



GEORG-AUGUST-UNIVERSITÄT
GÖTTINGEN IN PUBLICA COMMODA
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Structural variants and tandem repeats in horses and their potential impact on withers height

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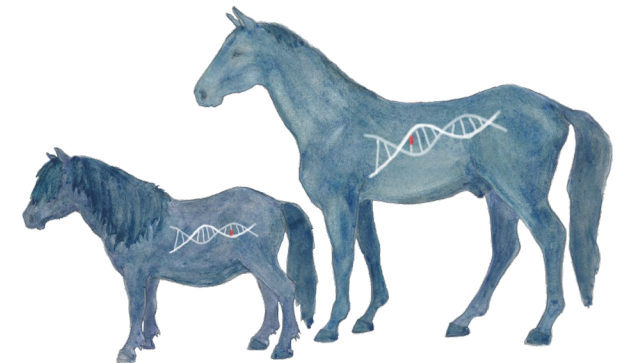
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Background

Structural variants (SVs)

- genomic alterations > 50 bp
- highly variable in size and type
 - insertions
 - deletions
 - duplications
 - inversions
 - translocations

Tandem repeats (TRs)

- repetitive DNA regions
- classification by length of **repeat unit**
 - 1 - 6 bp = microsatellites/STRs
 - > 6 bp = minisatellites/VNTRs

...TAGAC TCA TCA TCA TCA GGCATCGAC...

Background

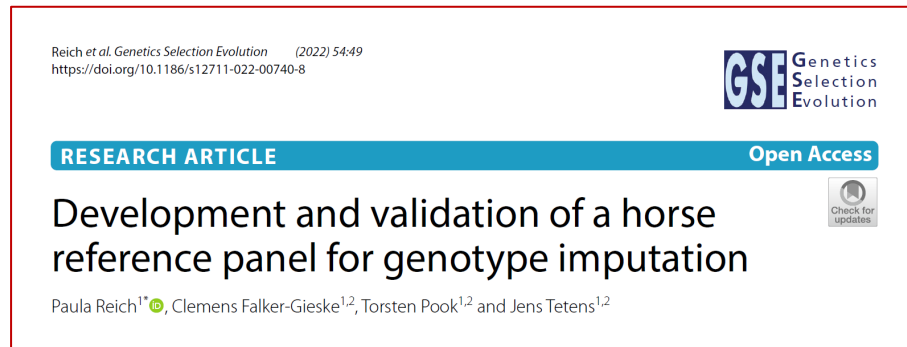
- substantial contribution to **genomic variation** between individuals
- **associations** with diseases and other phenotypes of interest
- BUT: most genomic studies in livestock **restricted** to SNPs and short INDELs



Aims:

- **identification** and **characterisation** of SVs and TRs in horses
- establishment of a **multi-variant-type reference panel**
- investigation of a potential **impact** of SVs and TRs on **withers height**

