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# Haplotype tests for economically important traits of dairy cattle

***J.B. Cole, P.M. VanRaden, D.J. Null, J.L. Hutchison, and S.M. Hubbard***
Animal Genomics and Improvement Laboratory, Agricultural Research Service, USDA, Beltsville, MD 20705-2350
301-504-8334 (voice) • 301-504-8092 (fax) • paul.vanraden@usda.gov • http://go.usa.gov/xybuq

Haplotype tests are used routinely to identify animals with desirable traits of economic importance, discover new genetic disorders, and track carrier status of genotyped animals. Recessive haplotypes that affect fertility and stillbirth in dairy cattle (haplotypes BH1–BH2, HH1–HH5, and JH1–JH2 were described in detail by VanRaden et al. (2011, 2013, 2014). A recessive mutation that causes embryo death (haplotype HH6) was discovered by Fritz et al. (2018). Carrier status for Holstein haplotypes with mutations for brachyspina (haplotype HH0), bovine leucocyte adhesion deficiency (BLAD; haplotype HHB), complex vertebral malformation (CVM; haplotype HHC), deficiency of uridine monophosphate synthase (DUMPS; haplotype HHD), mulefoot (syndactyly; haploptype HHM), polledness (haplotype HHP), red coat color (haplotypes HBR, HDR, and HHR), and cholesterol deficiency (HCD) are reported by the Council on Dairy Cattle Breeding (Bowie, MD). Brown Swiss haplotype tests for spinal dismyelination (SDM; haplotype BHD), spinal muscular atrophy (SMA; haplotype BHM), and Weaver Syndrome (haplotype BHW) also are provided. Polledness haplotypes are reported for Brown Swiss (BHP) and Jerseys (JHP). A haplotype that affects conception rate in Ayrshires (AH1) was reported by Cooper et al. (2014), an Ayrshire haplotype that affects fertility (AH2) was discovered by Null et al. (2017), and a haplotype that results in curly calves in Ayrshires (AHC) as reported by Agerholm et al. (2016). A haplotype associated with Jersey neuropathy with splayed forelimbs (JNS) has been identified (Al-Khudhair et al., 2022). Haplotypes BH1 and JH2 were discontinued in December 2018 (VanRaden and Null, 2018).

The table below lists all of the haplotypes currently tracked in the U.S. genomic evaluation system, the frequency of the minor (less common) haplotype, and the location in base pairs (bp) of the haplotype based on the 2018 ARS-UCD1.2 genome assembly (www.ncbi.nlm.nih.gov/assembly/GCF_002263795.1/reference; Rosen et al., 2018). Locations are exact (single bp) when the causative mutation is known and approximate (range of bp) when it is unknown, a duplication, a deletion, or multiple mutations. The frequency of carriers in the population is generally twice the haplotype frequency because carriers have 1 defective and 1 normal haplotype.

Recessives with very low frequencies (e.g., HH4) can be identified because many Holsteins have been genotyped (current exact counts of genotyped animals are shown in the Council on Dairy Cattle Breeding's "Genotype Counts by Chip Type, Breed Code, and Sex Code"). Generally, recessives in breeds with fewer genotyped animals and smaller populations will not be detected until they have a high frequency in the population. Haplotype tests are less accurate than loss-of-function (LOF) mutation tests, and retesting valuable animals that have been identified as carriers using a haplotype test is recommended if an exact test is available. Further information on combining LOF mutation tests with haplotype tests is available (VanRaden et al., 2012) as is further detail on genetic defects (Nicholas and Hobbs, 2014; OMIA - Online Mendelian Inheritance in Animals, 2014).

| Breed | Haplotype | OMIA 9913 ID[1] | Functional/ *gene* name | Haplotype frequency (%) | Chromo-some | ARS-UCD region (bp) | Reference |
|---|---|---|---|---|---|---|---|
| Ayrshire | AH1 | 001934 | PIRM/ *UBE3B* | 11.16 | 17 | 63,668,380 | Cooper et al. (2014), Venhoranta et al. (2014) |
| | AH2 | 002134 | *RPAP2* | 10.50 | 3 | 51,086,099–51,119,146 | Null et al. (2017) |
| | AHC | 002022 | *CHRNB1* | 15 | 19 | 27,121,939-27,131,139 | Agerholm et al. (2016) |
| Brown Swiss[2] | BH2 | 001939 | *TUBD1* | 6.65 | 19 | 10,833,921 | Schwarzenbacher et al. (2016) |
| | BHD | 001247 | SDM/ *SPAST* | 1.31 | 11 | 13,246,972–14,736,876 | Hafner et al. (1993), Thomsen et al. (2010) |
| | BHM | 000939 | SMA/ *KDSR*(*FVT1*) | 3.24 | 24 | 61,620,374 | El-Hamidi et al. (1989), Krebs et al., 2007 |
| | BHP | 000483 | Polledness/ *POLLED* | 1.22 | 1 | 2,578,598 | Medugorac et al. (2012), Rothammer et al. (2014) |

