



# from Mendel to Genom



- GENOMIC SELECTION
- SNP-BASED INBREEDING MANAGEMENT
- SELECTION ON POLLED LOCUS
- BETA CASEIN A2
  - SNP-BASED MONITORING OF RECESSIVES

FH2

- THROMBOPATHIA
- ARACHNOMELIA

FH4 FH5 BH2

EARLY DETECTION OF  
NOVEL MUTATIONS

LONGITUDINAL STUDIES

CASE-CONTROL STUDIES

GENOTYPE-BASED MONITORING

DETECTION OF CRYPTIC MUTATIONS



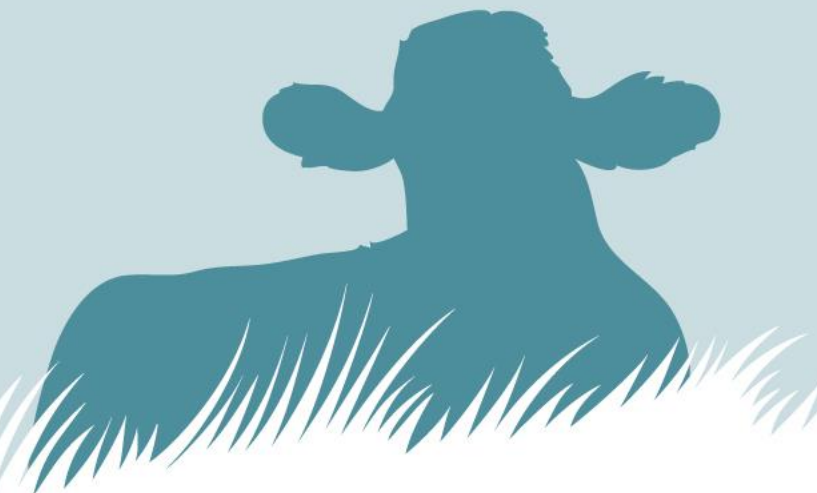


# SNP-Based Monitoring of Mendelian Traits in Fleckvieh Cattle: From Genetic Defects to Beneficial Variants

*Schwarzenbacher H., Himmelbauer J., Fuerst C.*

ZuchtData EDV-Dienstleistungen GmbH, 1200 Vienna, Austria

World Simmental-Fleckvieh Congress  
Brno, Czech Republic, 16<sup>th</sup>/21<sup>st</sup> September 2026



# Outline



01 Genomic toolbox to handle Mendelian traits

02 Desirable genetic variants

03 Unfavourable variants

04 SNP-based monitoring

05 Take-home message



*The ,novel‘ genomic toolbox  
to manage genetic variants*



# Case-Control Study

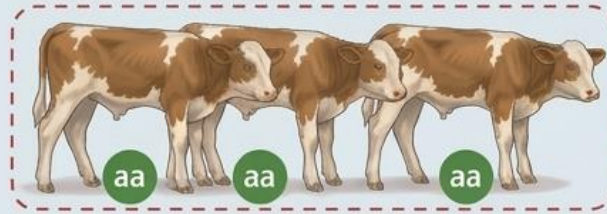
## Case-Control Study in Fleckvieh – Monogenic Recessive Lethal Factor

Comparison of affected calves (Cases) with healthy control calves (Controls)

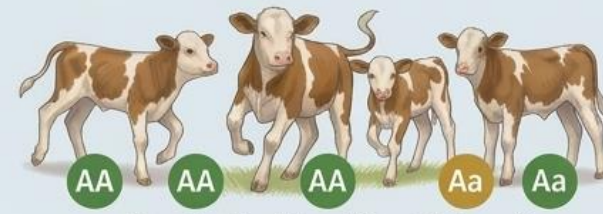
1

### Phenotyping: Cases vs. Controls

Distribution of trait carriers (sick calves) and healthy control animals based on external traits (phenotype).



Cases (Sick Calves)



Controls (Healthy Calves)

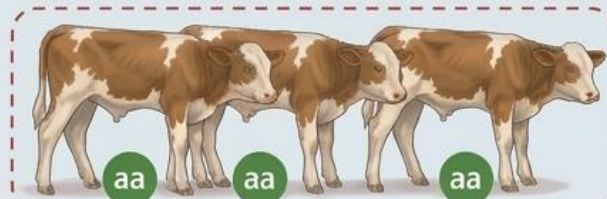
# Case-Control Study

## Case-Control Study in Fleckvieh – Monogenic Recessive Lethal Factor

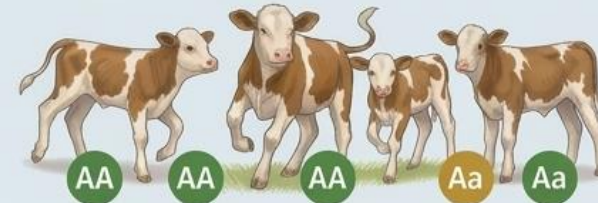
Comparison of affected calves (Cases) with healthy control calves (Controls)

### 1 Phenotyping: Cases vs. Controls

Distribution of trait carriers (sick calves) and healthy control animals based on external traits (phenotype).



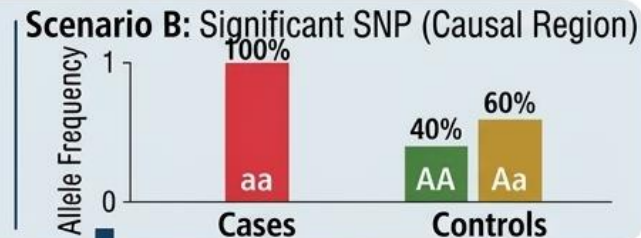
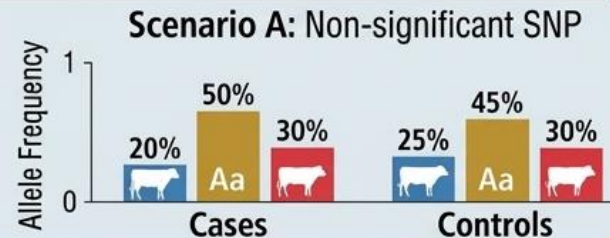
Cases (Sick Calves)



Controls (Healthy Calves)

### 2 SNP Genotyping (Comparison)

Comparison of two exemplary SNP scenarios and their association with the phenotype.



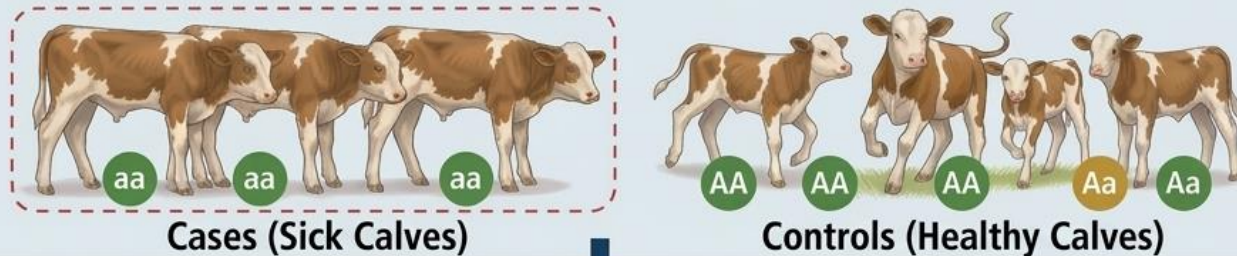
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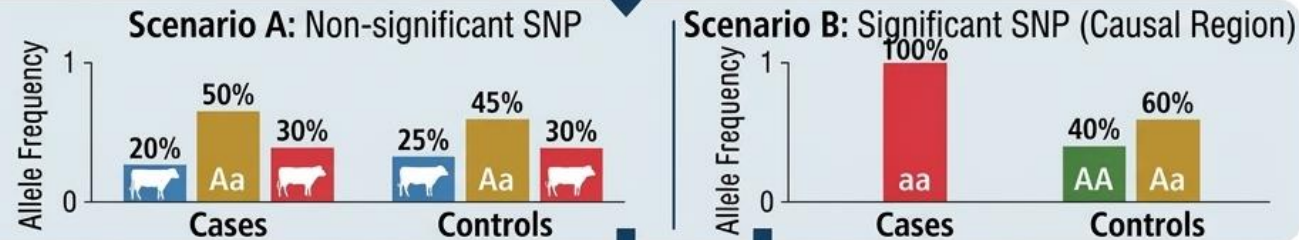
### 1 Phenotyping: Cases vs. Controls

Distribution of trait carriers (sick calves) and healthy control animals based on external traits (phenotype).



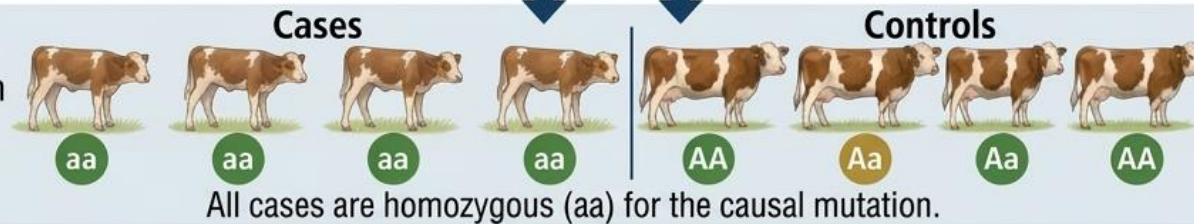
### 2 SNP Genotyping (Comparison)

Comparison of two exemplary SNP scenarios and their association with the phenotype.



### 3 Proof of Recessive Inheritance

Identification of the causal mutation through co-segregation analysis. Only homozygous recessive animals (aa) display the lethal phenotype.



