The Role of Deleterious Variants in Crop Genomes

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The mutational process results in a constant influx of new mutations into populations, with fitness effects that vary from lethal to advantageous. The distribution of fitness effects (DFE) of mutations is not directly observable (Eyre-Walker & Keightley 2007), but among mutations that impact fitness (those that are non-neutral), most will be deleterious (Keightley & Lynch 2003). Deleterious mutations comprise mostly disruption of phylogenetically conserved sites (Doniger et al. 2008) or loss-of-function mutations (Yampolsky et al. 2005). Strongly deleterious mutations, particularly those that are lethal in the heterozygous state, are quickly removed from populations by purifying selection. Likewise, advantageous mutations increase in frequency and fix (Robertson 1960). Mildly deleterious mutations have the potential to persist in populations and contribute significantly to reduction in fitness (Eyre-Walker et al. 2006; Doniger et al. 2008).

Ignoring the effects of linkage, the persistence of mutations as segregating variants depends on both the effective population size ($N_e$), and the selective coefficient for each variant ($s$). Deleterious mutations can effectively be removed from populations by purifying selection if the product of $N_e$ and $s$ is greater than one ($N_e s > 1$) (Kimura 1962). Smaller $N_e$ results in less effective purifying selection, meaning that selection can act on only strongly deleterious mutations. Weakly deleterious mutations will be subject only to drift, and have the potential to reach moderate frequencies in populations (Robertson 1960; Fay & Wu 2000; Fay et al. 2001). While mating system, ranging from self fertilization to obligate outcrossing, influences the segregation of deleterious mutations, the effect is relatively minor. In self-fertilizing species, homozygous lethal mutations are exposed more frequently, and are thus purged from the population more quickly than in outbreeding species (Lande & Schemske 1985; Henter 2003). Similarly, advantageous mutations are brought to homozygosity more readily, and thus increase in frequency more rapidly (Robertson 1960).

In domesticated species, both the demographic effects of domestication and genetic hitchhiking associated with strong selection for genetic variants associated with adaptation to domestication could impact the frequency of deleterious mutations in crop plants. The domestication event involved a strong bottleneck (Eyre-Walker et al. 1998), which would
allow deleterious mutations to drift to moderate frequency (Robertson 1960). Additionally, the selective sweeps involved during domestication (Wright et al. 2005) would push deleterious mutations to high frequencies (Hill & Robertson 1966). In cultivated rice, there is an excess of segregating nonsynonymous variants compared to wild relatives, which suggests an accumulation of deleterious mutations (Lu et al. 2006).

In humans, examination of the contribution of relatively rare genetic variants to trait variation has resulted in the emergence of personalized genomes as a major field of study, with particular emphasize on the contribution of rare deleterious variants to human disease. Current estimates suggest that the genome of individual humans carry at least several hundred loss-of-function mutations, with potentially many more deleterious noncoding variants (Abecasis et al. 2010; Agrawal & Whitlock 2012). Humans are not unique in harboring substantial numbers of deleterious polymorphisms; it is estimated that almost 40% of nonsynonymous mutations in yeast are deleterious (Doniger et al. 2008). Similar patterns are observed in rice (Lu et al. 2006), dogs (Cruz et al. 2008) and Drosophila (Fay et al. 2002). The identification, and targeted elimination of deleterious mutations has been proposed as a potential means of improving plant fitness and crop yields in elite cultivars (Morrell et al. 2012).

In this study, we examine the distribution of deleterious mutations in barley and soybean using exome resequencing technology. We find that deleterious mutations are present in crop genomes, and that selection against deleterious mutations is a potential approach to crop improvement.


