Genome-wide copy number variants associated with calving ease and retained placenta in Holstein cows

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Background

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Understanding Calving Disorders

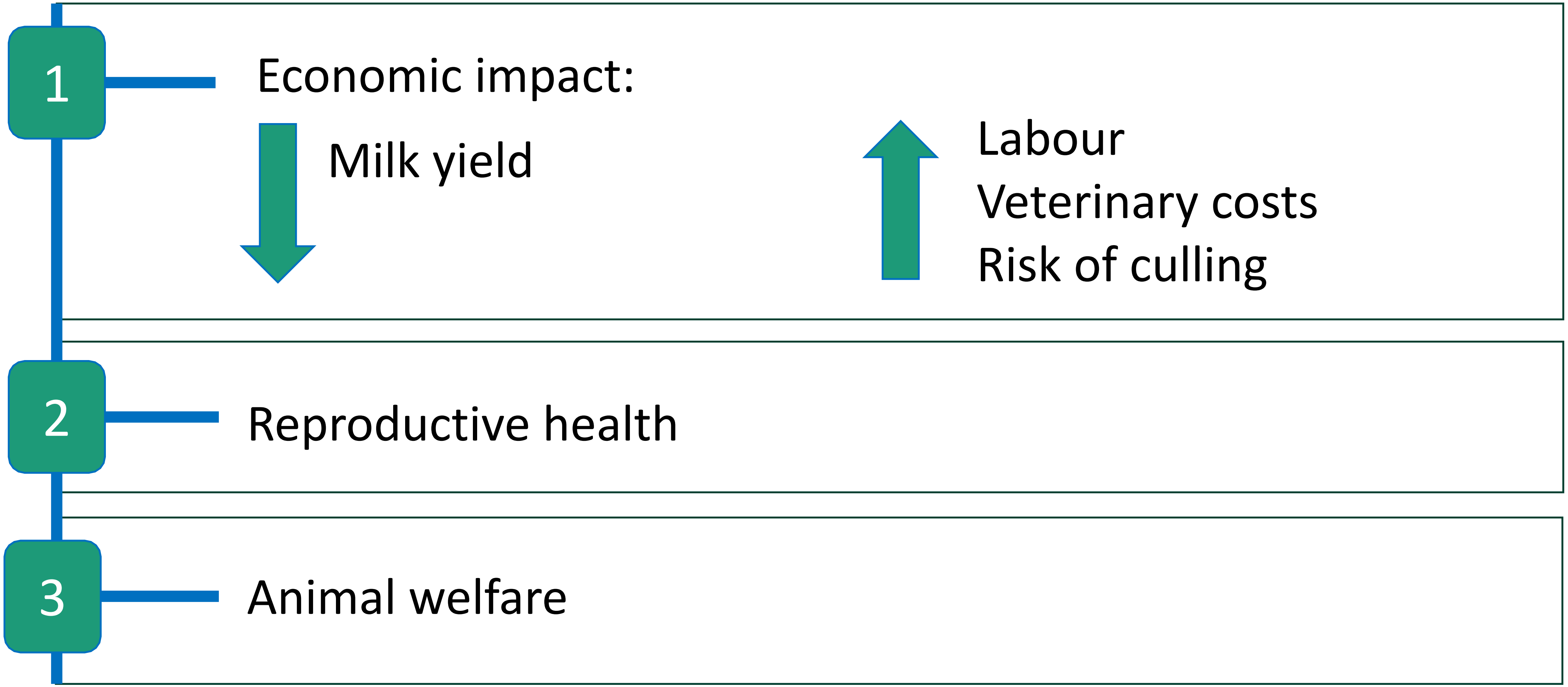
Calving ease

The ability of a cow to give birth without assistance from the farmer

Retained placenta

A condition where the cow fails to expel the fetal membranes after calving

Impact of calving disorders on dairy production



1. Economic impact:
   - ↓ Milk yield
   - ↑ Labour
   - ↑ Veterinary costs
   - ↑ Risk of culling
2. Reproductive health
3. Animal welfare

