Mapping a Gene for Harelip in Cattle

Brian W. Kirkpatrick, University of Wisconsin-Madison, Madison, WI and Donagh P. Berry, Teagasc-Moorepark, Ireland

Abstract Text:

A harelip phenotype was detected at apparent low frequency among offspring of a phenotypically normal Holstein bull. Pedigree analysis of affected calves did not display obvious inbreeding to a common ancestor, suggesting the causative allele was not a rare recessive. The normal phenotype of the sire suggests a dominant allele with incomplete penetrance or a mosaic mutation. Half-sib offspring characterized as harelip (n=22) or normal (n=44) were genotyped with the BovineHD SNP chip to both test the hypothesis of a single gene controlling the phenotype and to map the gene. Phased genotype data were used to predict paternally inherited haplotypes; Bovine50 Beadchip genotype data were available on the sire. Segregation and mapping of a single gene was tested and performed by linkage analysis in two alternative approaches. In the first, association of the paternally inherited haplotype with harelip phenotype utilized both harelip and phenotypically normal offspring in a typical linkage analysis. In the second, only offspring with the harelip phenotype were used, testing the deviation of paternal haplotype inheritance from the expectation of equal representation of alternative haplotypes under the null hypothesis of no association. In both analyses the most significant association was observed for a region on distal BTA13, though results were more significant for the analysis using only the harelip offspring (nominal $p<1x10^{-24}$) vs harelip and normal offspring (nominal $p<2x10^{-5}$) likely owing to the uncertain relationship between the normal phenotype and underlying harelip genotype for the latter. Subsequent research will sequence at least two affected half-sibs.