Mapping & variant calling

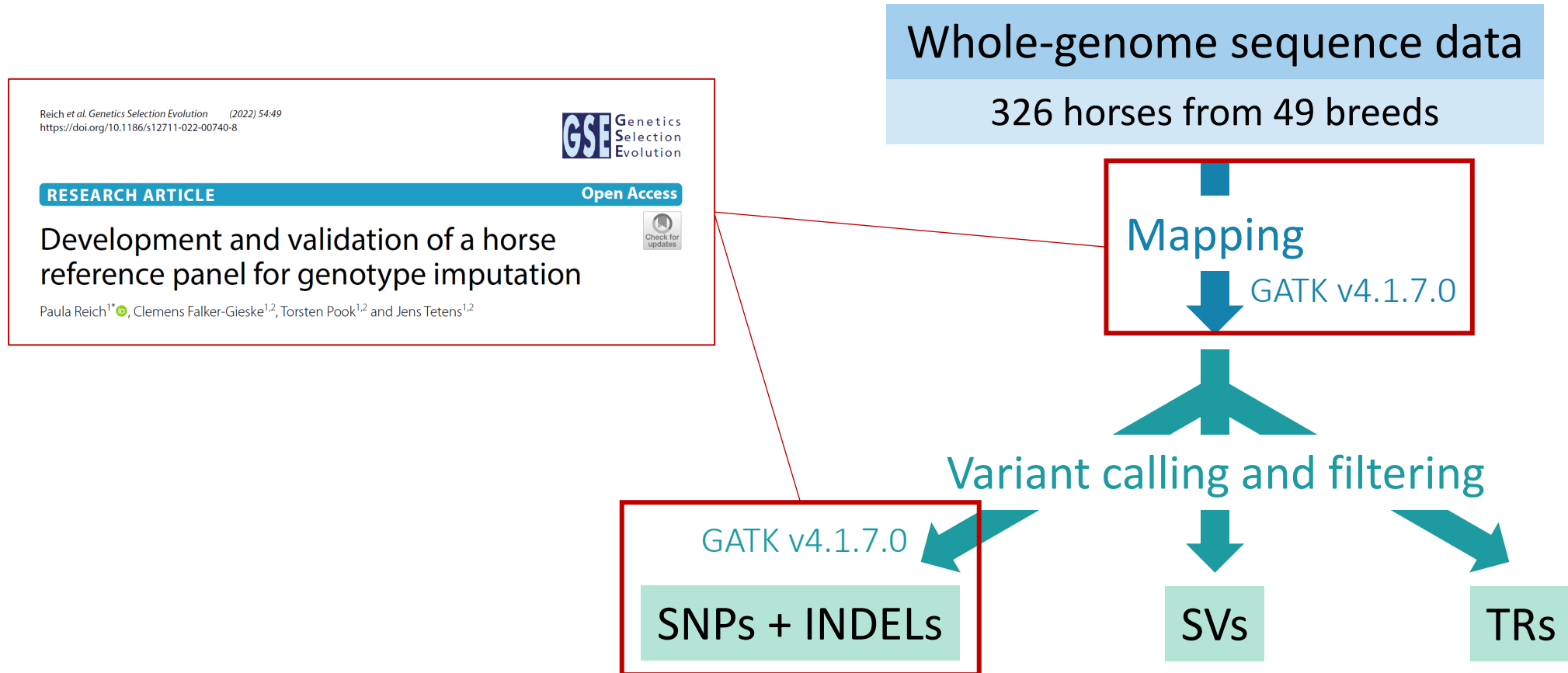


Whole-genome sequence data

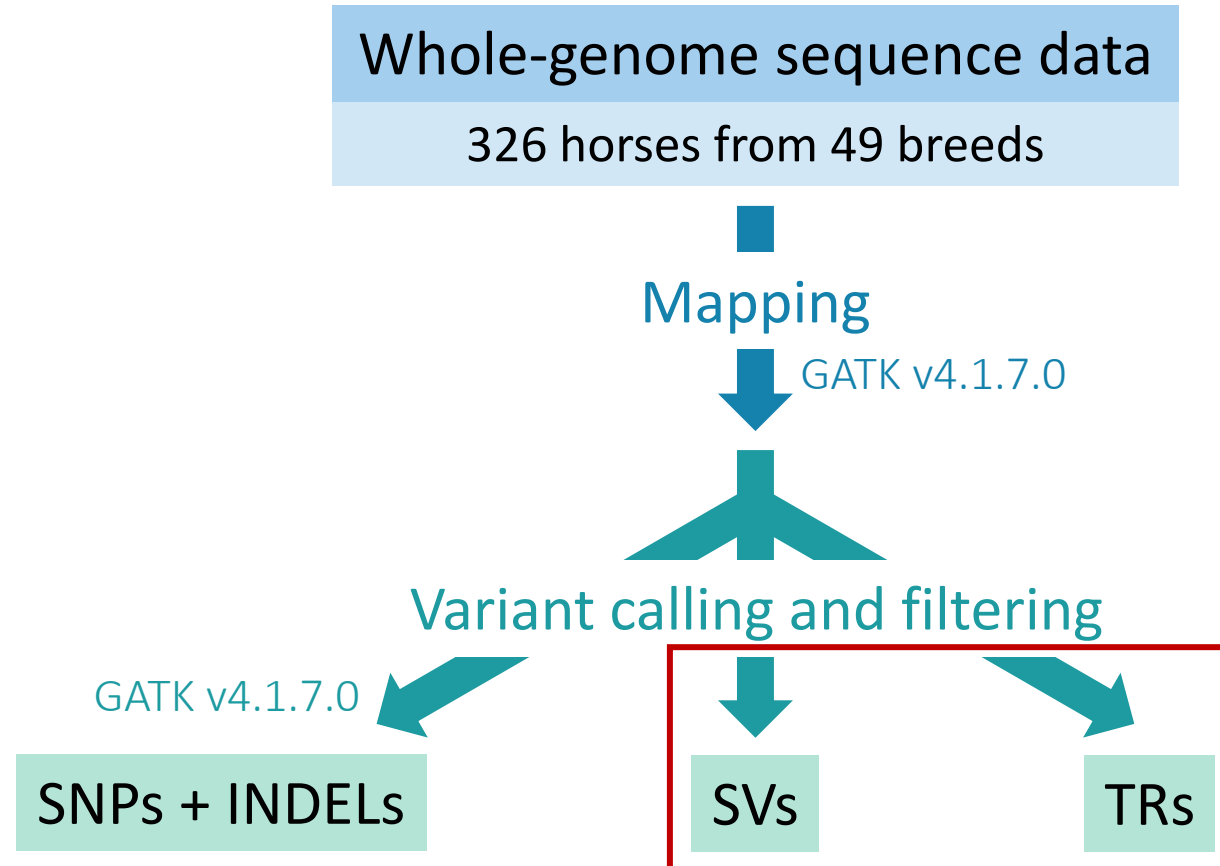
326 horses from 49 breeds

Mapping
↓ GATK v4.1.7.0

Mapping & variant calling

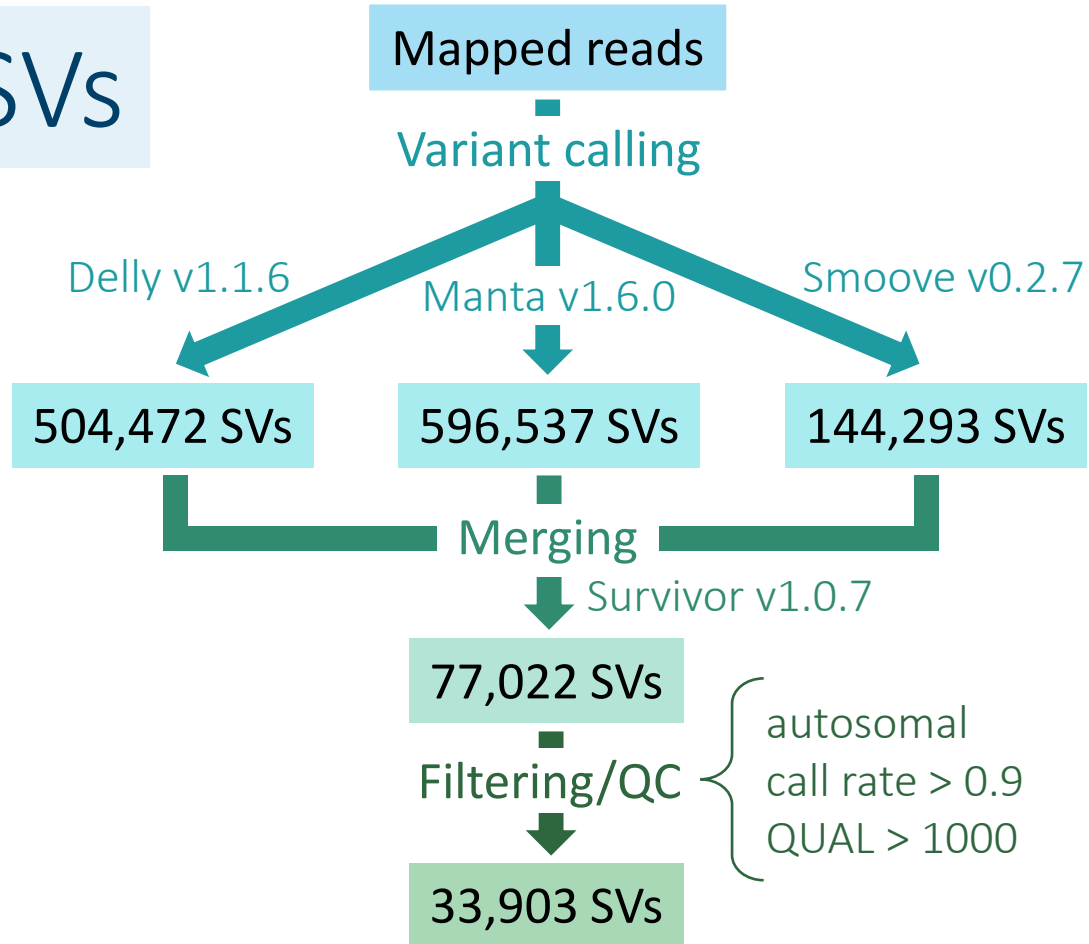


Mapping & variant calling

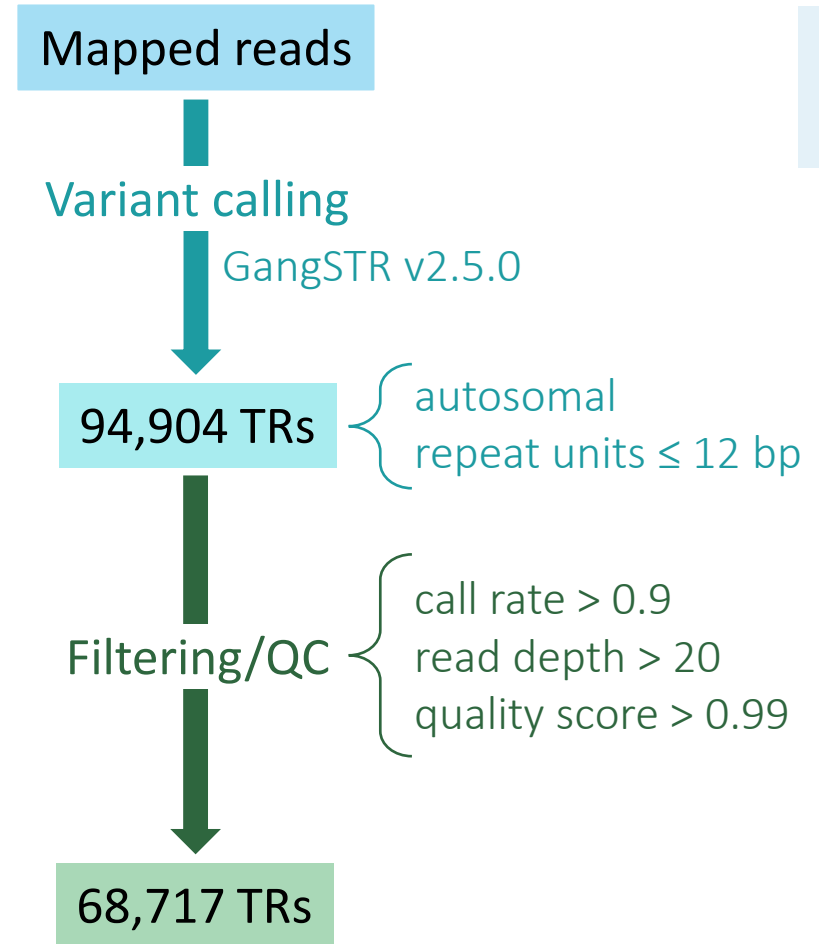


Variant calling & filtering

SVs



TRs



Variant effect prediction

SVs

33,903 SVs
33,625 biallelic | 278 multiallelic



