STRUCTURAL VARIATION AT THE *KIT* LOCUS IN RESPONSIBLE FOR THE PIEBALD PHENOTYPE IN HEREFORD AND SIMMENTAL CATTLE

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ABSTRACT

The *Spotted* locus is responsible for white spotting (piebald) coat color phenotypes in cattle. Since the Hereford breed is fixed for this phenotype, we postulate that a selective sweep occurred during breed formation to fix the *Spotted* locus while concurrently fixing nearby hitchhiking loci. *Spotted* has been linkage mapped to BTA6 between 64.7 Mb and 85.5 Mb (Grosz & McNeil, 1999). We examined SNP minor allele frequencies across this region in 811 fullblood Herefords using Illumina BovineHD genotypes and identified four stretches of homozygosity individually greater than 75 kb. The largest of the four is 415 kb and extends into *KIT*, a tyrosine kinase responsible for the migration melanocytes during development. To pinpoint the locus, one Hereford and three Angus (non-spotted) sire-son pair *de novo* assemblies were constructed and aligned. We predicted 323 fixed differences (SNPs or indels) from the alignments. However, none were in coding regions. Comparing the genomes of 29 spotted and 55 non-spotted cattle, we also found two duplications unique to spotted animals. One ~50 kb upstream of *KIT* and one in the first *KIT* intron. These appear to be duplicated 6X in Hereford and 3X and 6X, respectively, in fullblood Simmental. We predict either the upstream duplication interrupts a long-range regulatory element of *KIT* or the intron duplication reduces the transcriptional efficiency of *KIT* causing the piebald phenotype. Determining which variant is causal will require allele-specific expression analyses from animals homozygous and heterozygous for spotted and non-spotted alleles or extensive experimentation with developing embryos.