Background

Genomics: Unleashing the Potential

Fertility traits in dairy cows, have long been known for their low heritability

Inclusion of genomic information

Early identification of genetically superior animals

Increasing genetic gain

Table 1. Heritabilities for the traits analysed in the present study

Trait	Heritability
Calving Ease[1]	0.121
Calving Ease[2]	0.085
Retained Placenta[1]	0.033
Retained Placenta[2]	0.030

[1]: measured in heifers

[2]: measured in cows

Oliveira, et al., *in prep.*

Copy number variants (CNVs)
What we need to know

CNVs usually occur due to deletions or duplications of DNA segments larger than 50bp

Sudmant et al., 2015

CNVs have strong effects on gene expression as they may alter coding sequences and regulatory elements

Levy et al., 2011

CNVs can account for up to 18% of the genetic variation in gene expression

Stranger et al., 2007

Challenges in Detecting CNVs

Methodology	• The lack of formal methods to detect the region of a CNV (CNVR) makes it hard to incorporate them into genome-wide association studies (GWAS)
Sources of data	• SNP panels: May not capture the entire genomic signal • Whole-genome sequencing (WGS): High cost for large sample sizes
Validation	

Objectives

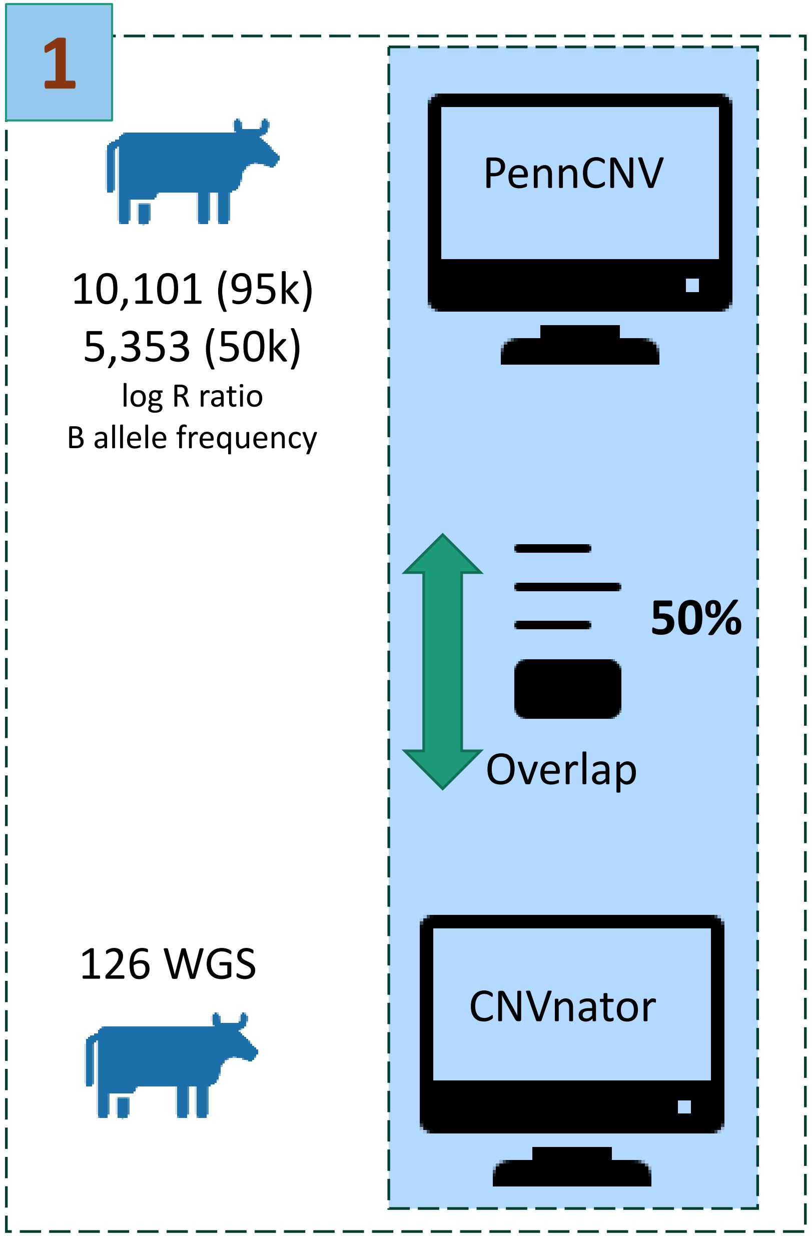
Identify CNVs using genotypes obtained from two different SNP arrays (50K and 95K)