Splitting

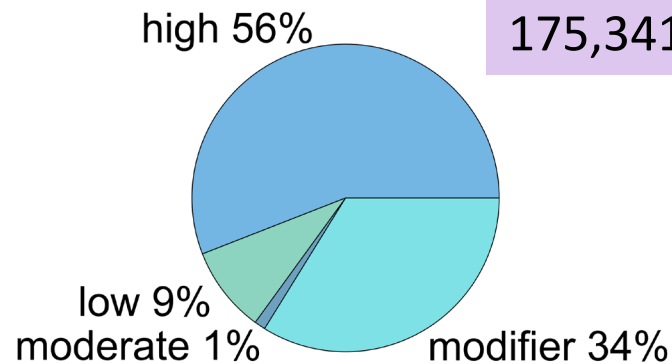


34,378 biallelic SVs

Variant effect prediction

↓ SnpEff v5.2

175,341 annotations



TRs

68,717 TRs
417 biallelic | 68,300 multiallelic



Splitting

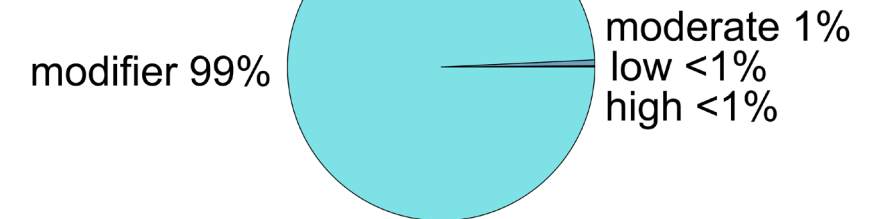


967,033 biallelic TRs

Variant effect prediction

↓ SnpEff v5.2

1,987,875 annotations

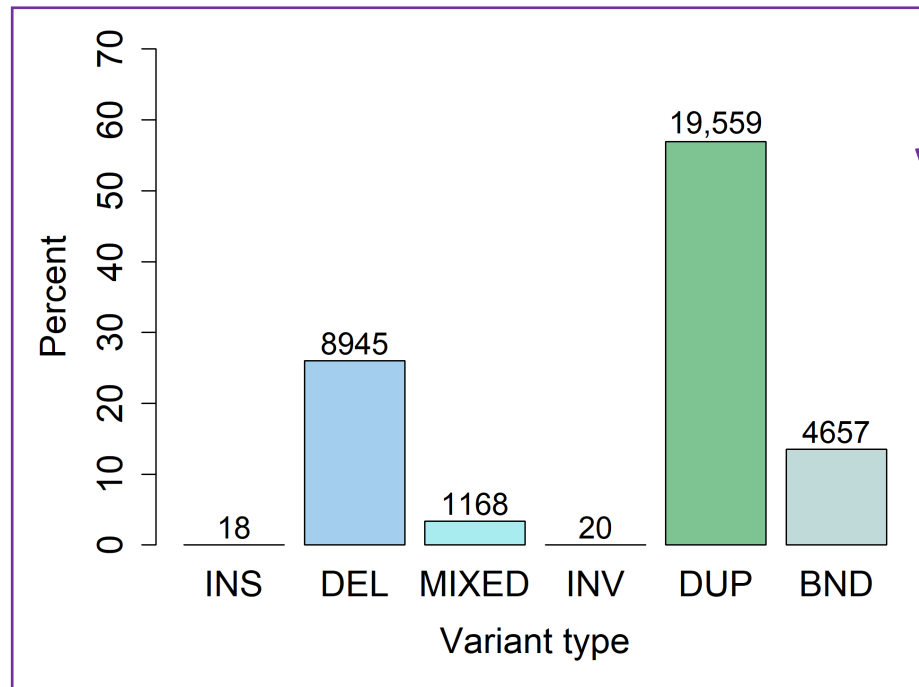


Variant effect prediction

SVs

34,378 biallelic SVs

