-linked duplication

To date, only one Mendelian trait — a form of hearing impairment — has been linked to the human Y chromosome. A study now uncovers the molecular basis of this disorder and shows that duplicated genes originating from chromosome 1 are probably responsible for the trait.

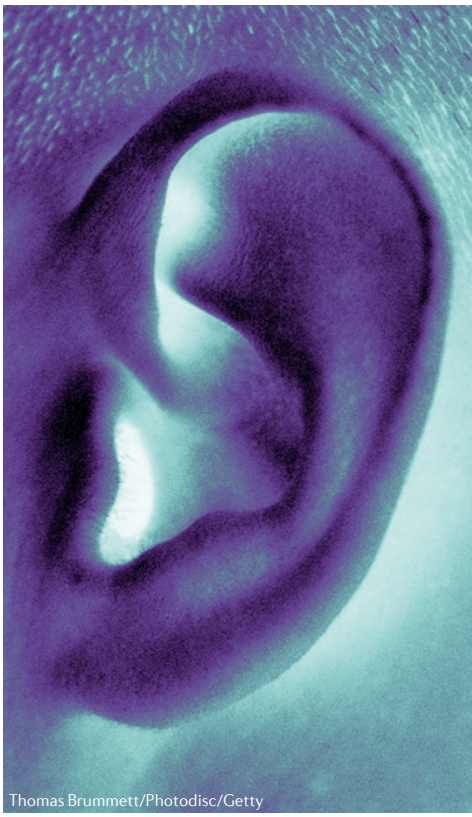
The hearing impairment, termed DFNY1, was found in a Chinese family, and in this study Wang *et al.* sequenced representative Y chromosomes from affected and unaffected branches of the family. Comparison of the relative read depth along the chromosomes, plus other methods, revealed a duplicated region in the DFNY1 Y chromosome.

Detailed characterization of the duplicated region using fibre fluorescence *in situ* hybridization and PCR-based methods showed that the duplicated region arises from a complex rearrangement and includes three sections of the Y chromosome and sequence from chromosome 1. The breakpoint sequences include regions of microhomology that implicate a mechanism called fork stalling and template switching (FoSTeS) in the generation of this rearrangement. Notably, this is the first report of an interchromosomal rearrangement resulting from FoSTeS.

The duplicated Y-chromosome portion includes one known protein-coding gene: *TSPY1*. Multiple copies of *TSPY1* have previously been reported but have not been associated with deafness. By contrast, the chromosome 1 material includes five annotated genes and arises from a region previously associated with hearing loss. The conclusion that this Y-linked trait is actually a result of chromosome 1 sequences is also consistent with the lack of a hearing impairment in individuals with gain or loss of an entire Y chromosome.

Mary Muers

ORIGINAL RESEARCH PAPER Wang, Q. *et al.* Genetic basis of Y-linked hearing impairment. *Am. J. Hum. Genet.* 24 Jan 2013 (doi:10.1016/j.ajhg.2012.12.015)



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