Summary

Recent advances in genomic technologies have enabled the development of genotype-driven approaches to monitor recessive genetic defects in cattle populations such as reverse genetics and the search for depletions in homozygous genotypes among large cohorts of animals genotyped for genomic selection.
In this study, analyzing Illumina BovineSNP50 genotypes from more than 250,000 animals and 396 whole genome sequences, we identified two new embryonic lethal mutations (called HH6 and HH7) in Holstein cattle.
HH6 is a non-synonymous mutation affecting the initiator codon of the gene encoding the SDE2 Telomere Maintenance Homolog (SDE2), a protein essential for genomic stability in eukaryotes. Initiation of translation at the closest in-frame methionine codon would truncate the SDE2 precursor by 83 amino acids, including the cleavage site necessary for its activation.
HH7 is a four base pair deletion starting three base pair downstream the splice donor site of the antepenultimate exon of the gene encoding the Centromere Protein U (CENPU), which plays a key role in mitosis. Notably this deletion affects a guanine that is entirely conserved among Mammals. The mutation is predicted to disturb the splicing of CENPU and to result in important modifications of the primary structure of the protein after residue Q327.
No homozygote for the derived allele was observed in a large population of 29,000 and 109,000 Holstein animals genotyped with the Illumina EuroG10K SNP chip for HH6 and HH7, respectively. In addition, both mutations showed significant negative effects on the conception rate and the non return rate at 56 days in at risk- versus control mating, which is consistent with an early death of homozygous embryos.
The low frequency of the derived alleles in the French population (respectively 1.3% and 0.9%) and the availability of a diagnostic test on the Illumina EuroG10K SNP chip routinely used for genomic evaluation will enable a rapid and efficient selection against these deleterious mutations.

Keywords: embryonic lethality, deficit in homozygote, HH6,HH7, SDE2, CENPU