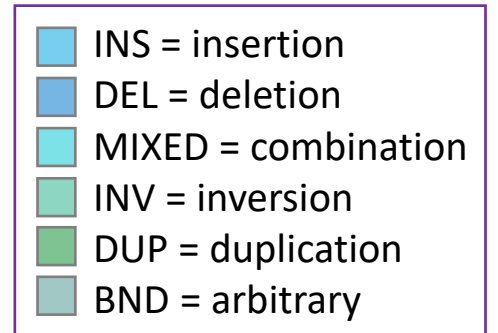
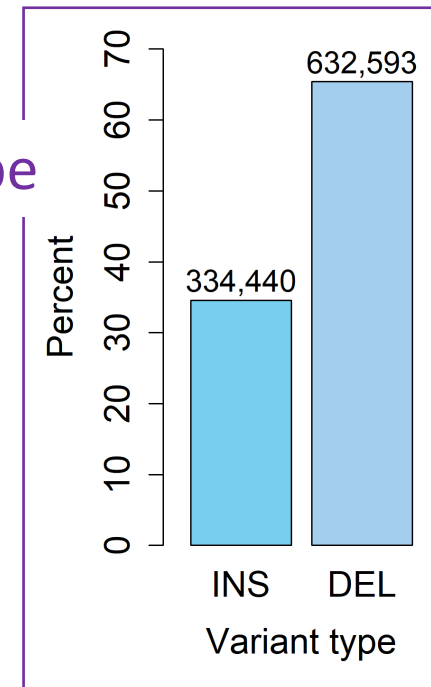
Variant effect prediction
↓ SnpEff v5.2



Variants by type

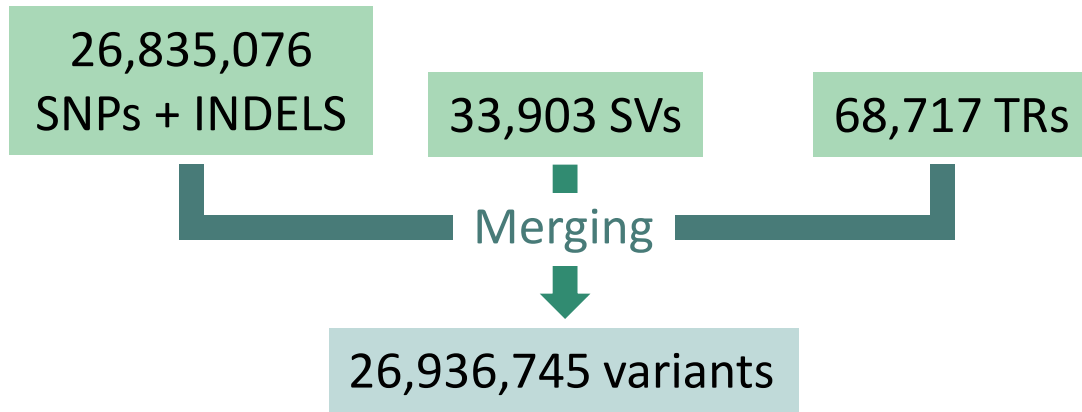
967,033 biallelic TRs

Variant effect prediction
↓ SnpEff v5.2

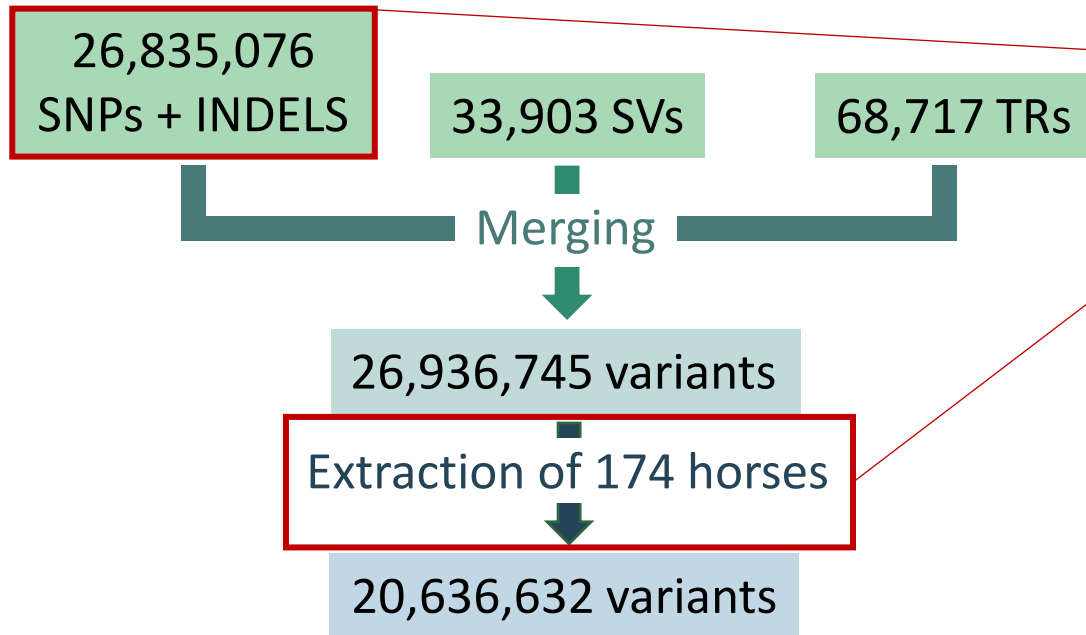


TRs

Genotype imputation



Genotype imputation



Reich et al. *Genetics Selection Evolution* (2022) 54:49
<https://doi.org/10.1186/s12711-022-00740-8>