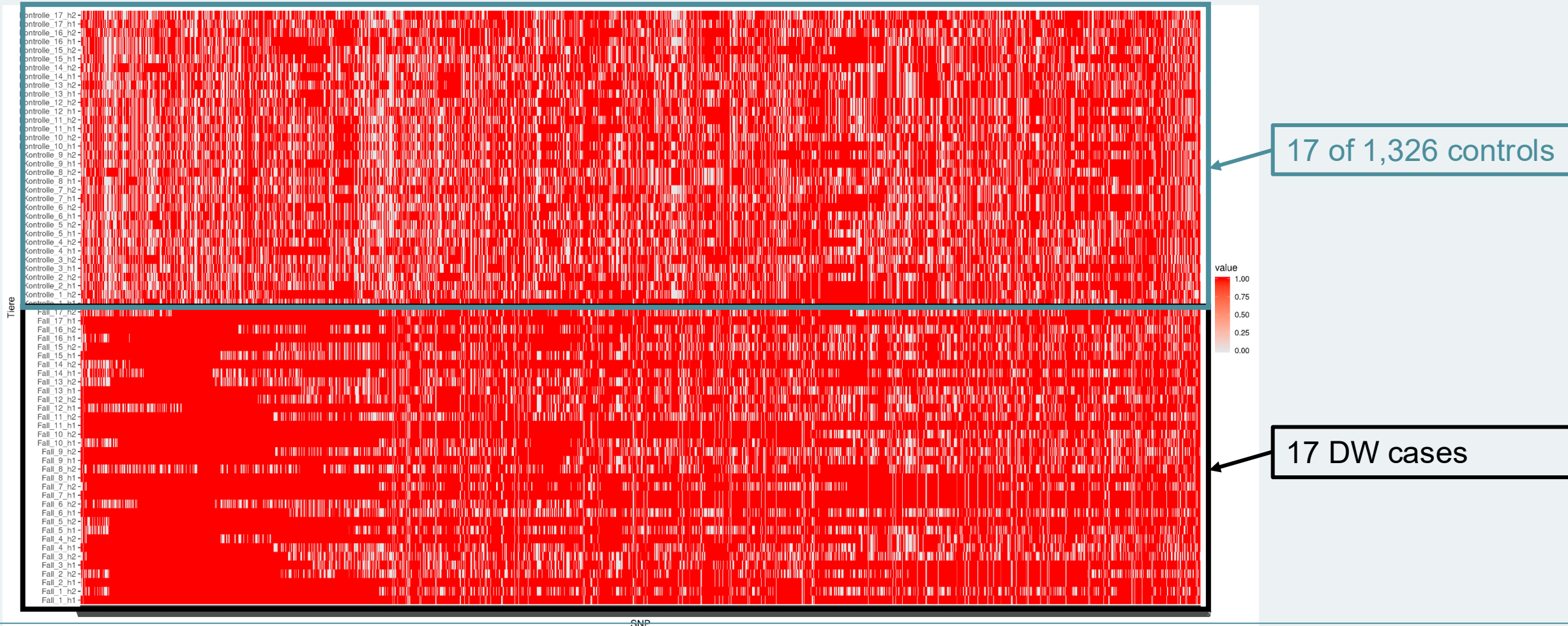
#### Conclusion:

Significant SNP shows enrichment of aa in cases and absence of aa in controls;  
causal mutation identified.

*Illustration generated with Gemini, 2026*

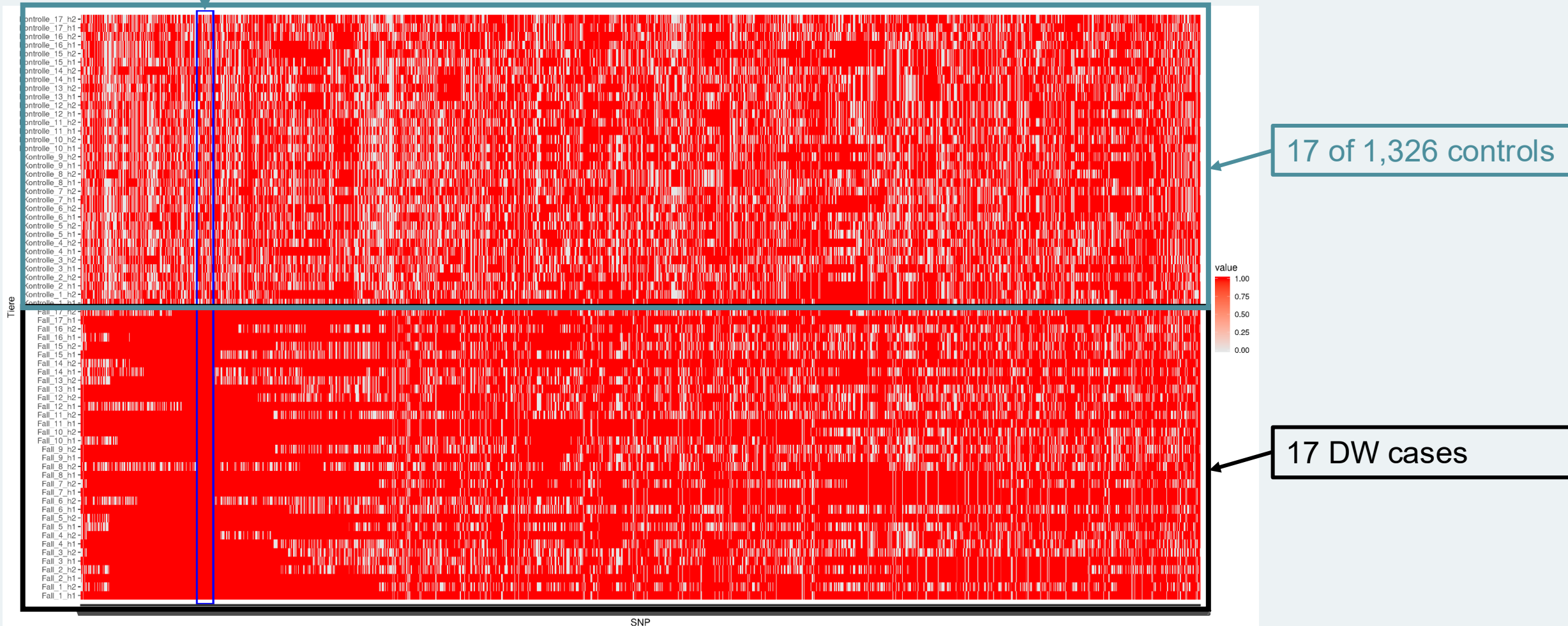
# Dwarfism in Fleckvieh

Chromosome 3, 2,005 SNP, 17 DW-cases, 1,326 controls



# Dwarfism in Fleckvieh

**Haplotype:** *Homozygous in all cases but never on controls*



# Genotype-based monitoring

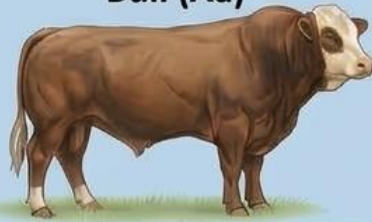
## VanRaden et al. (2008) – Genotype-Based Monitoring

Gene loci with underrepresentation of homozygous genotypes relative to allele frequency

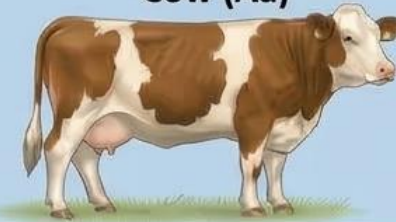
### 1 Initial Situation

For each SNP, genotype data (AA, AB, BB) and allele frequencies ( $p$ ,  $q$ ) are evaluated.

Bull (Aa)



Cow (Aa)



# Genotype-based monitoring

## VanRaden et al. (2008) – Genotype-Based Monitoring

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### 1 Initial Situation

For each SNP, genotype data (AA, AB, BB) and allele frequencies ( $p$ ,  $q$ ) are evaluated.

Bull (Aa)



Cow (Aa)



### 2 Expected Genotypes after Mating

Under Hardy-Weinberg conditions, expected genotype frequencies are calculated based on allele frequencies.

AA

25 %  
( $p^2$ )

Aa

50 %  
( $2pq$ )

aa

25 %  
( $q^2$ )

# Genotype-based monitoring

## VanRaden et al. (2008) – Genotype-Based Monitoring

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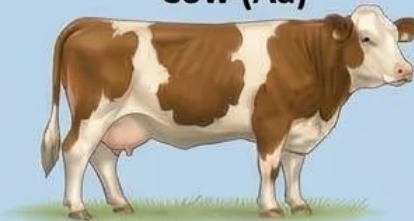
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Bull (Aa)



Cow (Aa)



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Under Hardy-Weinberg conditions, expected genotype frequencies are calculated based on allele frequencies.

AA  
25 %  
( $p^2$ )

Aa  
50 %  
( $2pq$ )

aa  
25 %  
( $q^2$ )



### 3 Observation in Genotyped Population

The actual observed genotype frequencies are compared with the expected values.



AA



AA



AA



Aa



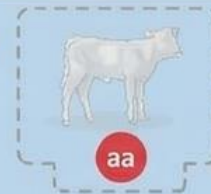
Aa



Aa



Aa



aa

No homozygous aa animals observed

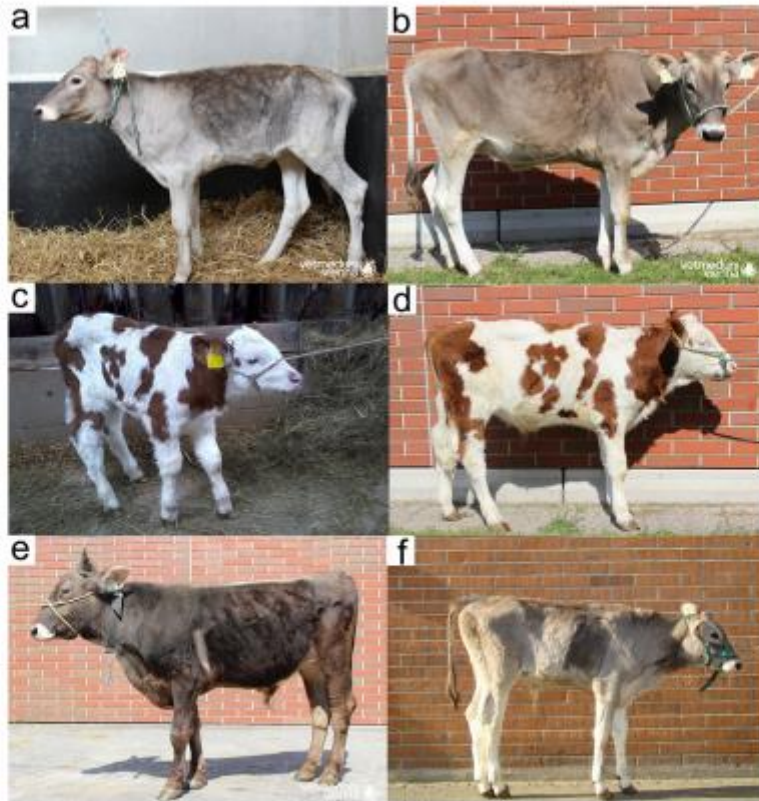


### Conclusion:

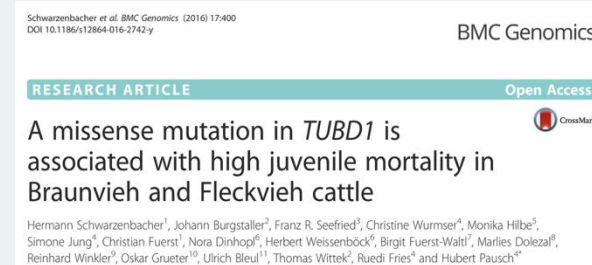
Haplotypes with likely recessive lethal alleles are identifiable by underrepresented homozygous genotypes.

