

# Degrees of similarity

A study has reversed the common but untested assumption that orthologous gene pairs are functionally more similar to each other than paralogous pairs are. This finding could influence the practice of using evolutionary relationships to infer function from sequence.

Paralogous pairs have been considered to be an unreliable source of information for annotating genes because of their high rate of sequence evolution after duplication. Feeling dubious that sequence divergence paralleled functional divergence, the authors compared the ability of paralogues or orthologues to predict the function of 8,900 genes that are present in mice and humans and for which function had been experimentally validated. Contrary to the current working hypothesis, functional similarity between orthologues was <70%, whereas it was >70% for paralogues.

Surprisingly, for orthologues, protein sequence divergence was a

poor predictor of functional divergence; proteins were likely to fall into the same [Gene Ontology](#) category whether their sequence identity was 50% or 99%. By contrast, functional similarity between paralogues went hand in hand with sequence identity: paralogous sequences from the same species were functionally the most similar. These conclusions held true when gene expression levels were used as readouts of functional similarity.

The rapid pace at which genomes are being sequenced calls for a more effective way of computationally assigning gene function. Now, this task no longer needs to rely on transferring function from one gene to a single orthologue but can instead take advantage of several gene duplicates with a single genome.

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**ORIGINAL RESEARCH PAPER** Nehrt, N. L. *et al.*  
Testing the ortholog conjecture with comparative  
functional genomic data from mammals.  
*PLoS Comp. Biol.* 7, e1002073 (2011)