GSE Genetics Selection Evolution

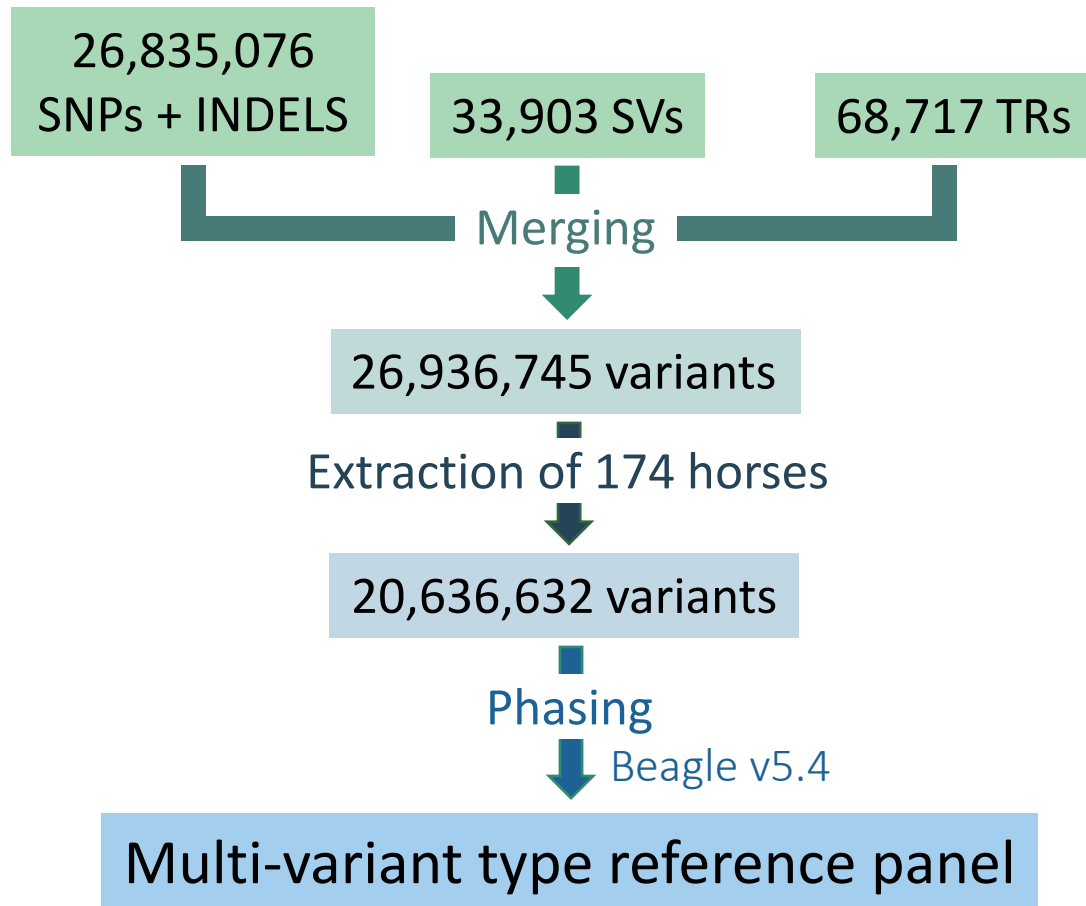
RESEARCH ARTICLE Open Access

Development and validation of a horse reference panel for genotype imputation

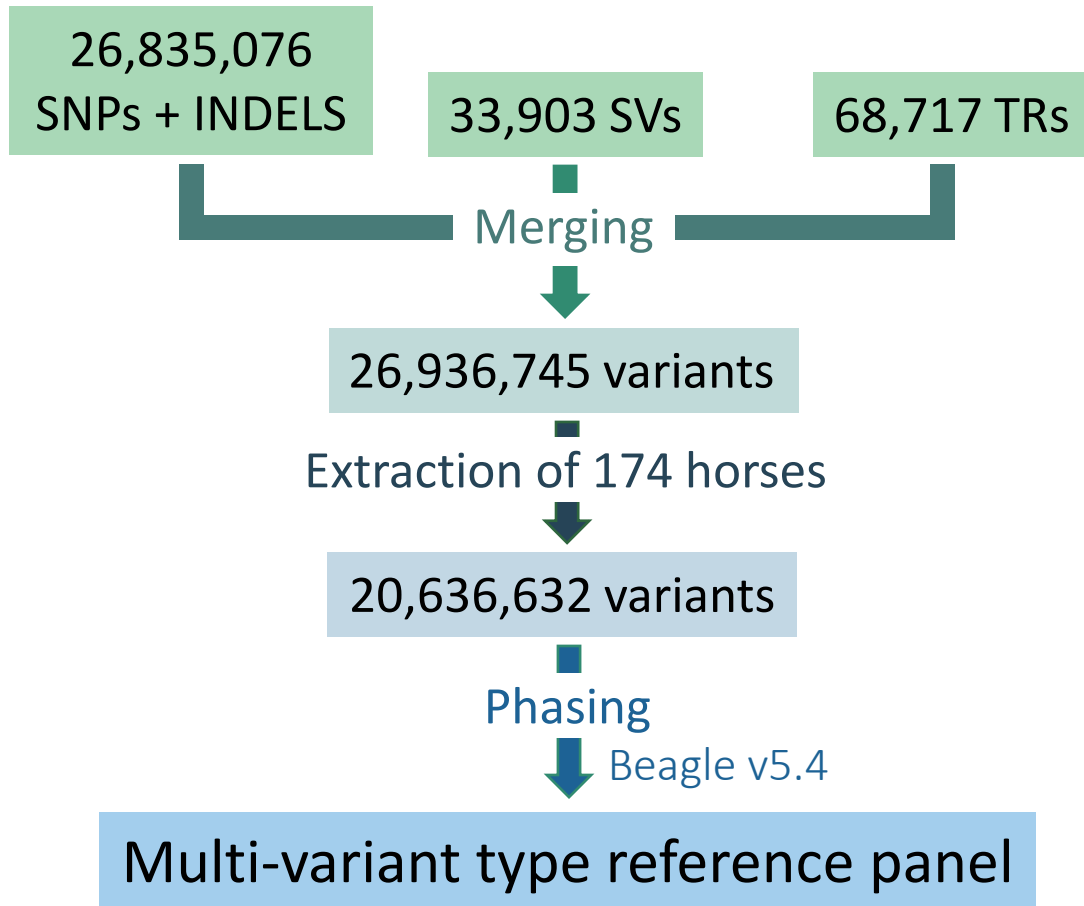
Paula Reich^{1*}, Clemens Falker-Gieske^{1,2}, Torsten Pook^{1,2} and Jens Tetens^{1,2}