*Illustration generated with Gemini, 2026*

# Example: Brown Swiss Haplotype 2: (B2)



**Fig. 2** Phenotypic manifestation of homozygosity for BH2 in four animals. Pictures of BV2 (a, b), FV1 (c, d), BV5 (e) and BV4 (f) were taken at the time of admission in the animal clinic (a, c) and shortly before euthanasia (b, d, e, f), respectively. A detailed description of the disease manifestations is available in Table 4

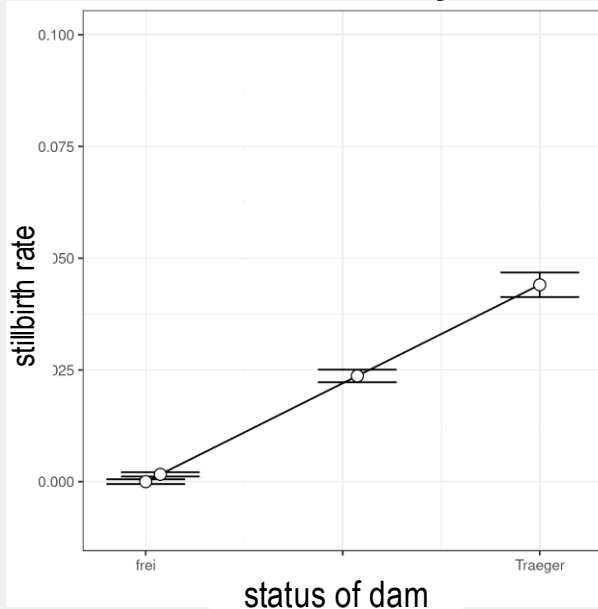


segregates also in Fleckvieh ...  
below-average birth weight  
higher stillbirth rate  
markedly increased mortality  
during the first seven weeks of life  
typical clinical signs are **nasal discharge and pneumonia**

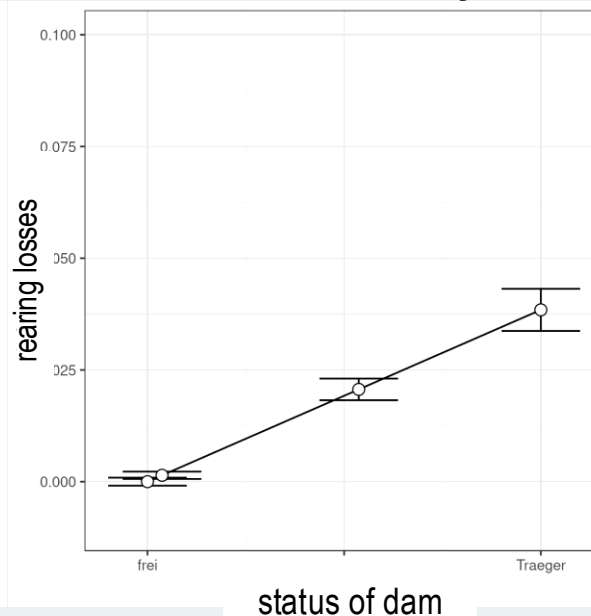
# B2 risk-matings

Risk matings with B2-carrier bulls,  
effect of B2-status of dam on still birth and rearing losses

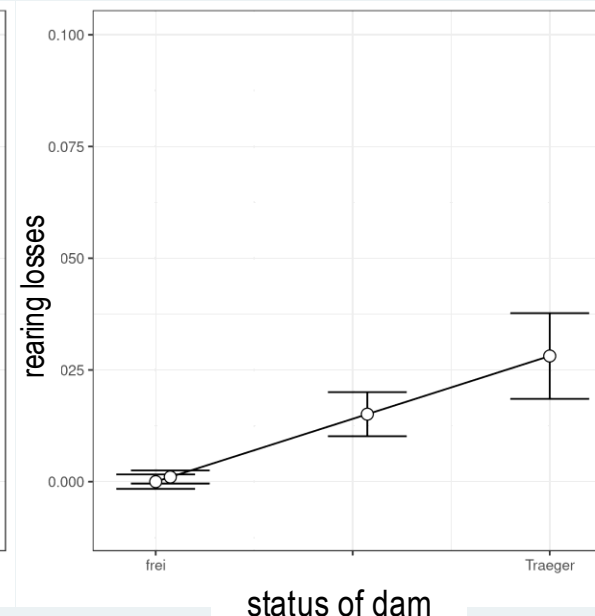
still birth rate  
0 to 2<sup>nd</sup> day



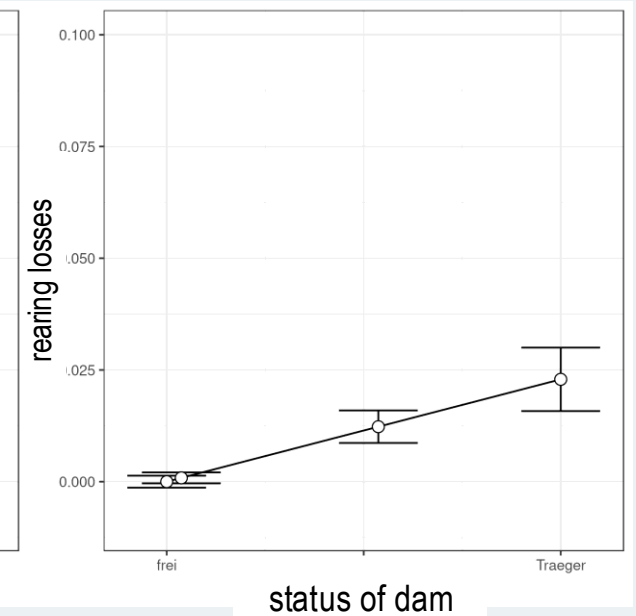
rearing losses  
3<sup>rd</sup> to 30<sup>th</sup> day



rearing losses  
31<sup>st</sup> d.-10 m. males



rearing losses  
31<sup>st</sup> d.-15 m. females



# Longitudinal Study

## Detection of Cryptic Mutations in Fleckvieh Cattle

Shift in Genotype Frequencies Across Life Stages & Phenotypic Causes (e.g. Besnard et al., 2024)

### 1. Genotype Shift Across Life Stages

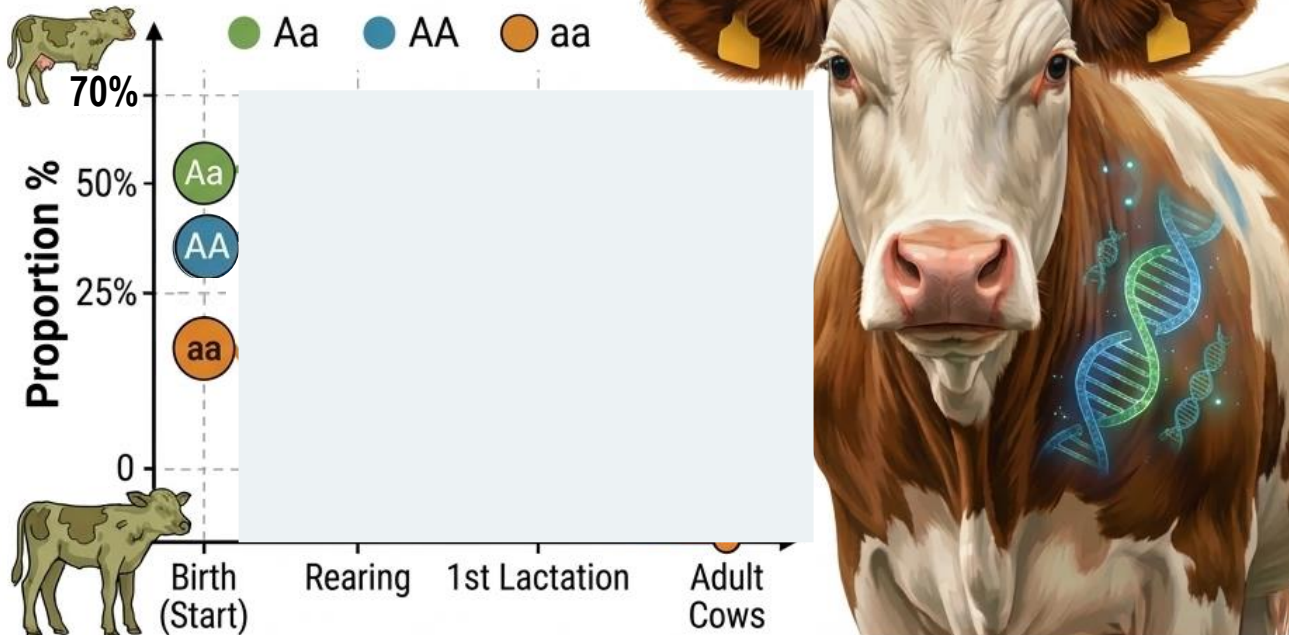
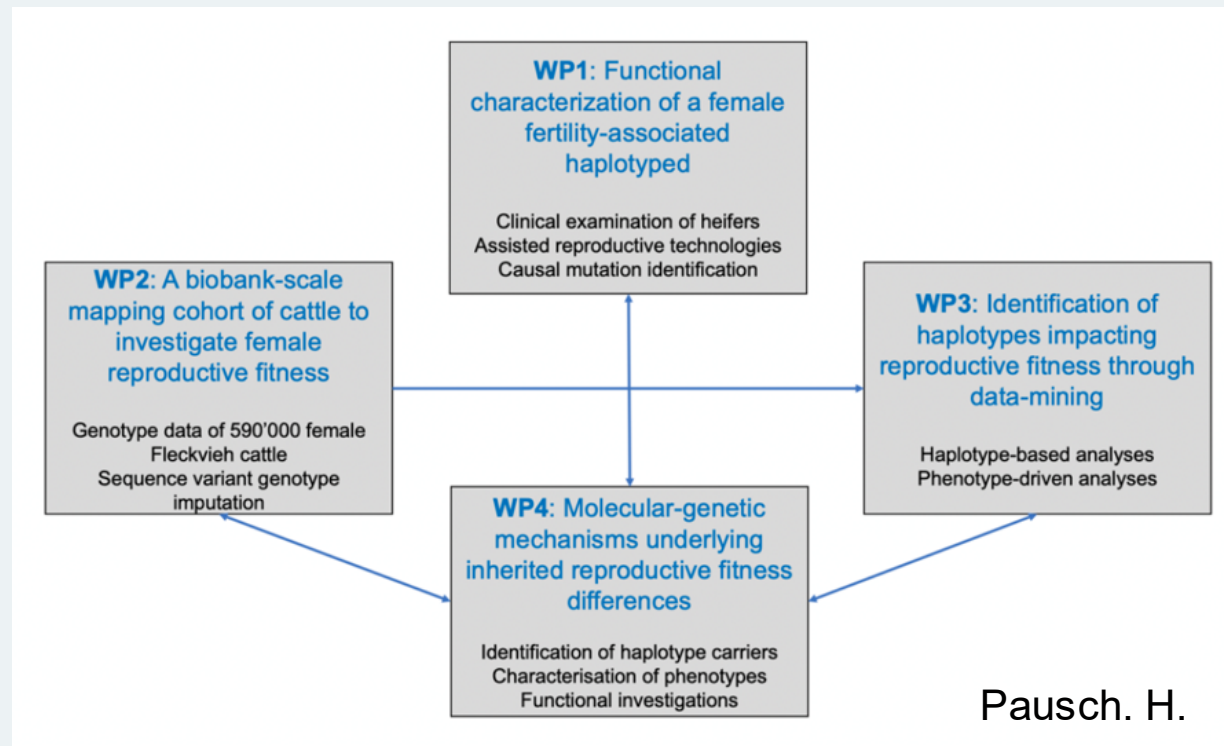