| Breed | Haplotype | OMIA 9913 ID[1] | Functional/ *gene* name | Haplotype frequency (%) | Chromo-some | ARS-UCD region (bp) | Reference |
|---|---|---|---|---|---|---|---|
| | BHW | 000827 | Weaver/ *PNPLA8* | 0.58 | 4 | 49,339,002–49,461,342 | McClure et al. (2013), Kunz et al., 2016 |
| Holstein | HBR | 001199 | Black/red coat color/ *MC1R*(*MSHR*) | 0.75 | 18 | 14,705,501 | Lawlor et al. (2014) |
| | HCD | 001965 | Cholesterol deficiency/*APOB* | 2.28 | 11 | 77,872,709 | Kipp et al. (2015), Charlier (2016), Menzi et al. (2016), Schütz et al. (2016) |
| | HDR | 001529 | Dominant red coat color | 0.03 | 3 | 9,361,962 | Capitan et al. (2014), Lawlor et al. (2014), Dorshorst et al., 2015 |
| | HH0 | 000151 | Brachyspina/ *FANCI* | 1.65 | 21 | 20,775,563 | Agerholm et al. (2006), Charlier et al. (2012) |
| | HH1 | 000001 | *APAF1* | 1.28 | 5 | 62,810,245 | Adams et al. (2012) |
| | HH2 | 001823 | — | 1.21 | 1 | 93,501,204–95,581,556 | VanRaden et al. (2011), McClure et al. (2014) |
| | HH3 | 001824 | *SMC2* | 2.64 | 8 | 93,753,358 | Daetwyler et al. (2014), McClure et al. (2014) |
| | HH4 | 001826 | *GART* | 0.23 | 1 | 1,997,582 | Fritz et al. (2013) |
| | HH5 | 001941 | *TFB1M* | 2.39 | 9 | 91,847,117–91,937,003 | Cooper et al. (2013), Schütz et al. (2016) |
| | HH6 | 002149 | *SDE2* | 0.44 | 16 | 29,015,336–29,059,673 | Fritz et al. (2018) |
| | HHB | 000595 | BLAD/ *ITGB2* | 0.21 | 1 | 144,770,078 | Shuster et al. (1992) |
| | HHC | 001340 | CVM/ *SLC35A3* | 1.10 | 3 | 43,261,946 | Agerholm et al. (2001) |
| | HHD | 000262 | DUMPS/ *UMPS* | 0.01 | 1 | 69,151,931 | Shanks et al. (1984) |
| | HHM | 000963 | Mulefoot/ *LRP4* | 0.05 | 15 | 76,807,960 | Eldridge et al. (1951), Duchesne et al. (2006) |
| | HHP | 000483 | Polledness/ *POLLED* | 0.88 | 1 | 2,578,598 | Medugorac et al. (2012), Rothammer et al. (2014) |
| | HHR | 001199 | Red coat color/ *MC1R*(*MSHR*) | 3.29 | 18 | 14,705,965 | Joerg et al. (1996) |
| Jersey[2] | JH1 | 001697 | *CWC15* | 9.21 | 15 | 15,449,431 | Sonstegard et al. (2013) |
| | JHP | 000483 | Polledness/ *POLLED* | 2.04 | 1 | 2,578,598 | Medugorac et al. (2012), Rothammer et al. (2014) |
| | JNS | 002298 | *UCHL1* | 8.2 | 6 | 60,158,901 | Al-Khudhair et al. (2022) |

[1]Online Mendelian Inheritance in Animals (OMIA) identification number for *Bos taurus* (National Center for Biotechnology Information species code 9913).
[2]Discontinued haplotypes: BH1, JH2.

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