Validate the CNVR identified using WGS data

Association between CNVRs and calving ease and retained placenta

Materials and Methods

1



2

	N	dEBV[3]
Calving ease[1]	2,464	102.76 (3.67)
Calving ease[2]	2,275	101.58 (3.15)
Retained placenta[1]	2,465	101.64 (4.67)
Retained placenta[2]	2,461	99.78 (4.01)

[1]: measured in heifers; [2]: measured in cows; [1]: dEBV mean (SD)

3

Theoretical reliability > 0.1

CNVRs identified >1% of animals

Linear regression CNVRs X dEBVs

Population stratification

False discovery rate < 0.05

CNV identification – CNVR creation

Pseudo-phenotypes

Association analyses

Association Analyses

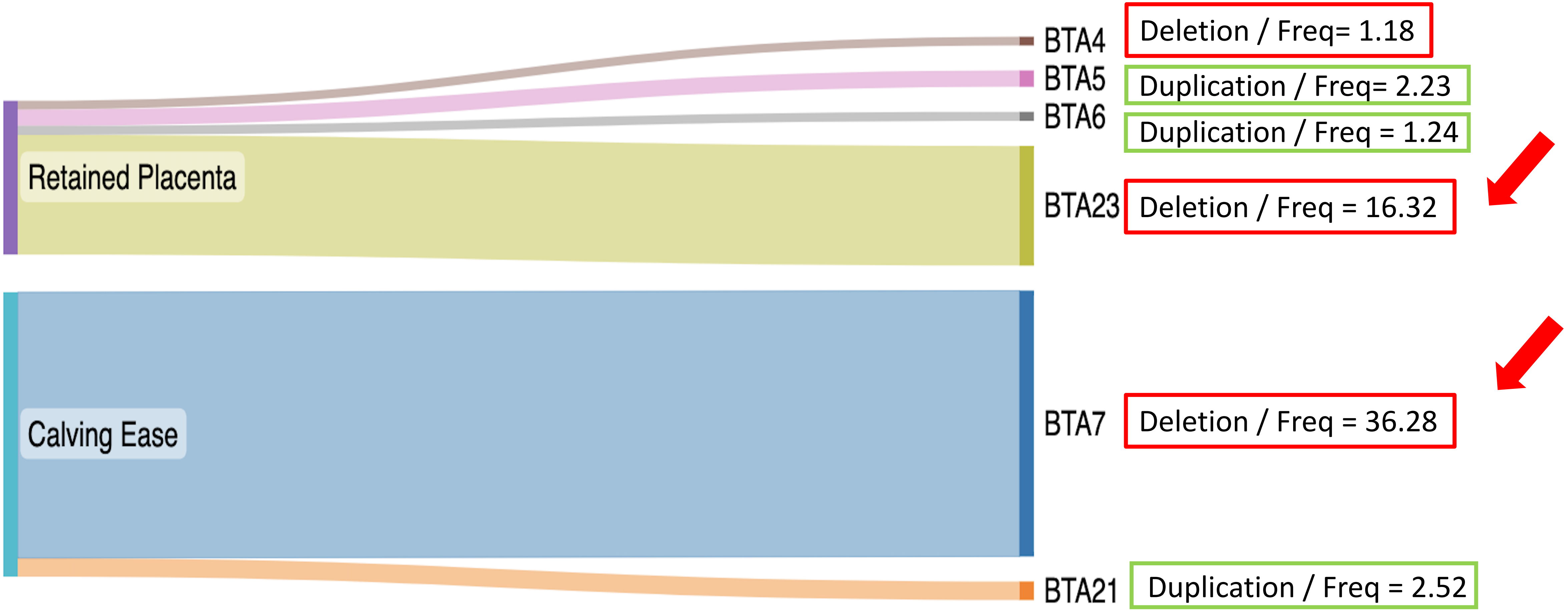
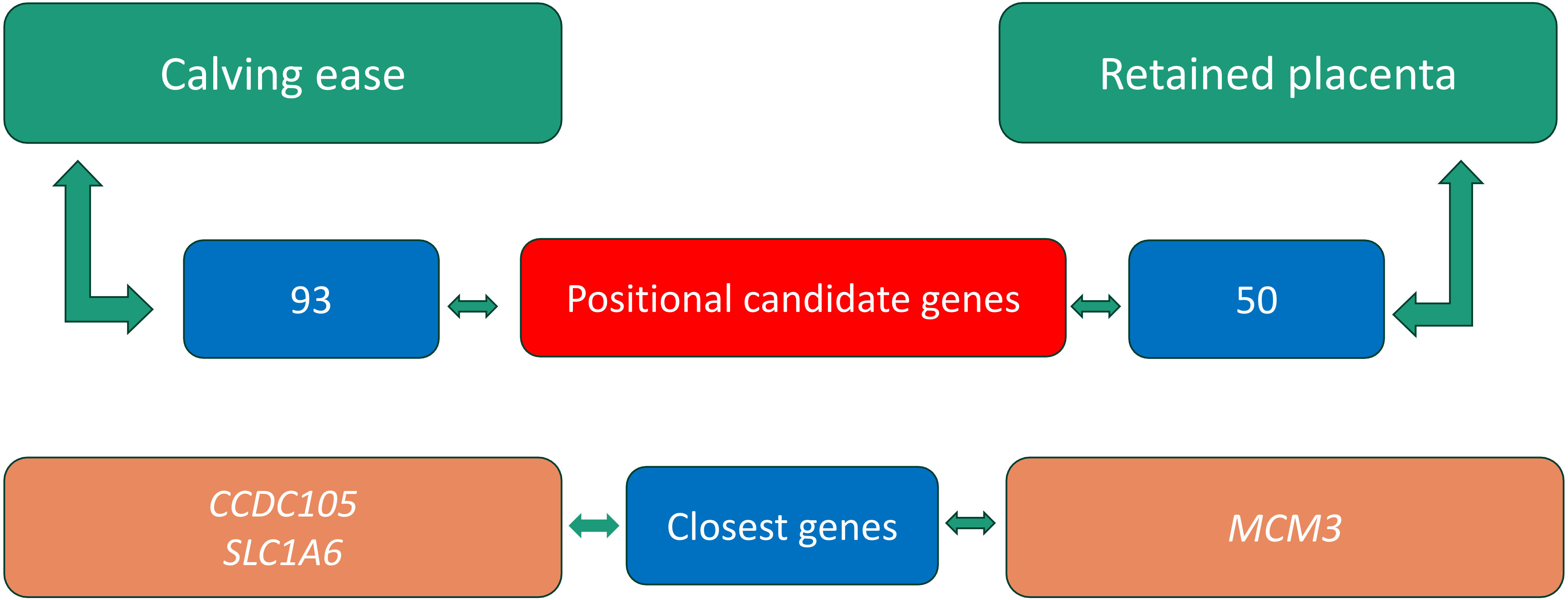