Illustration generated with Gemini, 2026

# Longitudinal Study

*Research Project, ETH Zürich, Prof. Pausch and colleagues:*

**“A data-mining approach to detect genomic regions impacting female reproductive fitness in cattle.”**



variants that lead to losses in **later life** come with **higher costs!**

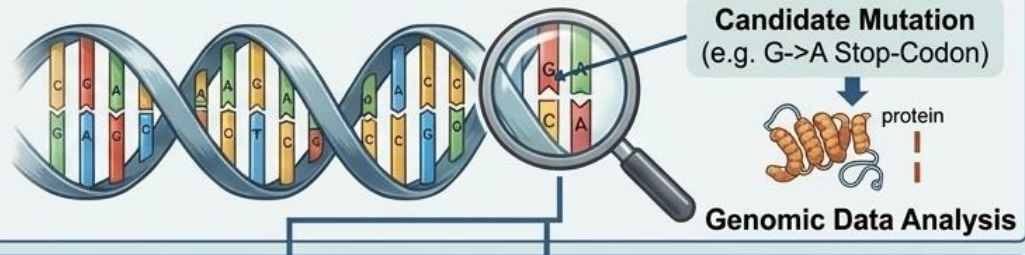
# Reverse Genetics

## Reverse Genetics in Fleckvieh – From Mutation to Phenotype

1

### DNA Sequencing & Variant Identification

Investigation of Fleckvieh genome data to discover potential loss-of-function mutations (e.g. Loss-of-Function).

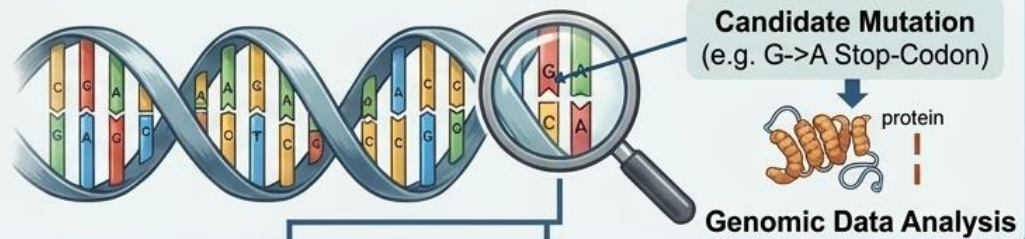


# Reverse Genetics

## Reverse Genetics in Fleckvieh – From Mutation to Phenotype

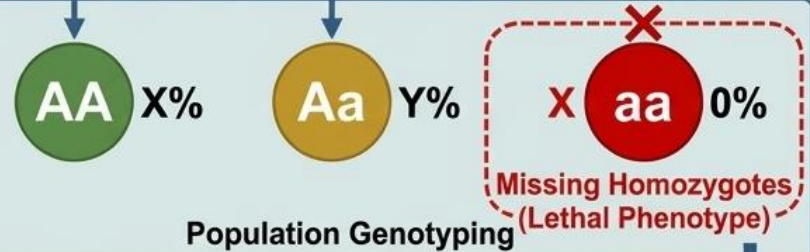
### 1 DNA Sequencing & Variant Identification

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### 2 Genotype Classification in Population

Checking the frequencies of AA, Aa, and aa animals (homozygotes) in a representative population.

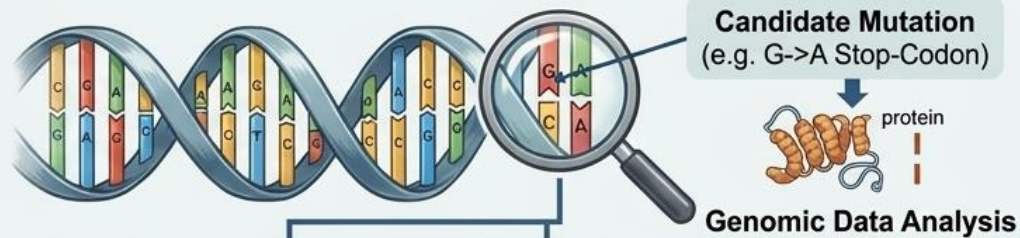


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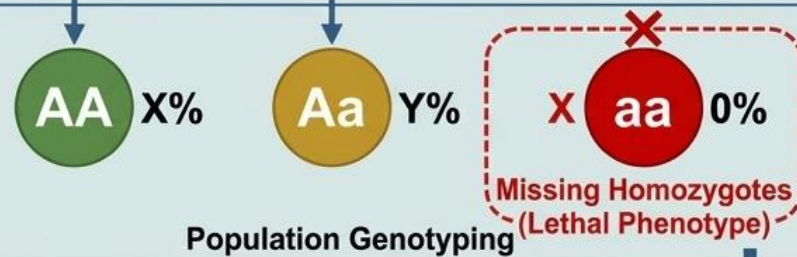
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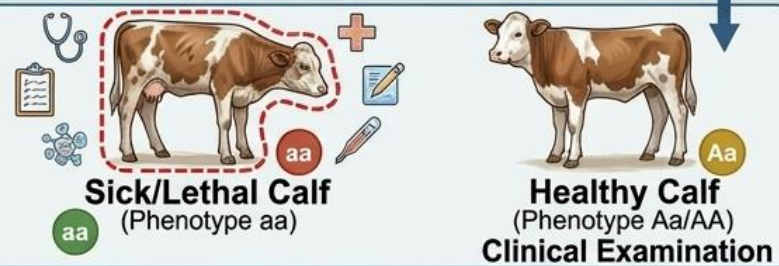
### 2 Genotype Classification in Population

Checking the frequencies of AA, Aa, and aa animals (homozygotes) in a representative population.



### 3 Phenotypic Validation (Reverse Search)

Clinical evaluation and phenotyping of rare homozygous (aa) or heterozygous (Aa) offspring for symptom documentation.



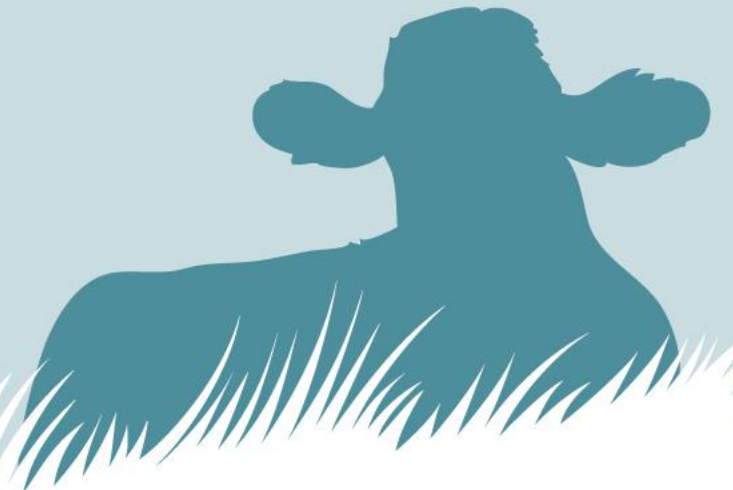
**Conclusion:** Reverse genetics first identifies functional DNA variants and subsequently investigates their phenotypic impact in the Fleckvieh population.

