

# Identification of Genetic Variants Associated with Conformation Traits in Swiss Dairy Cattle

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## Background

- Hoof and leg conformation traits influence health, welfare, longevity, and productivity in dairy cattle.

## Objective

- To estimate heritabilities ( $h^2$ ) and to identify candidate variants of hoof and leg conformation traits in Holstein (HO) and Brown Swiss (BS)

## Material and Methods

- Sample size and phenotypes:** HO = 21,535; BS = 15,724; leg and hoof conformation corrected scores
- Genotypic data:** Imputed to WGS SNPs
- $h^2$ :** Estimated with GCTA-REML on HD SNP panel (~777k SNPs)
- GWAS:** GCTA-MLMA (additive, recessive, dominant models) with HD panel; suggestive threshold  $P < 5 \times 10^{-6}$
- Fine-mapping:** on chromosomes harboring suggestive QTLs using a second MLMA with WGS imputed SNPs,  $P < 5 \times 10^{-8}$
- Candidate variant prioritization:** 95% credible sets; variants filtered for LD with lead SNP:  $R^2 \geq 0.75$ , MAF  $\geq 0.01$ , gene function

## Results

- $h^2$ :** For HO, values ranged from 0.10 (LOC) to 0.28 (BST); for BS, from 0.10 (DHE) to 0.26 (HQU) (Table 1)

Table 1: Estimated  $h^2$  of the hoof and leg conformation traits studied.

| Trait | HO    |       | BS    |       |
|-------|-------|-------|-------|-------|
|       | $h^2$ | SE    | $h^2$ | SE    |
| BST   | 0.28  | 0.01  | -     | -     |
| RLR   | 0.21  | 0.009 | -     | -     |
| RLS   | 0.24  | 0.009 | -     | -     |
| DHE   | 0.13  | 0.008 | 0.1   | 0.009 |
| FAN   | 0.14  | 0.008 | 0.14  | 0.01  |
| LOC   | 0.1   | 0.007 | -     | -     |
| HQU   | -     | -     | 0.26  | 0.01  |
| RLV   | -     | -     | 0.21  | 0.01  |

BST = bone structure; RLR = rear leg rear view; RLS = rear leg set; DHE = deep heel; FAN = foot angle; LOC = locomotion; HQU = hock quality; RLV = rear leg side view HO = Holstein; BS = Brown Swiss

- Significant regions:** 26 QTLs were identified, including 16 in HO (7 additive, 7 dominant, 2 recessive) and 10 in BS (6 additive, 4 dominant). Among these, 10 QTLs harbored candidate variants.

Table 2: Candidate variants from additive and non-additive GWAS.

| Trait | Breed | Model     | Chr | P-log | Variant type | Gene    |
|-------|-------|-----------|-----|-------|--------------|---------|
| LOC   | HO    | additive  | 5   | 8.26  | intronic     | CACNA1C |
| LOC   | HO    | additive  | 11  | 14.13 | missense     | GCC2    |
| BST   | HO    | recessive | 22  | 16.78 | stop gained  | HYAL1   |
| DHE   | BS    | additive  | 13  | 7.7   | synonymous   | TPX2    |
| DHE   | BS    | additive  | 25  | 9.69  | upstream     | ABCA3   |
| HQU   | BS    | additive  | 3   | 7.26  | intronic     | NDUFA10 |
| HQU   | BS    | additive  | 25  | 7.01  | synonymous   | CLCN7   |
| HQU   | BS    | additive  | 26  | 7.84  | missense     | FGF8    |
| HQU   | BS    | dominant  | 6   | 10.26 | intronic     | ANKRD17 |
| HQU   | BS    | additive  | 18  | 7.17  | frameshift   | RIPOR1  |

P-log = -log of 10 of the P-value; BST = Bone Structure; LOC = Locomotion; HQU = hock quality; DHE = deep heel; HO = Holstein; BS = Brown Swiss