Figure 1. Sankey diagram illustrating the relationship between CNVRs and the analysed traits, along with the frequency of significantly ($P< 0.05$) associated CNVRs across chromosomes.

Candidate genes identified



Calving ease

Retained placenta

93

Positional candidate genes

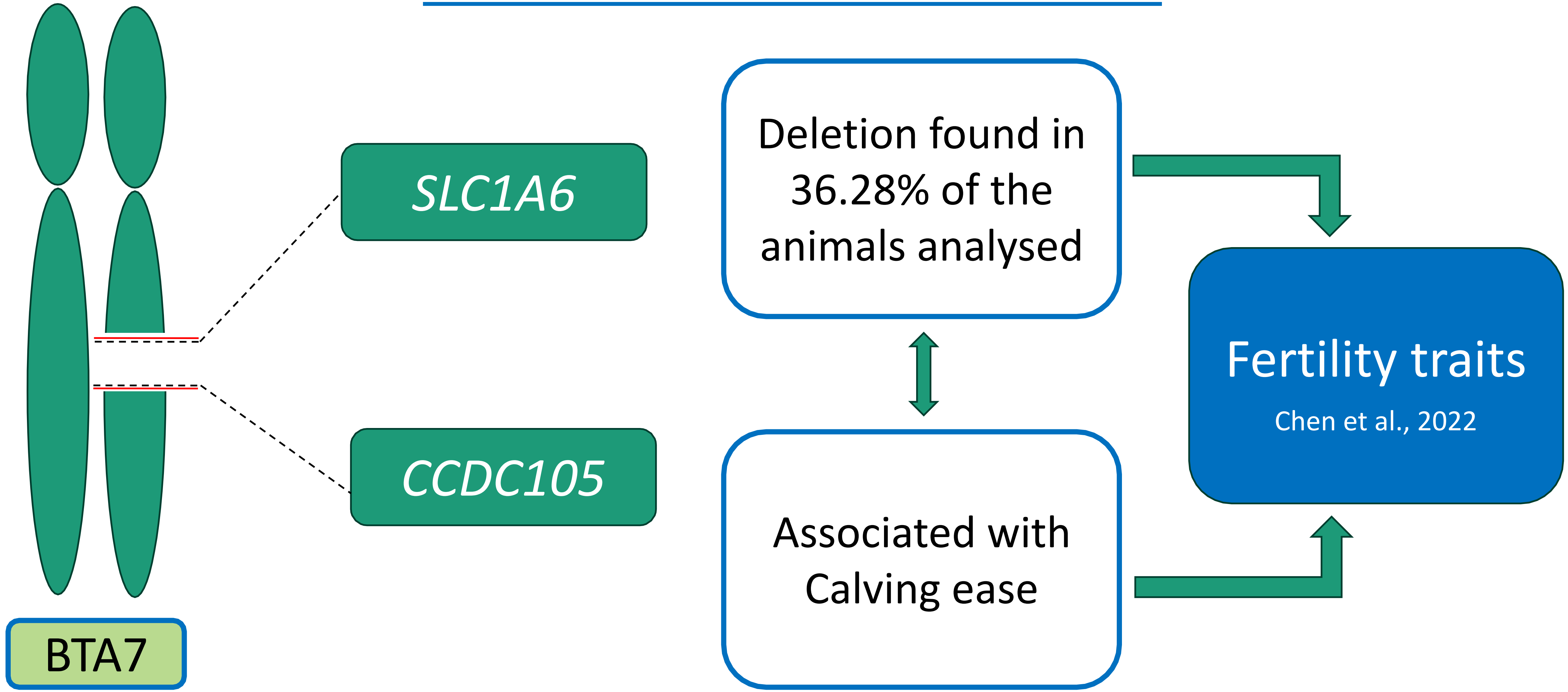
50

CCDC105
SLC1A6

Closest genes

MCM3

Calving Ease



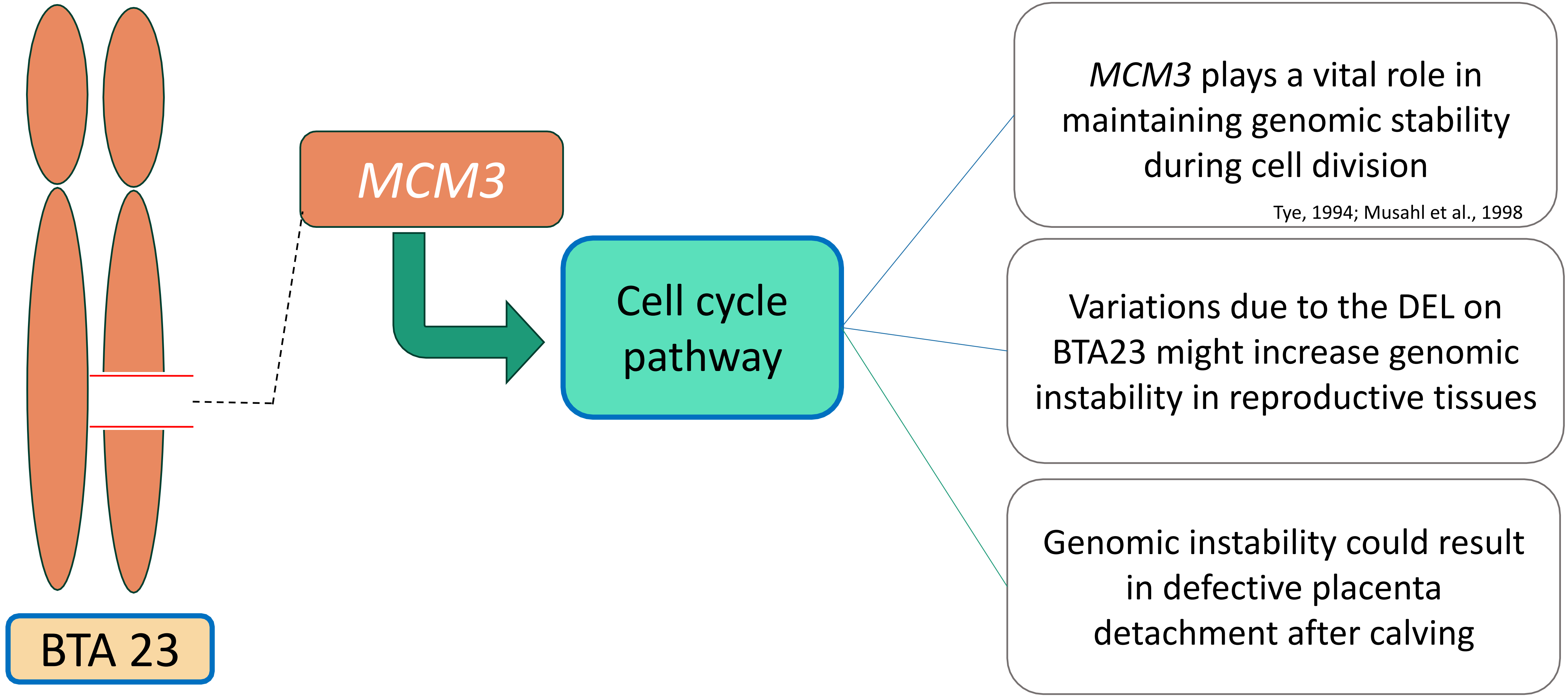
Deletion found in 36.28% of the animals analysed

Associated with Calving ease

Fertility traits

Chen et al., 2022

Retained Placenta



BTA 23

MCM3

Cell cycle pathway

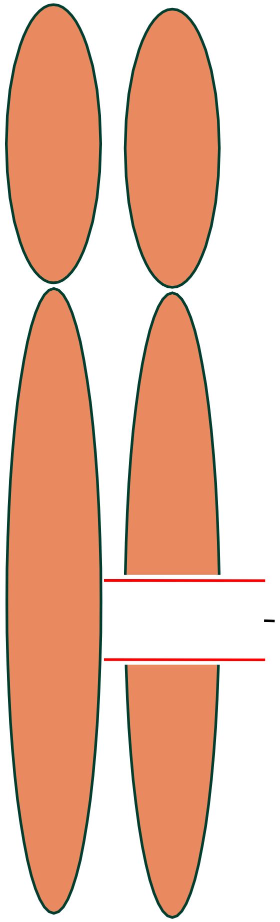
MCM3 plays a vital role in maintaining genomic stability during cell division

Tye, 1994; Musahl et al., 1998

Variations due to the DEL on BTA23 might increase genomic instability in reproductive tissues

Genomic instability could result in defective placenta detachment after calving

Retained Placenta



BTA 23

MCM3

Progesterone-mediated oocyte maturation

Progesterone imbalances or deficiencies can affect oocyte maturation, thereby affecting fertility as a consequence

López-Gatius and Garcia-Ispierto, 2022

Decline in progesterone levels prior to uterine contraction during parturition is a crucial process

Janszen et al., 1990; Mesiano, 2022

Disturbances in hormonal balance can affect placenta expulsion

Conclusions

CNV Insights:	Valuable insights for low heritable traits in dairy cattle
High Frequency Associations:	CNVRs on BTA7 and BTA23
Improving EBVs:	Incorporating this information might increase the accuracy of genomic selection
Advancing the Dairy Industry:	Strategy for healthier and more productive cattle
Future Directions:	Further investigations are needed to fully understand the implications of these CNVRs

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