*Illustration  
generated with  
Gemini, 2026*

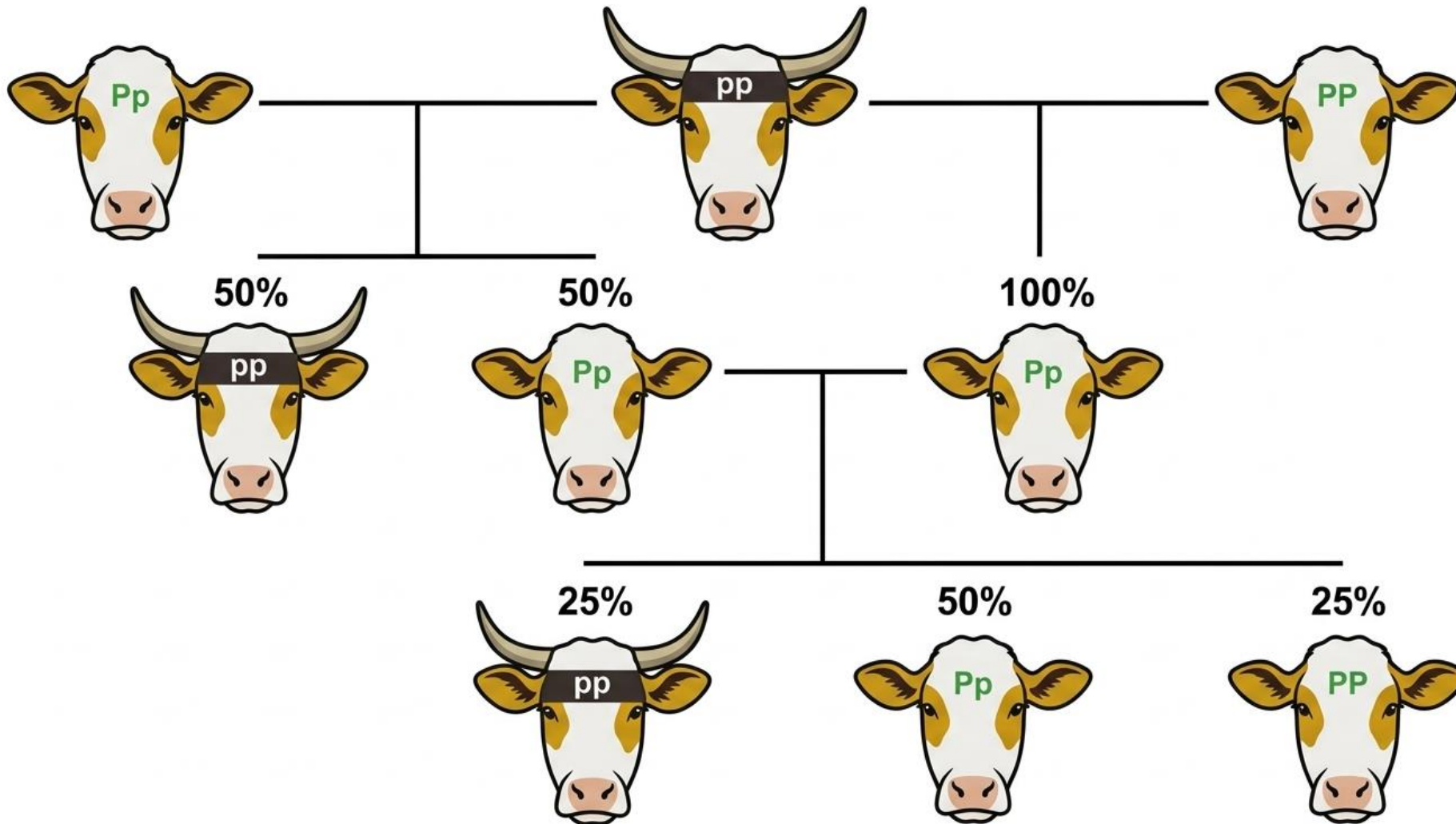


# *Desirable Genetic Variants*

*Polled*  
 *$\kappa$ -Casein*  
 *$\beta$ -Casein*



# Inheritance of polled



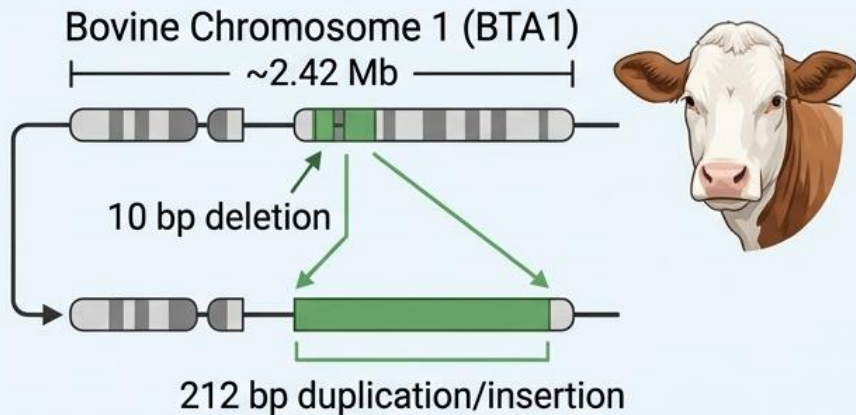
*Illustration generated with Gemini, 2026*

# The genetics of polled

## Genetics of Polledness: Celtic (PC) vs. Friesian (PF) Mutations (BTA1 POLLED Locus)

### Polled Celtic Variant (PC)

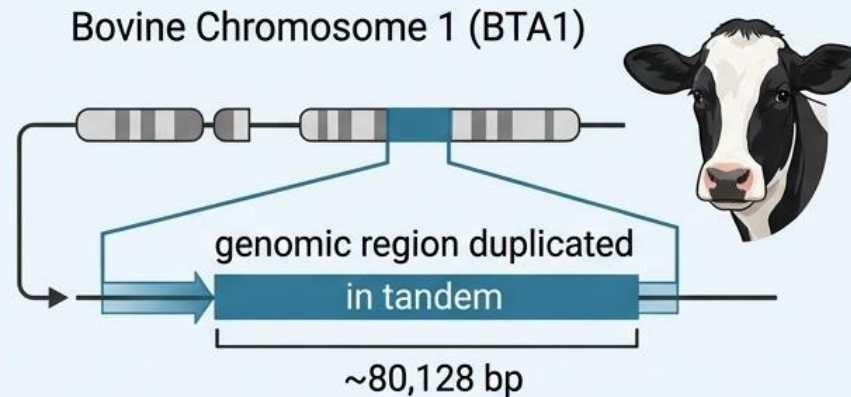
#### 212 bp Complex Indel (Insertion-Deletion)



- Commonly found in Fleckvieh, Simmental, Angus, and Hereford.

### Polled Friesian Variant (PF)

#### ~80 kb Tandem Duplication



- Commonly found in Holstein-Friesian and Fleckvieh lines.

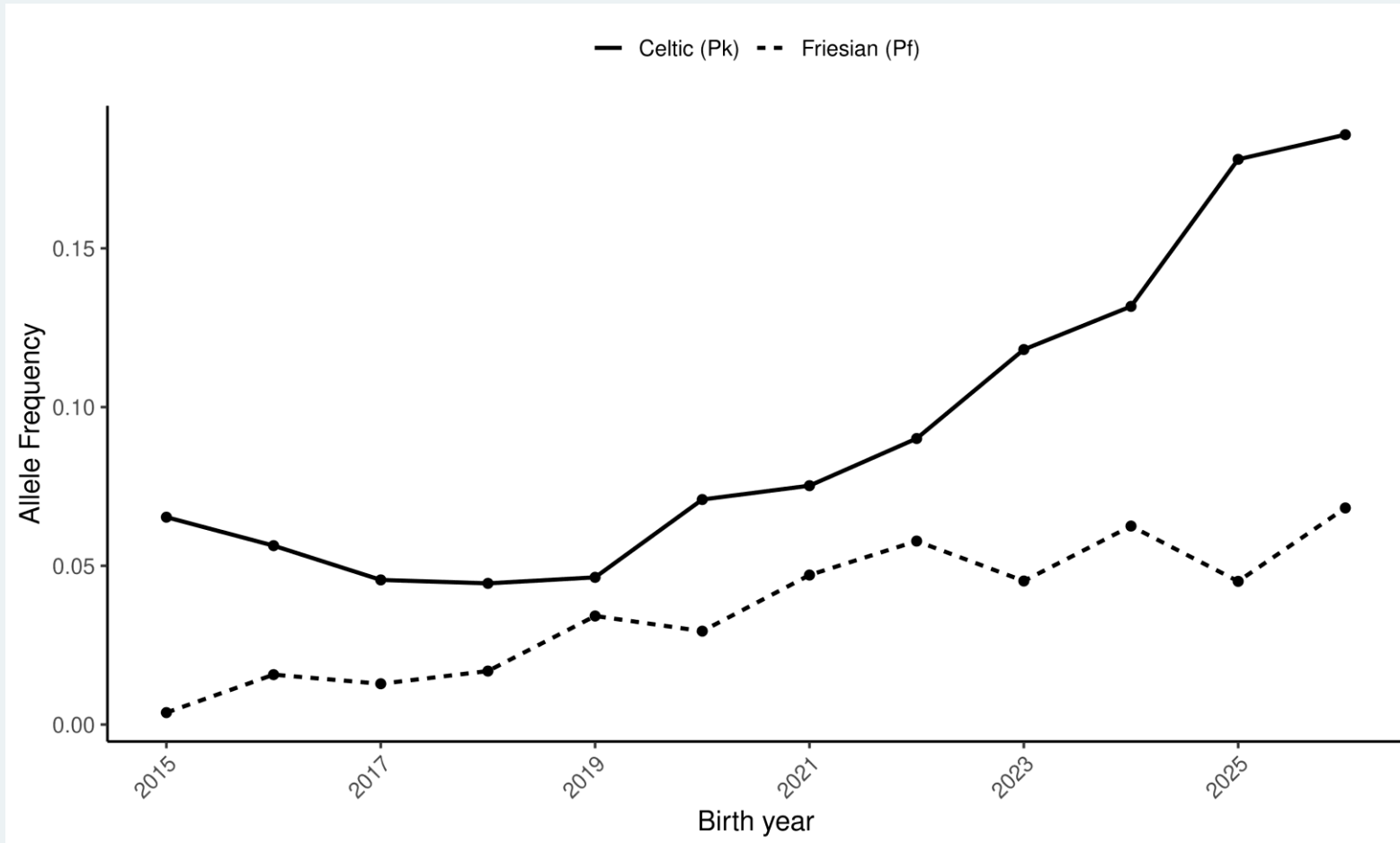


**Conclusion:** Both PC and PF mutations lie on Chromosome 1 (POLLED locus) and show Autosomal Dominant inheritance, resulting in a naturally hornless phenotype.

*Illustration generated  
with Gemini, 2026*

# The genetics of polled

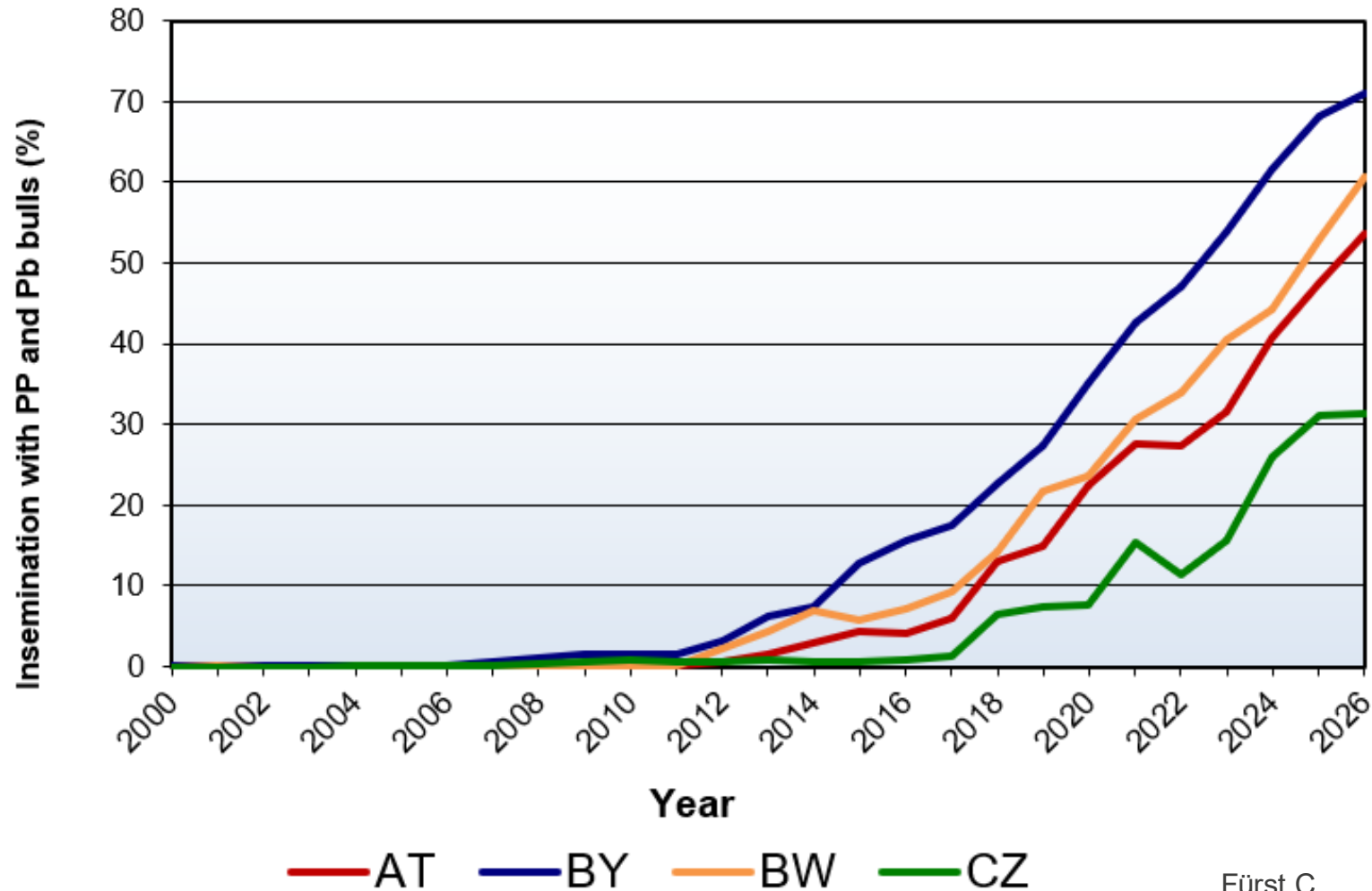
## Polled allele frequencies in female genotyped Fleckvieh population