## Workflow of bone structure (BST) in HO

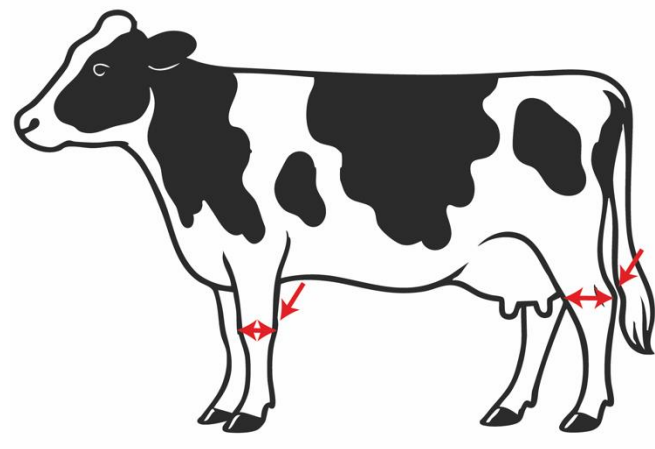


Figure 1: BST phenotype in HO, with scores from 1 (wide) to 9 (narrow)

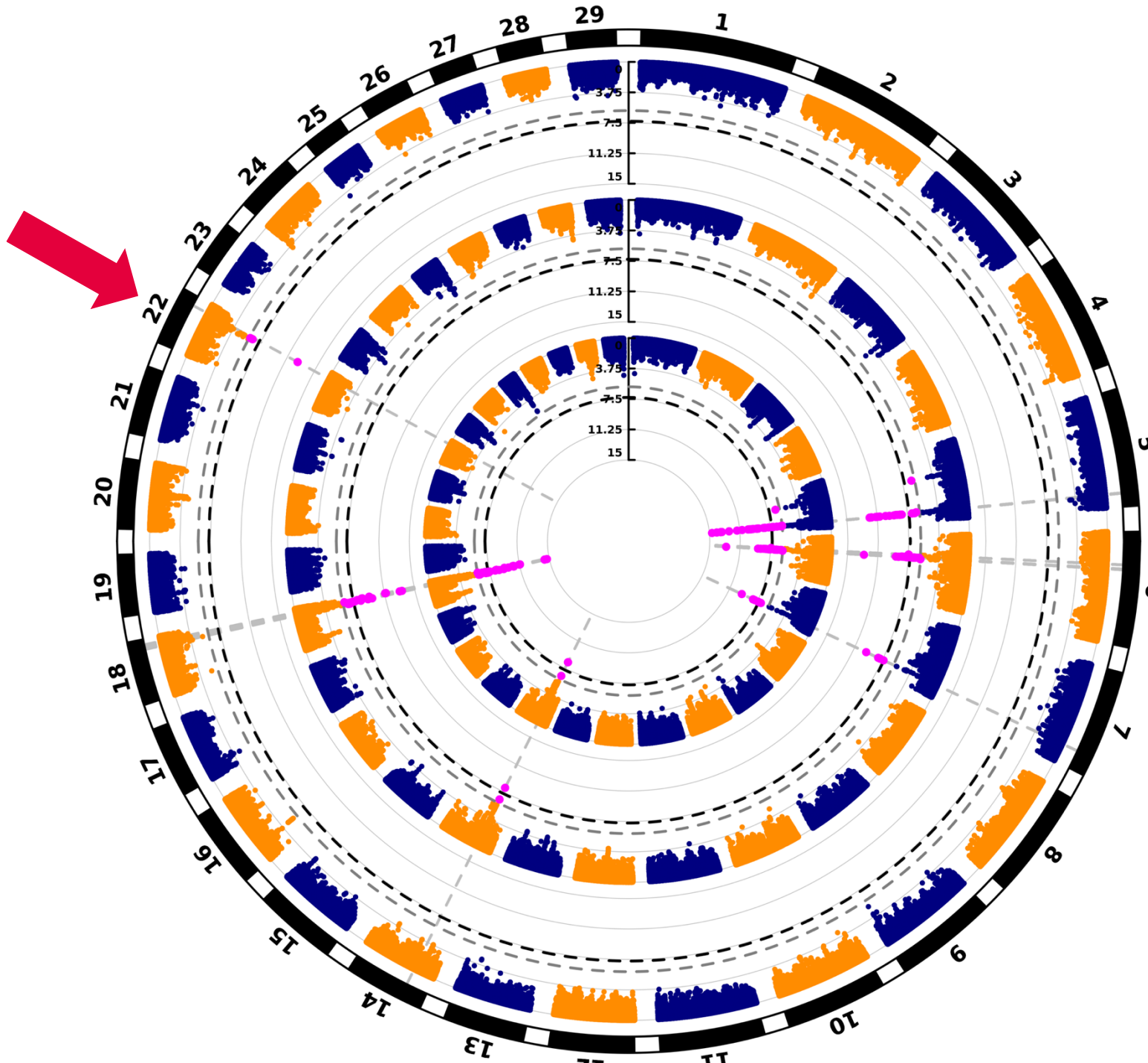


Figure 2: Circular Manhattan plot of GWAS for BST in HO for recessive (outer), dominant (middle), and additive (inner) models

