

Management of Mendelian Traits in Breeding Programs by Gene Editing

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High-density single nucleotide polymorphism genotypes have recently been used to identify a number of novel recessive mutations that adversely affect fertility in dairy cattle, as well as to track conditions such as polled. Recent findings suggest that the use of sequential mate allocation strategies that account for increases in genomic inbreeding and the economic impact of affected matings result in faster allele frequency changes than strategies which do not consider inbreeding and monetary losses. However, the effect of gene editing on selection programs also should be considered because gene editing has the potential to dramatically change allele frequencies in livestock populations. A simulation program developed to evaluate dairy cattle breeding schemes was extended to include the use of clustered regularly interspaced short palindromic repeat (CRISPR), transcription activator-like effector nuclease (TALEN), and zinc finger nuclease (ZFN) technologies for gene editing. A hypothetical technology with a perfect success rate was used to establish an upper limit on attainable progress, and a case with no editing served as a baseline for comparison. The technologies differed in the rate of success of gene editing, as well as the success rate of the embryo transfer step, based on estimates in the literature. The number of alleles edited was assumed to have no effect on success rate. The two scenarios evaluated considered only the horned locus, or 12 recessive alleles currently segregating in the U.S. Holstein population. The top 1, 5, or 10 % of bulls were edited each generation, and either no cows or the top 1 % of cows were edited. Inefficient editing technologies produced less cumulative genetic gain and lower level of inbreeding than efficient ones. Gene editing was very effective at reducing the frequency of the horned haplotype (increasing the frequency of polled animals in the population), and allele frequencies of the 12 recessives segregating in the US Holstein population decreased faster with editing than without. These results suggest that gene editing can be an effective tool for reducing the frequency of harmful alleles or increasing the frequency of desirable alleles in a dairy cattle population even if only a small proportion of elite animals are modified. The source code for the simulation and scripts used to analyze the data are available on GitHub: <https://github.com/wintermind/gene-editing>.

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