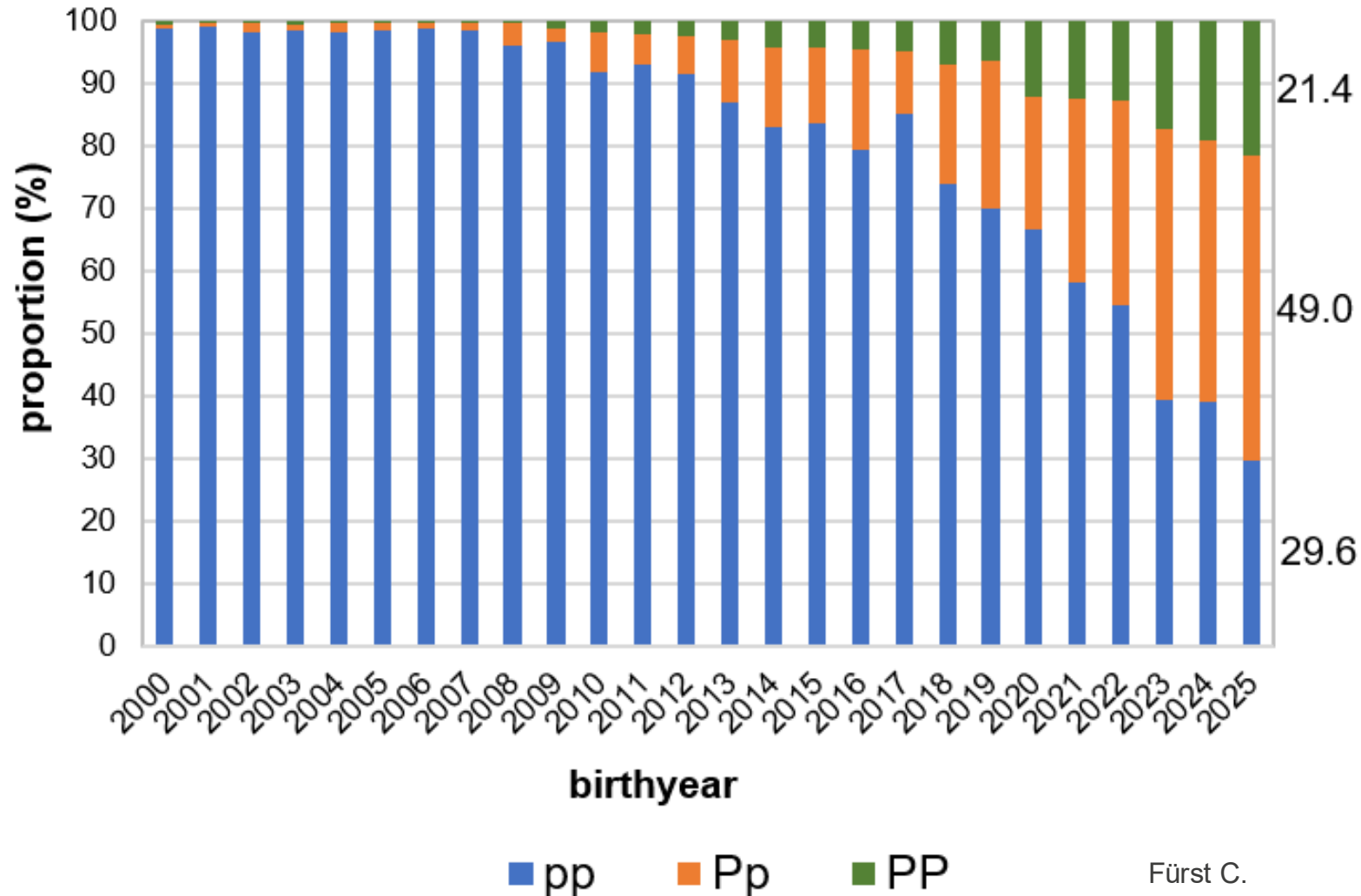
polled is under  
strong selection

mainly on celtic  
variant

# Inseminations with polled: Pp+PP

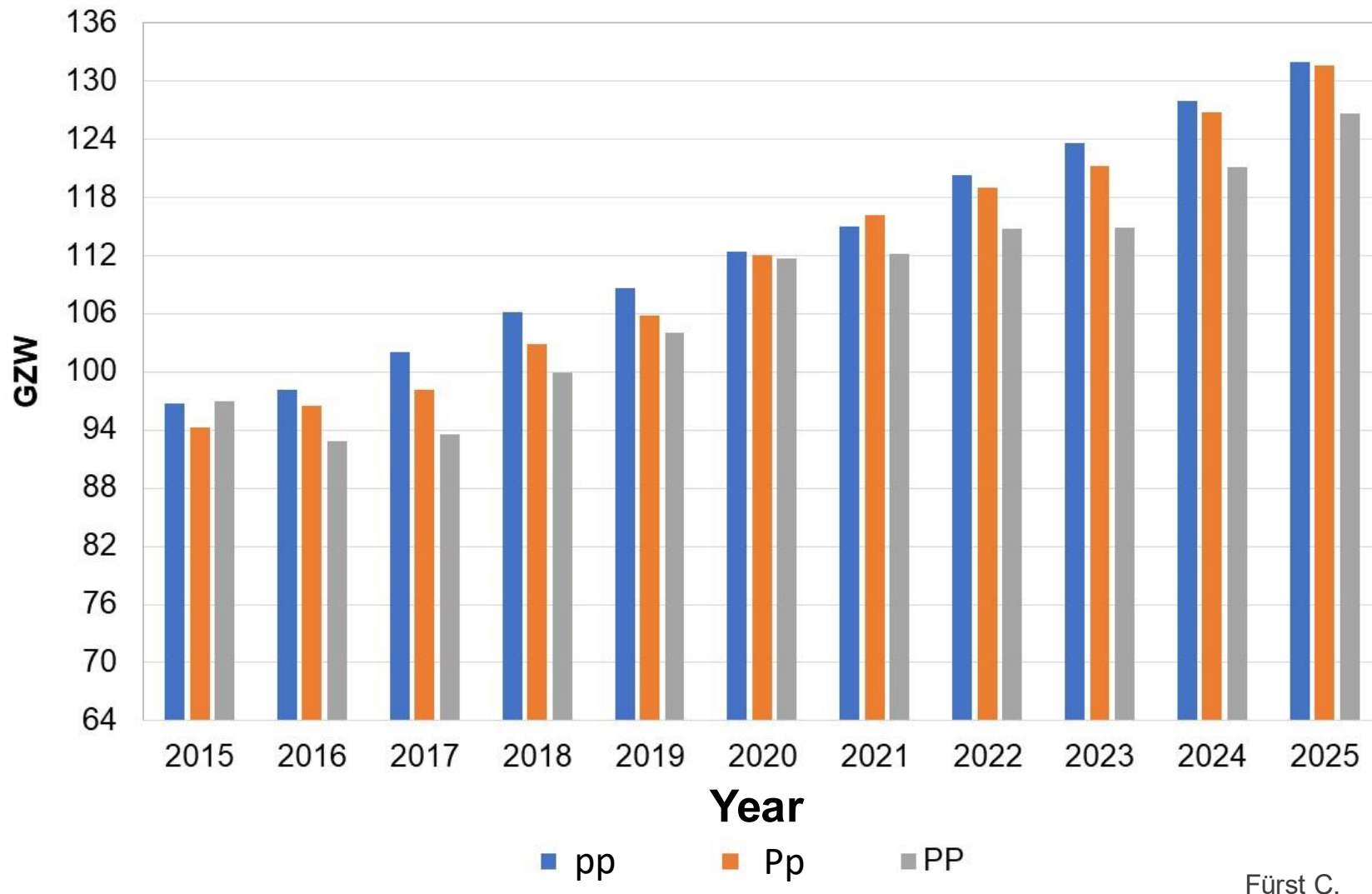


# Polled status of AI bulls (AT+DE+CZ)



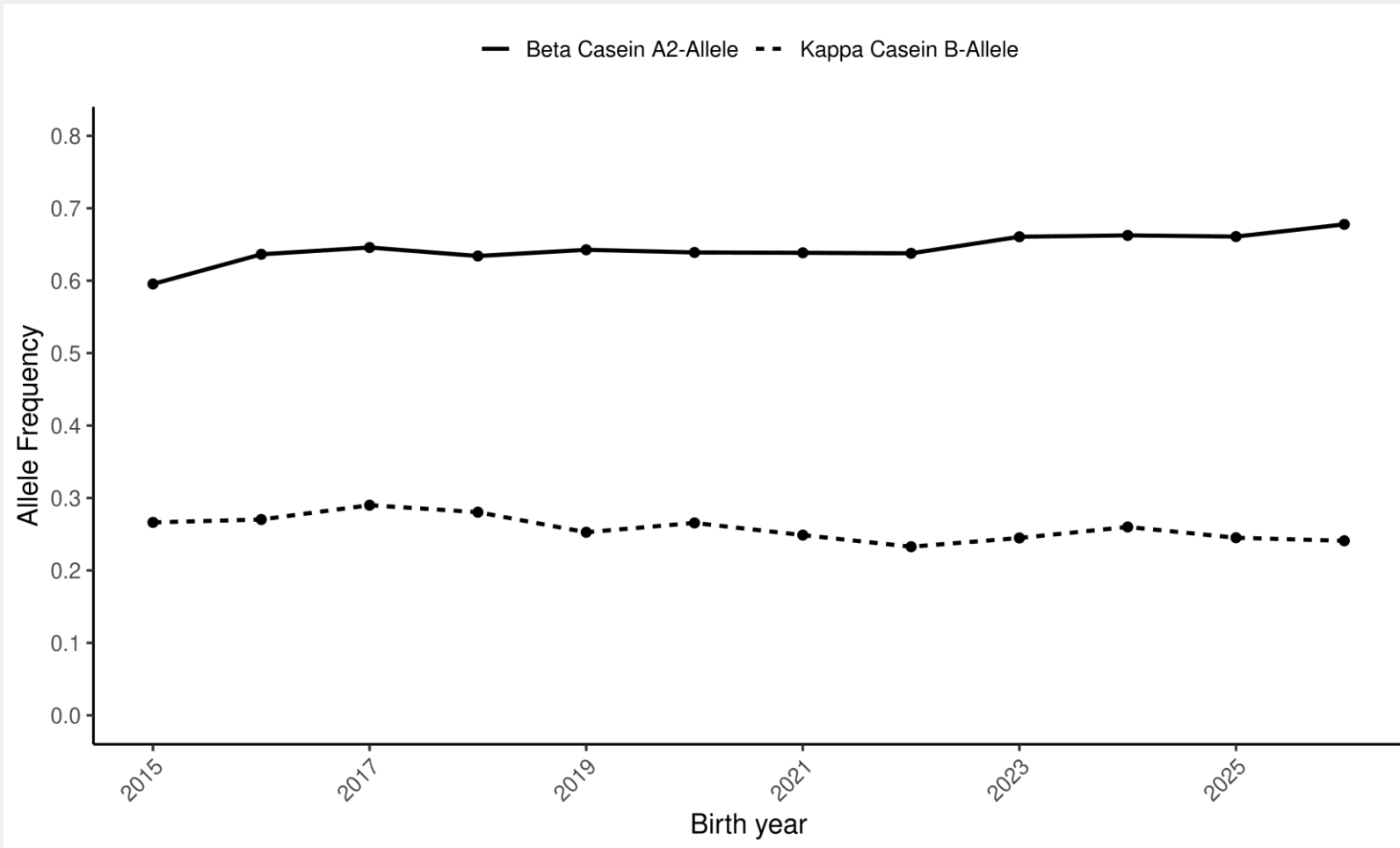
more than  
2/3 polled!

# TMI of used semen by horn status



# K-Casein and $\beta$ -Casein

Allele frequencies in female genotyped Fleckvieh population



not much selection  
visible on milk  
casein composition

**no price premium**  
for either trait

**scientific evidence**  
**still under debate**  
for  $\beta$ -casein

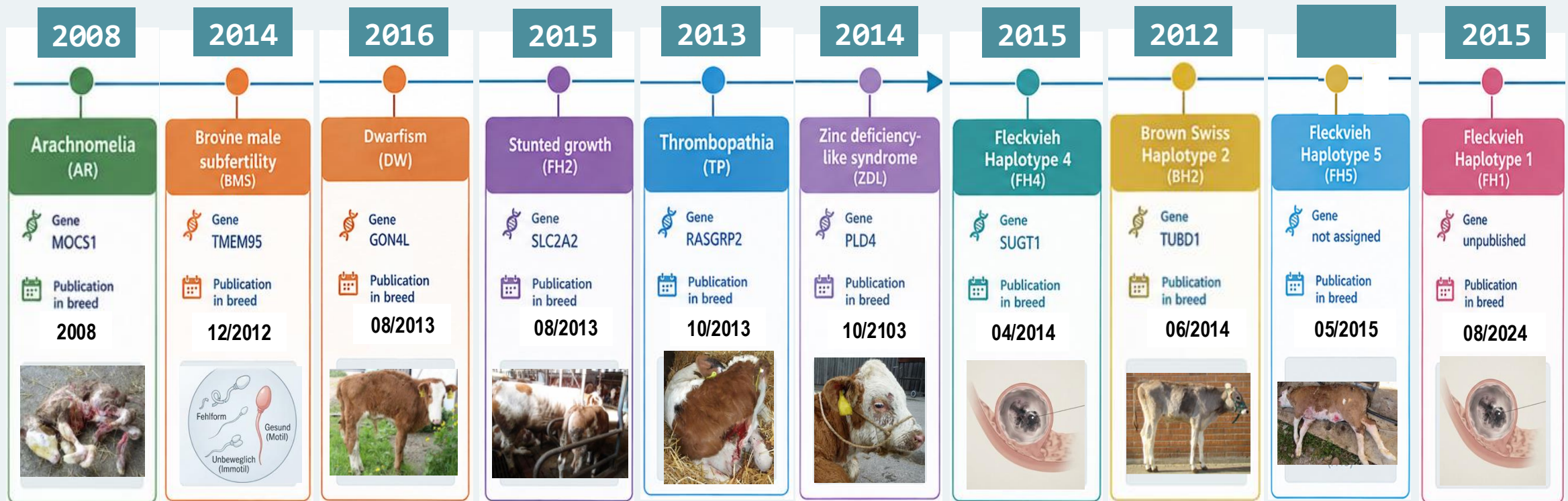


# *Unfavourable Genetic Variants*



# Unfavourable variants in Fleckvieh

Ordered by date of publication in breed  
year of scientific publication



# Genetic defect labeling



**Pos. 1-2/3:**      **Abbreviation for defect**

**Pos. 3/4:**      **Carrier status: C = carrier**

**F = free**

**S = homozygous carrier (sure)**

| Defect                         | Abbrev. |
|--------------------------------|---------|
| Arachnomalia                   | AR      |
| Bovine male Subfertility BMS   | MS      |
| Brown Swiss-Haplotype 2 BH2    | B2      |
| Fleckvieh-Haplotype 1 FH1      | F1      |
| Fleckvieh-Haplotype 4 FH4      | F4      |
| Fleckvieh-Haplotype 5 FH5      | F5      |
| Stunted growth FH2             | F2      |
| Thrombopathia TP               | TP      |
| Zinkdefizienz-like Syndrom ZDL | ZL      |
| Dwarfism                       | DW      |

