Up to 25% of beneficial mutations in protein sequences are not adaptive innovations in mammals

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Abstract

In this work based on genome-wide studies across species and populations, we estimated the proportion of beneficial mutations in protein coding sequences that are not adaptive innovations. Our study is based on the premise that slightly deleterious mutations scattered across the genome are reaching fixation due to genetic drift. These mutations are then subsequently reverted by beneficial back-mutations, generating a balance at which genomes are constantly both damaged and repaired simultaneously at different loci. Even though the existence of these back-mutations is predicted by the nearly neutral theory, they have been largely overlooked, and positive selection has been countlessly interpreted as adaptation to changing environments. In this work, we integrated datasets across the entire exome of 96 species at the mammalian scale, with polymorphism for 28 populations from 6 genera (*Equus*, *Bos*, *Capra*, *Ovis*, *Chlorocebus* and *Homo*). We then estimated selective effects of mutations inside mammalian protein coding sequences, under a model assuming no adaptation at the phylogenetic scale. We finally estimated the proportion of beneficial mutations that are not adaptive innovations among all beneficial mutations at the population scale. Our work confirms that deleterious substitutions have accumulated in mammals and are currently being eliminated. In modern humans, it results in around 25% of beneficial mutations that are not adaptive innovations, but instead are repairing previous deleterious changes.