Check for updates

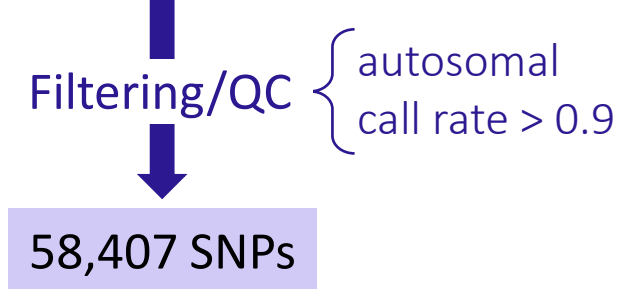
Genotype imputation



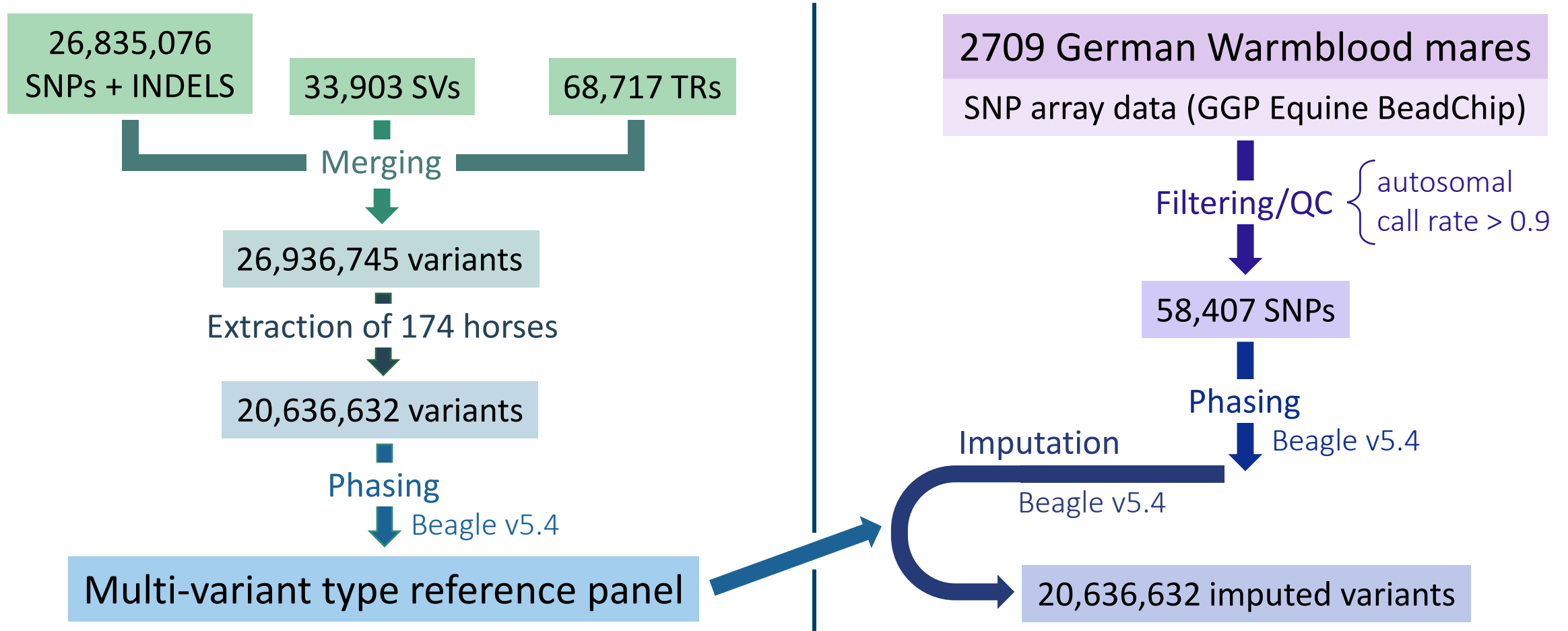
Genotype imputation



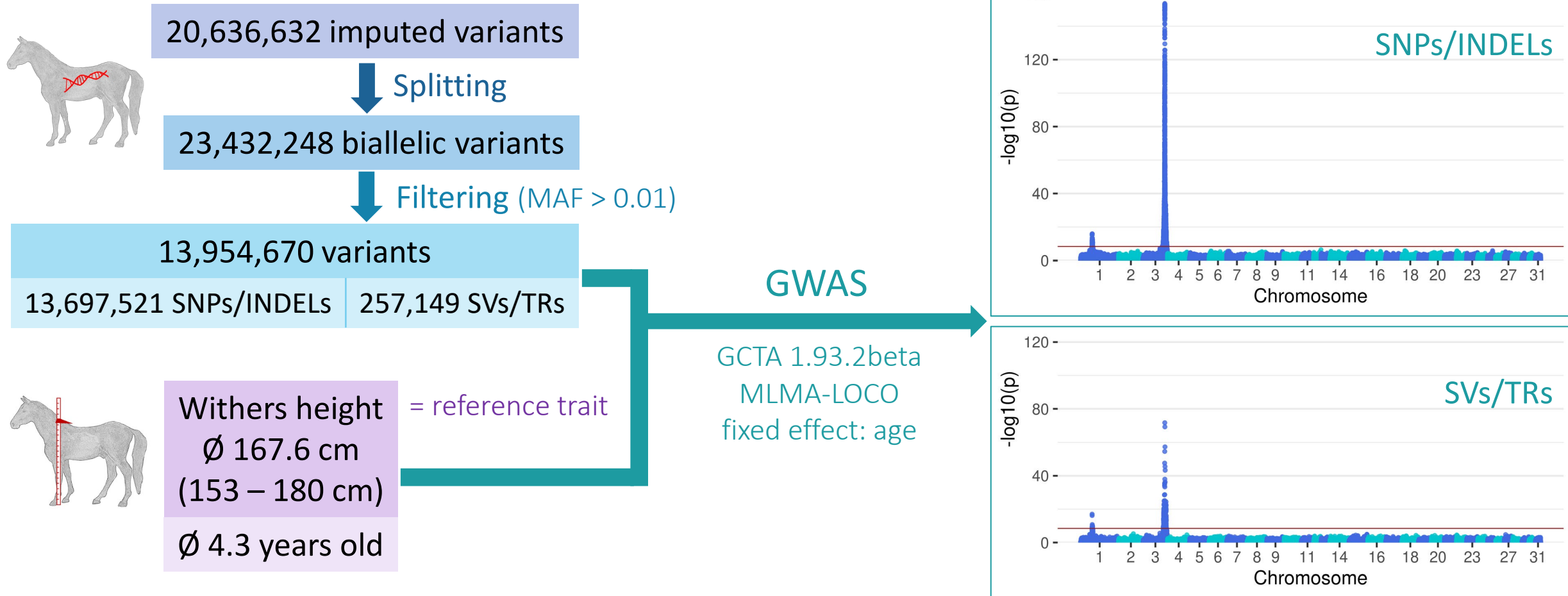
2709 German Warmblood mares
SNP array data (GGP Equine BeadChip)