**Examples:**

**B2C =**

heterozygous carrier of BH2

**ARF =**

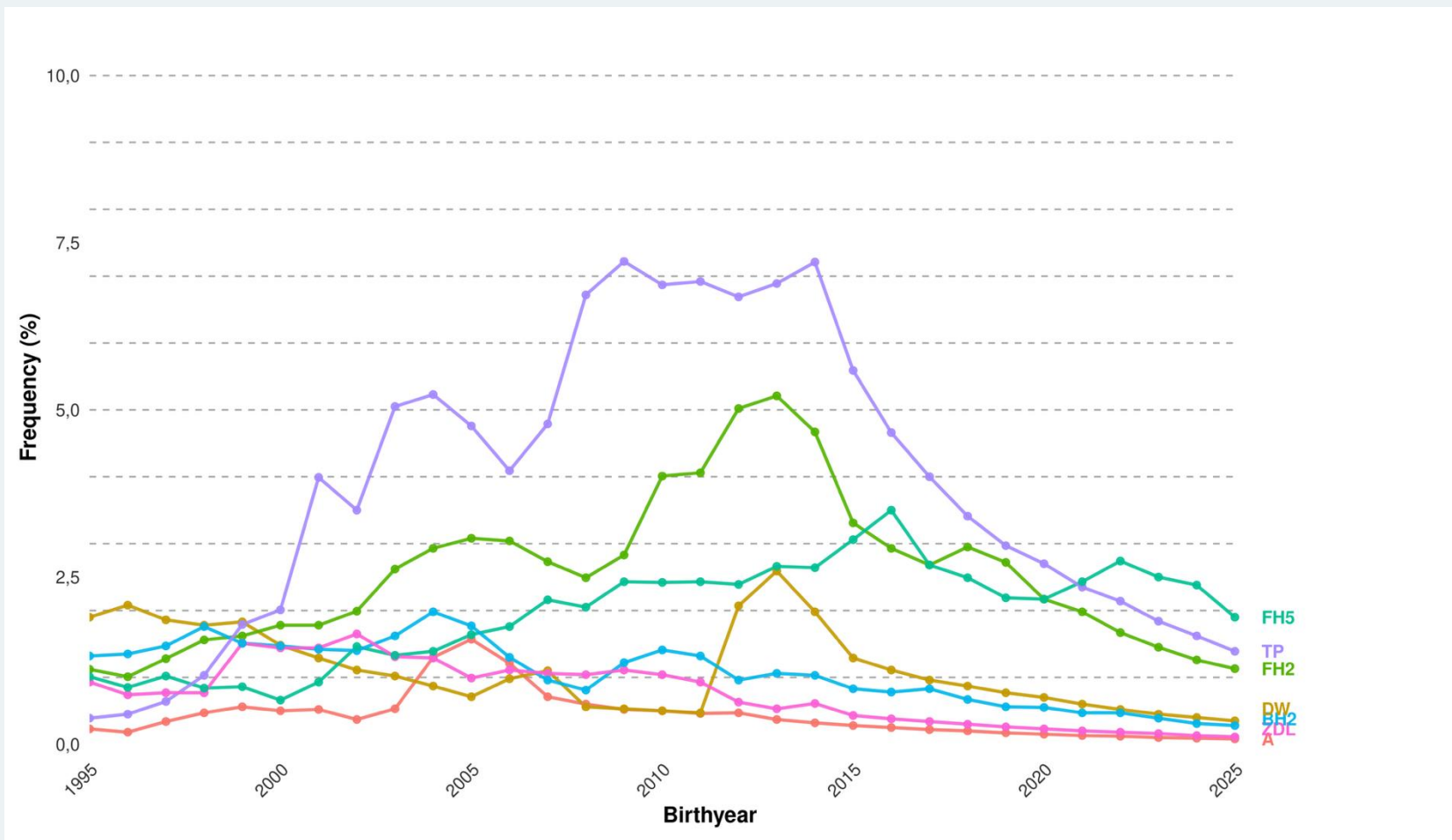
frei von Arachnomalia

**MSS =**

homozygus carrier of BMS

# Defects with visible cases

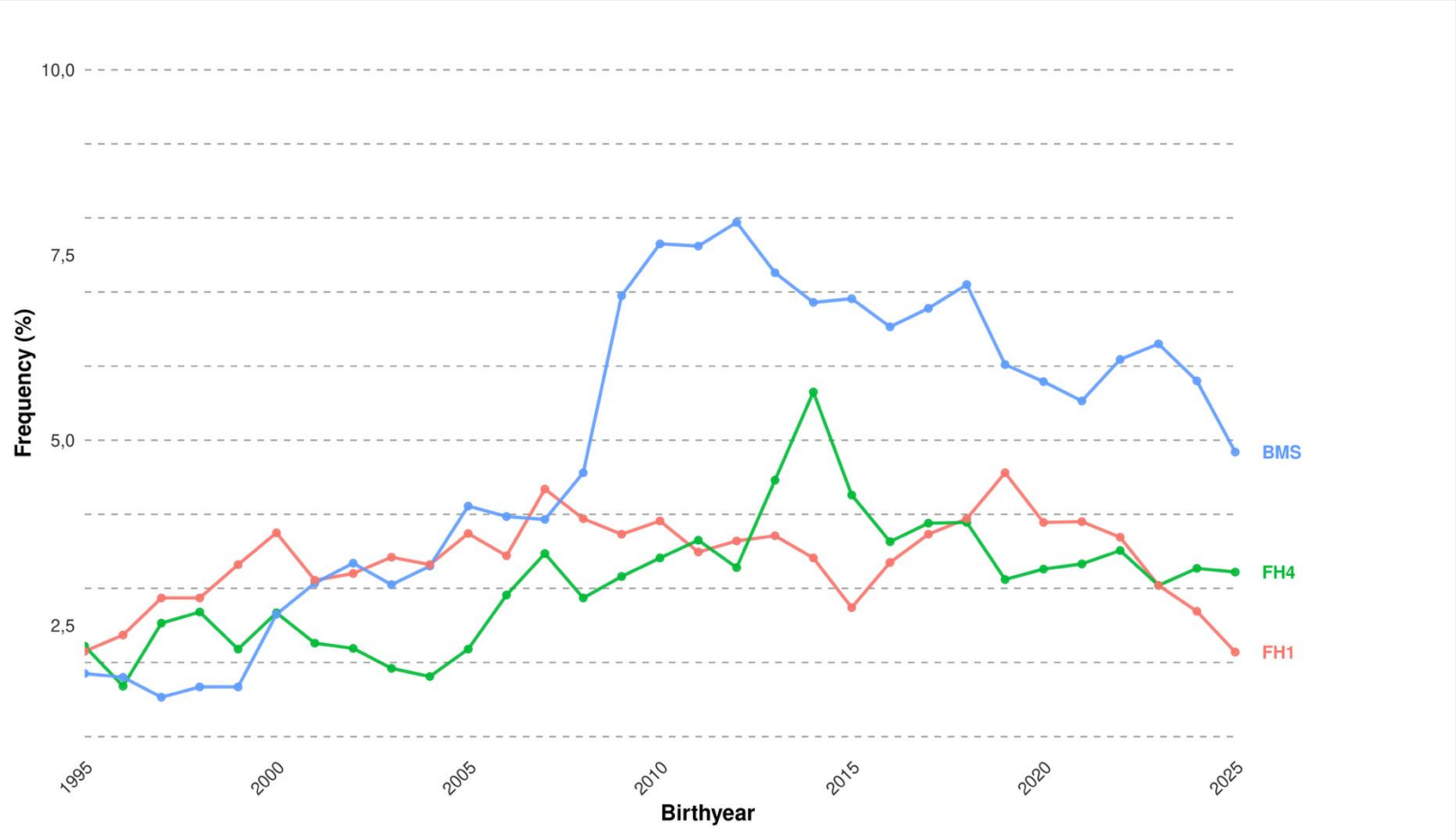
Frequencies in the female population (AT)



very strong  
selection against  
defects with  
visible cases

# Defects with no visible cases

Frequencies in the female population (AT)



moderate selection  
against defects with  
no visible cases



# *Genomic Monitoring using Custom SNPs*



# Genomic monitoring

Chips consist of different SNP groups

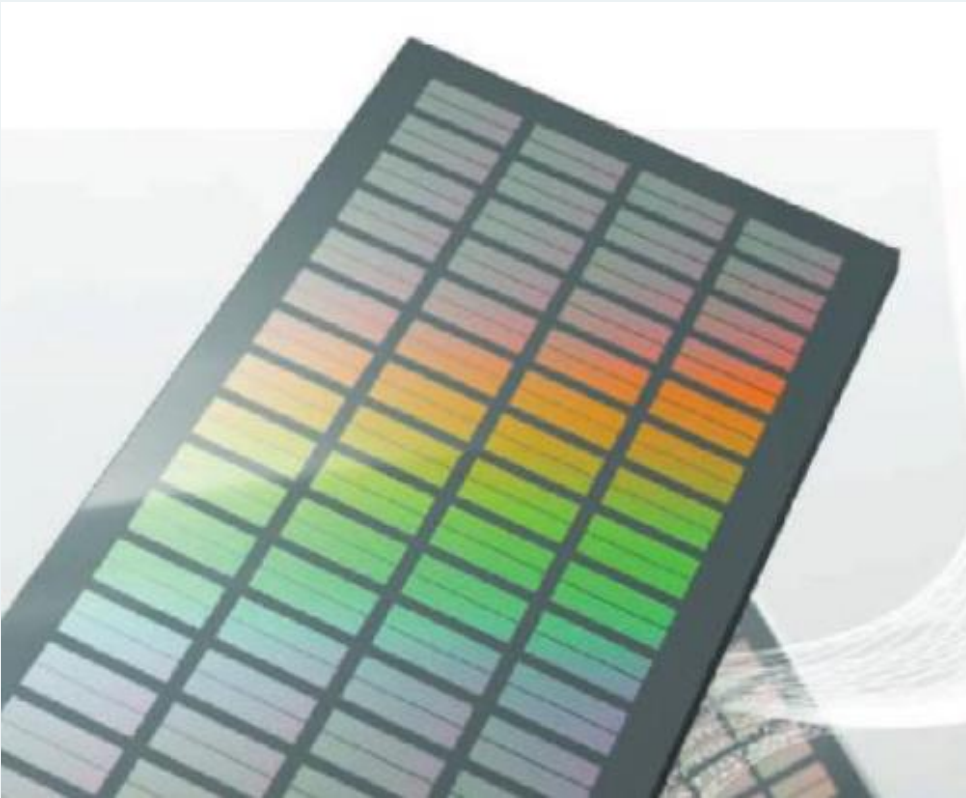
- SNPs for genomic breeding values
  - cover the genome well, no direct effect on the phenotype
- SNPs for parentage verification
  - reliable, occur in many breeds, no genomic prediction possible
- SNPs for direct genetic tests
  - genetic defects and genetic traits
  - usually commissioned and designed by the customer

Design of direct genetic tests based on own research and/or data bases such as OMIA (Online Mendelian Inheritance in Animals)

# SNP genotypes in data base (all breeds)

15/09/2026

| Chip version           | No. SNP | No. Custom SNP | No. Animals | No. Genotypes (bn) |
|------------------------|---------|----------------|-------------|--------------------|
| Illumina K50 V1A       | 54 001  |                | 6 301       | 0.34               |
| Illumina K50 V1B       | 54 001  |                | 24 683      | 1.33               |
| Illumina K50 V2        | 54 609  |                | 52 457      | 2.86               |
| Illumina K50 V3        | 53 218  |                | 1 200       | 0.06               |
| Illumina HD            | 777 962 |                | 1 254       | 0.98               |
| Illumina K80 GGPHD     | 76 879  |                | 2 975       | 0.23               |
| Illumina K50 Custom V1 | 56 263  | 1 718          | 15 691      | 0.88               |
| Illumina K50 Custom V2 | 56 715  | 2 181          | 33 091      | 1.88               |
| Illumina K50 Custom V3 | 45 994  | 2 323          | 14 547      | 0.67               |
| Illumina K50 Custom V4 | 46 691  | 2 364          | 100 261     | 4.68               |
| Illumina K50 Custom V5 | 56 460  | 2 508          | 118 977     | 6.72               |
| Illumina K50 Custom V6 | 59 003  | 3 058          | 120 545     | 7.11               |
| Illumina K50 Custom V7 | 59 117  | 3 161          | 284 788     | 16.84              |
| Illumina K50 Custom V8 | 57 805  | 3 773          | 525 686     | 30.38              |
| Total                  |         |                | 1 302 456   | 75                 |



# Genomic monitoring

currently...

- 114 genomic locations
  - in 27 cattle breeds
  - analysed as part of the 14-day routine
- 
- which variant segregates in which breed
  - check allele frequencies over time
  - carrier animals

# Many variants are NOT breed-specific



Frequencies of loci found in Fleckvieh that segregate in other breeds

| Locus [OMIA-ID*] | Angus | Blonde<br>Aquitaine | Brown Swiss | Charolais | Ennstaler<br>Bergscheck. | Galloway | Grauvieh | Kaerntner<br>Blondvieh | Limousin | Murbodner | Original<br>Braunvieh | Original<br>Pinzgauer | Pustertaler<br>Sprinzen | Schot.<br>Hochlandr. | Tuxer | Wagyu | Waldviertler<br>Blondvieh | Weiß-Blau<br>Belgier |
|------------------|-------|---------------------|-------------|-----------|--------------------------|----------|----------|------------------------|----------|-----------|-----------------------|-----------------------|-------------------------|----------------------|-------|-------|---------------------------|----------------------|
| A (FV) [001541]  |       |                     |             |           | 8.1                      |          |          |                        |          |           |                       |                       |                         |                      |       |       |                           |                      |
| BH2 [001939]     |       |                     | 1.9         |           |                          |          |          |                        |          |           |                       |                       |                         |                      |       |       | 18.6                      |                      |
| FH2 [000366]     |       |                     |             |           |                          |          |          |                        |          |           | 1.5                   |                       |                         |                      |       |       |                           |                      |
| FH5 [002960]     |       |                     |             |           |                          |          |          |                        |          |           |                       |                       |                         |                      | 0.8   |       |                           |                      |
| TP [002433]      |       |                     |             |           | 0.9                      |          |          |                        |          | 0.6       |                       |                       | 5.4                     |                      |       |       |                           |                      |



*Take-home message*



# Conclusions



**01** Genomic toolbox enable efficient management of Mendelian traits.  
Especially in large populations under genomic selection.

**02** Increased awareness among breeders and decision makers and less 'fear'.  
Rezessives with visible cases are under rigorous selection.  
Genetic defects are still a disruption of the breeding business!

**03** Higher speed needs clear vision and good breakes.



from Mendel  
to Genom

THANK  
YOU!

*Illustration generated with  
OpenAI, 2026*



- GENOMIC SELECTION
- SNP-BASED INBREEDING MANAGEMENT
- SELECTION ON POLLED LOCUS
- BETA CASEIN A2
  - SNP-BASED MONITORING OF RECESSIVES

FH2

- THROMBOPATHIA
- ARACHNOMELIA

FH4 FH5 BH2

EARLY DETECTION OF  
NOVEL MUTATIONS

LONGITUDINAL STUDIES

CASE-CONTROL STUDIES

GENOTYPE-BASED MONITORING

DETECTION OF CRYPTIC MUTATIONS

