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In the news

SILENT MUTATIONS
TURN UP THE VOLUME

Although a silent mutation doesn't affect the amino-acid sequence of a protein, it can affect protein folding and function, reports an intriguing *Science* paper. Chava Kimchi-Sarfaty and colleagues examined a silent mutation that is caused by a synonymous single nucleotide polymorphism (SNP) in *MDR1*, which encodes the protein pump P-gp. Previous results had indicated that this SNP was linked to reduced pump functionality, but through an unspecified mechanism. Startlingly, their results showed that the pump's conformation, and its functionality, were altered by this SNP, despite the protein's amino-acid sequence remaining unchanged.

How might this occur? "We think that this SNP affected protein function because it forced the cell to read a different codon than it usually does," answers co-author Michael Gottesman, and "this slight change might slow the folding rhythm, resulting in an altered protein conformation...", (*GenomicsProteomics.com*, 27 Dec 2006).

While this result is groundbreaking, not everyone was surprised. Ian Purvis and colleagues, at the University of Glasgow, UK, and Anton Komar, now at Cleveland State University, USA, had previously independently proposed that silent mutations could fine-tune protein folding and function. Furthermore, artificially engineered SNPs had already been shown to affect folding and function. This result, however, is the first demonstration that naturally occurring SNPs can have such effects.

These new results seem to add a new level of complexity to the creation of artificial genes and to the diagnosis of disease-causing mutations. Whether synonymous SNPs have adverse biological effects might have to be re-examined on a case-by-case basis, and researchers' ears will have to be perked up for what we now know are not-so-silent mutations.

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