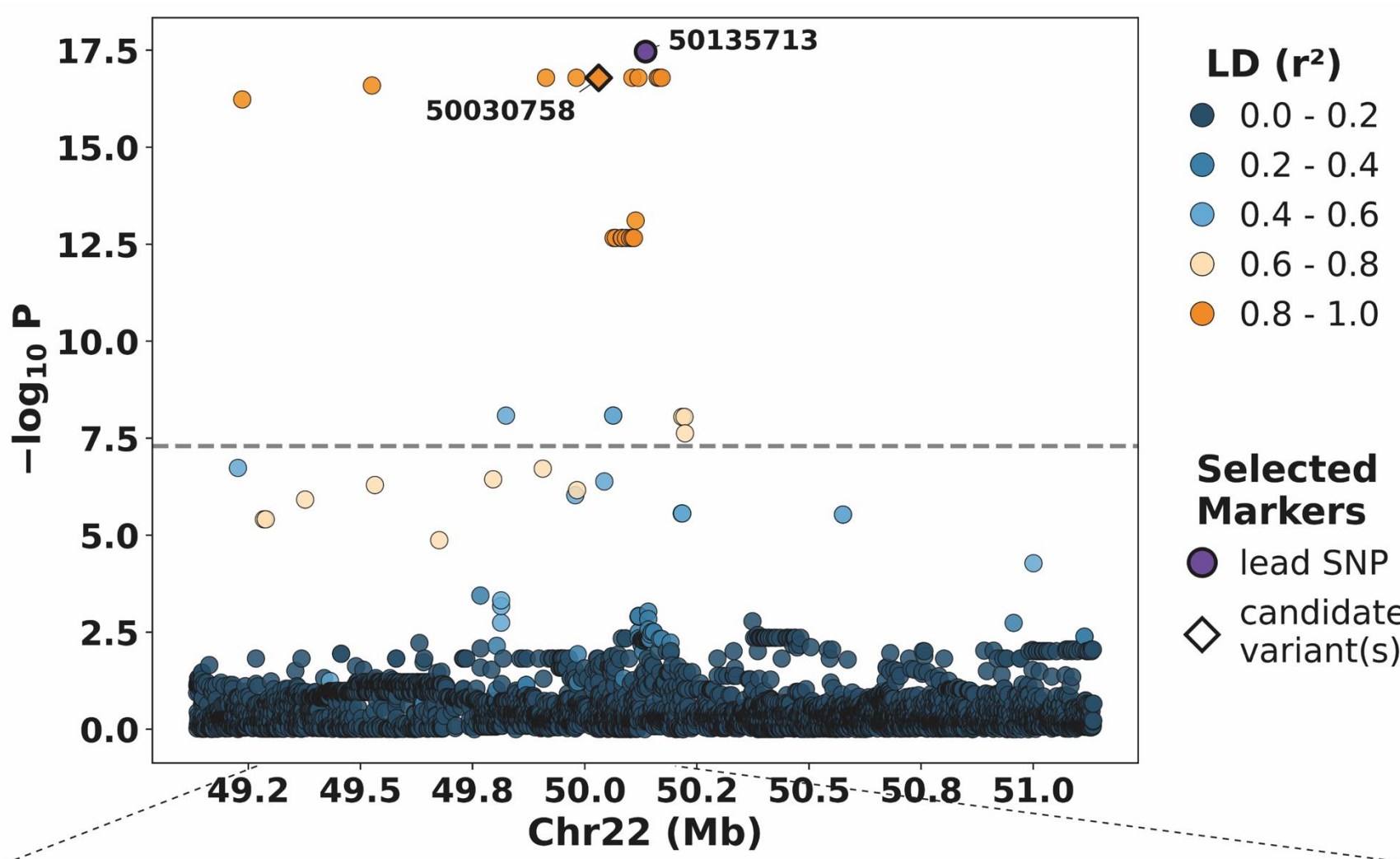


Figure 3: Regional association plot for BST in HO using the recessive model

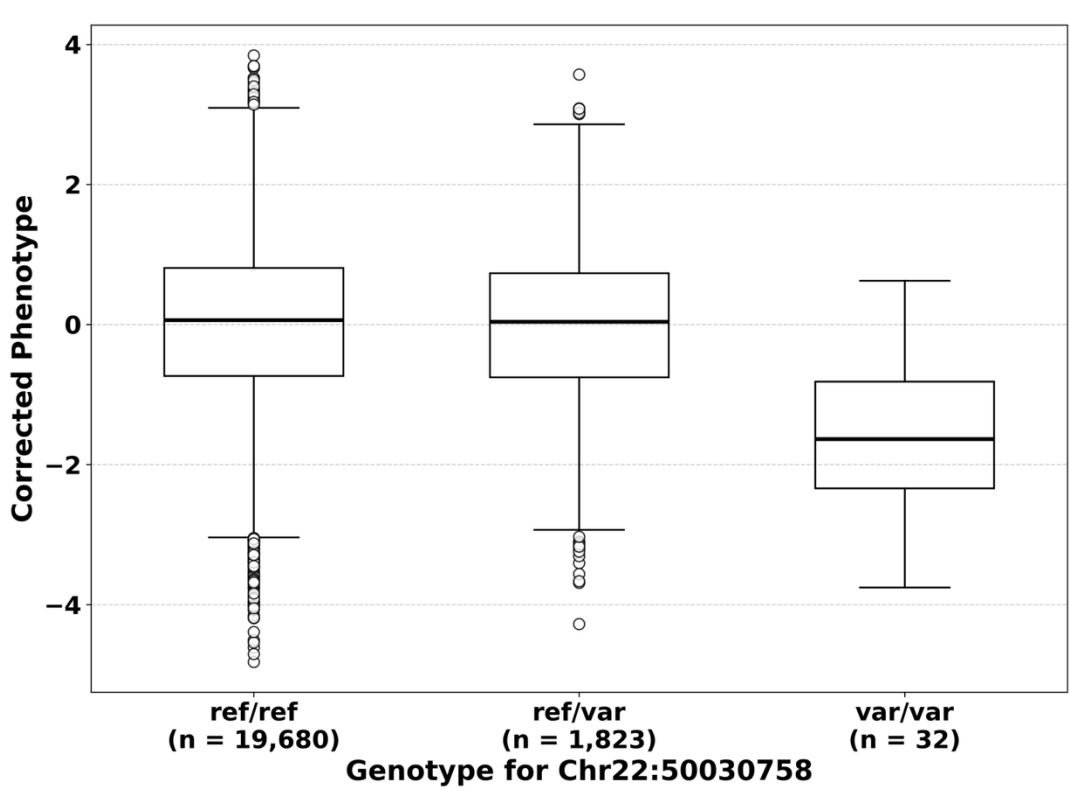


Figure 4: Corrected BST phenotypes by genotype at *HYAL1* variant in HO



Figure 5: HO cow homozygous for the alternative *HYAL1* allele showing tarsal synovitis

## Outlook and conclusion

- $h^2$ :** Moderate to low
- Plausible candidate genes:** *HYAL1*, *HDAC4*, *CACNA1C* and *CLCN7*, linked to skeletal and limb development
- HO homozygous for the *HYAL* show polysynovitis in the limb joints.

