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Letters.

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Heretical DNA Sequences?

When "Genomic clues to DNA treasure sometimes lead nowhere" (D. Monroe, News Focus, 10 July, p. 142), the apparent impasse should indeed stimulate more subtle interpretation. Exceptions to the "conservation equals function" rule for sequence evolution are "heretical" only when mutations are expected to occur at random and to be rejected by selection in functional sequences while accumulating unchecked elsewhere. However, that simplistic view is untenable (1). Intragenomic, site-specific mutation rates vary across orders of magnitude. Sequences critical for adaptation may well have higher-than-average mutation rates, leading to rapid divergence even among closely related species.

For example, Riley and Krieger (2, 3) recently described a set of simple sequence repeats (SSRs) that have been retained over deep evolutionary time even though neither the repeating motif nor the number of repeats is conserved. SSRs are mutation-prone stretches, once dismissed as meaningless stutters, that turn up within many functional domains. Earlier this year *Science* reported experimental confirmation (4) of a decades-old prediction (5) that SSRs' high mutation rates could promote efficient evolutionary adaptation. The SSRs discovered by Riley and Krieger are flanked by highly conserved upstream sequences within the untranslated regions of 22 genes, all but one of which have neurodevelopmental roles. These SSRs display recurring patterns of motif replacement across a wide range of vertebrates. Some function is evidently being preserved in the repetitive (and hypermutable) nature of these sites, one which can persist through, or perhaps even exploit, the accumulation of sequence-transforming mutations.

Genome treasure-hunters should expect the unexpected; additional gems surely remain buried within nonconserved sequences.

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