Genotype imputation



GWAS for withers height



GWAS for withers height

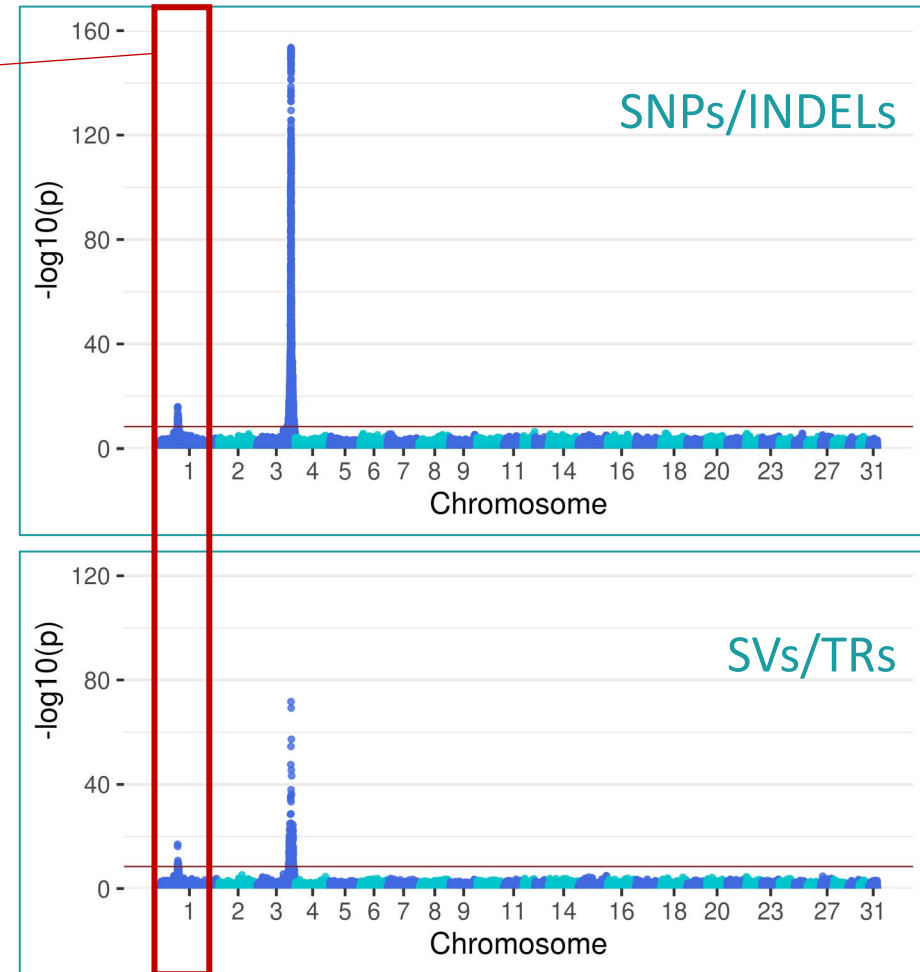
QTL on ECA1: 56-60 Mb

- top SNPs: ~56.6/56.9 Mb ($p = 2 \cdot 10^{-16}$)
- top INDEL: ~57.2 Mb ($p = 1 \cdot 10^{-16}$)
- top SV: –
- top TR: ~56.6 Mb ($p = 1 \cdot 10^{-17}$)
- 0 significant SVs, 13 significant TRs

intronic deletion
(modifying impact)
in *CTNNA3*

Variant effect prediction

- SVs: –
- TRs: only modifier and low impact



GWAS for withers height

QTL on ECA3: 96-119 Mb

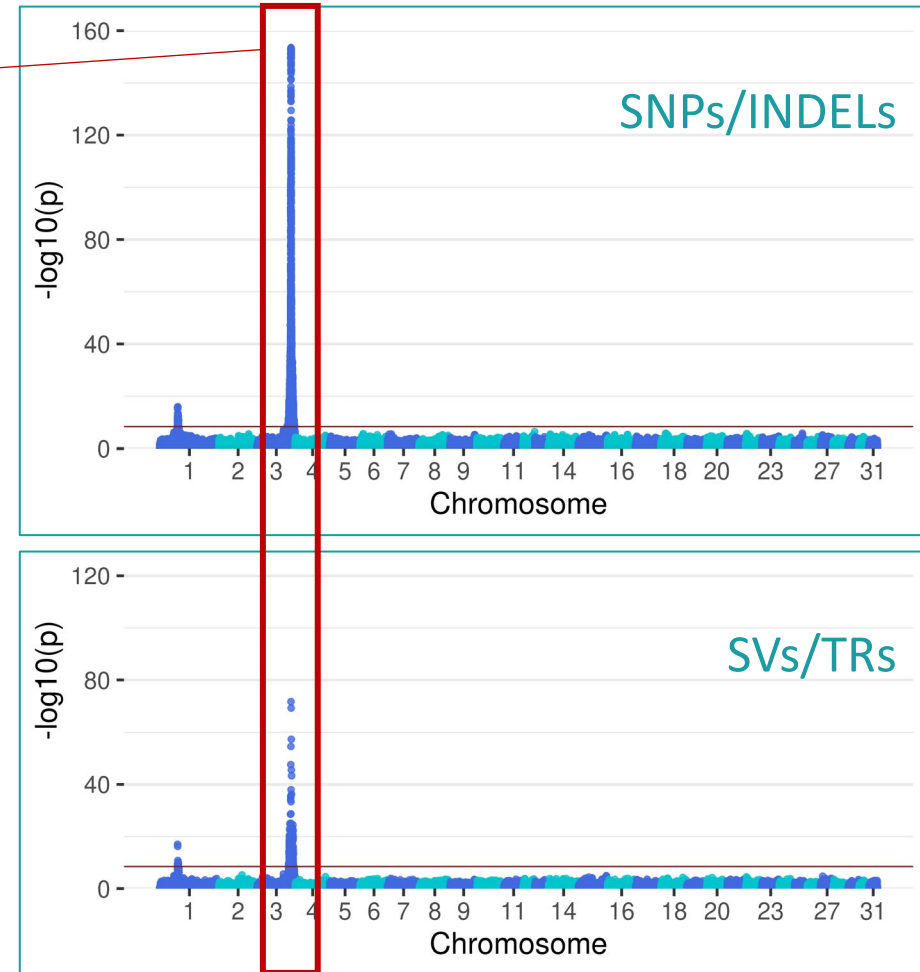
- top SNPs: ~107.4 Mb ($p = 4 \cdot 10^{-154}$)
- top INDEL: ~107.4 Mb ($p = 8 \cdot 10^{-154}$)
- top SV: ~111.2 Mb ($p = 5 \cdot 10^{-23}$)
- top TR: ~107.3 Mb ($p = 2 \cdot 10^{-72}$)
- 9 significant SVs, 227 significant TRs

