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advantageDOI:
10.1038/nrg1900

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Skewed patterns of polymorphism around a locus can imply that it has recently been subject to selection. Many studies have therefore looked for evidence of selection in the large sets of polymorphism data that have recently become available. Teshima *et al.* have now shown that the reliability of empirical approaches to assessing such data depends on demography and the nature and history of the allele being selected.

Polymorphism at neutral sites in the genome is not entirely free from the influence of selection. A neutral allele at a locus that happens to be close to an advantageous allele at a locus under selection will 'hitch-hike' to near-fixation along with the selected allele. Therefore, levels of polymorphism at neutral sites will be reduced if selection has acted nearby.

There are several models of expected neutral polymorphism against which data can be compared

when looking for selection. However, the results are often sensitive to the assumptions of the model. Therefore, a simple empirical approach is often used for genome-wide analyses, in which sites with the most skewed polymorphism patterns are assumed to be those that are linked to selected sites. But what are false-discovery and false-negative rates in this approach, and are there systematic biases against discovering certain types of selected site?

Teshima *et al.* simulated data sets for the evolution of modern humans and the domestication of maize. They attempted to make their data realistic by including bottlenecks (to mimic non-sub-Saharan human populations) or constant population sizes (for sub-Saharan populations), and strong selection on previously neutral alleles (for the relatively sudden artificial selection imposed by man in domesticating maize) compared with weaker selection on new mutations (for wild plant populations).

They found that their ability to detect genuine selection was best when the selection acted on new mutations in a population of constant size. This finding confirms what is intuitive: pre-existing, previously neutral mutations are expected to

exist in several haplotypes, so several different neutral alleles will hitch-hike with the mutation when it is selected, maintaining polymorphism; and population bottlenecks reduce polymorphism, so they will confound the observable effects of selection at surrounding sites.

The most serious implication of this paper is for how theories about the genetics of adaptation might be developed. Empirical scans will continue to detect many good candidate sites for selection. However, they will miss alleles that were selected after having previously been neutral, and also recessive alleles, which the authors showed to be harder to detect than co-dominant or dominant ones. The alleles that are likely to be missed might affect certain types of protein more than others, and the mutations might be of a certain functional type that is different from that of new, dominant mutations. So, this study is a word of caution to anyone hoping to use empirical screens to make global statements about the types of mutation that selection acts on.

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ORIGINAL RESEARCH PAPER Teshima, K. M., Coop, G. & Przeworski, M. How reliable are empirical genomic scans for selective sweeps? *Genome Res.* 10 May 2006 (doi:10.1101/gr.5105206)