intergenic fusion
(low impact)

intergenic insertion
(modifying impact)

Variant effect prediction

- SVs: 7 modifier, 1 low, 1 high impact
- TRs: only modifier and low impact



GWAS for withers height

QTL on ECA3: 96-119 Mb

- known QTL for withers height
- candidate causal SNPs:

Reich et al. *Genetics Selection Evolution* (2024) 56:45
<https://doi.org/10.1186/s12711-024-00914-6>

Genetics Selection Evolution

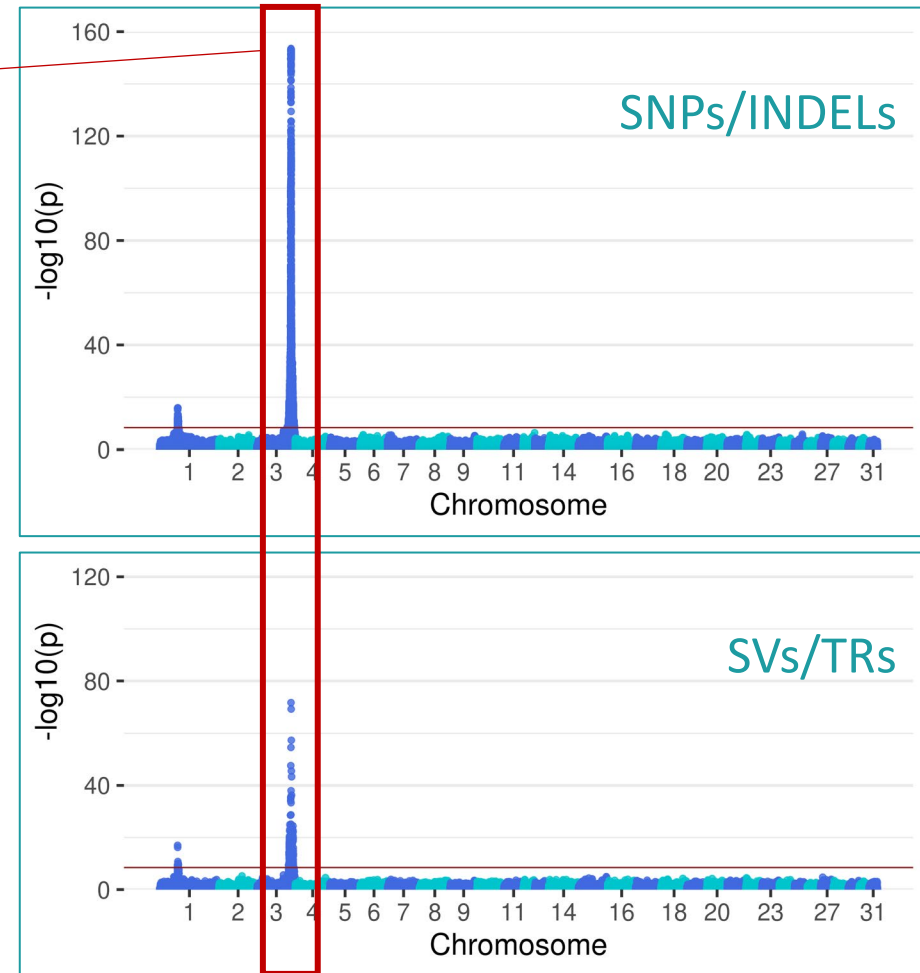
RESEARCH ARTICLE

Open Access

Genomic analyses of withers height and linear conformation traits in German Warmblood horses using imputed sequence-level genotypes

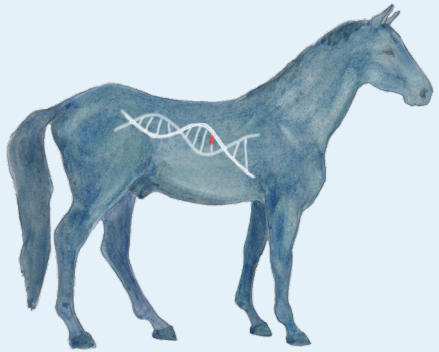
Paula Reich^{1,2*}, Sandra Möller¹, Kathrin F. Stock³, Wietje Nolte⁴, Mario von Depka Prondzinski⁵, Reinhard Reents³, Ernst Kalm⁶, Christa Kühn^{7,8,9}, Georg Thaller⁶, Clemens Falker-Gieske^{1,2†} and Jens Tetens^{1,2†}

→ additional role of SVs/TRs?



Conclusions

- ✓ **identification** and **characterisation** of SVs and TRs in horses
- ✓ establishment of a **multi-variant-type reference panel**
- multi-variant-type **GWAS** using imputed sequence-level data
 - ✓ identification of **QTL** for **withers height**
 - 🎯 investigation of candidate **causal SVs/TRs** for withers height
 - 🎯 application to **other** (conformation) **traits**



Thank you for your attention!



IAFH
International Association of Future
Horse Breeding GmbH & Co KG

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