COMMON GENOMIC REGIONS UNDERLIE HEIGHT IN HUMANS AND STATURE IN CATTLE

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ACKNOWELDEMENT
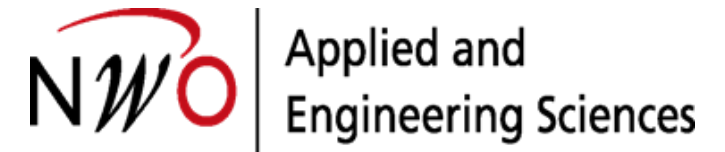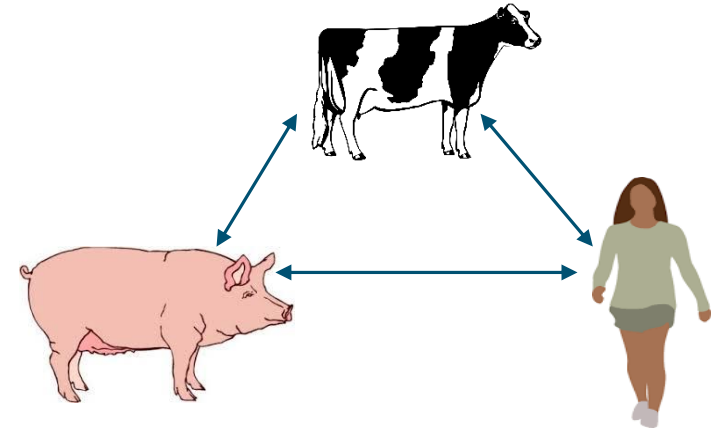
INTORDUCTION AND RESEARCH QUESTION

General Scientific interest

- Similarity in trait biology across species

- Potential use of across-species genetic information in the

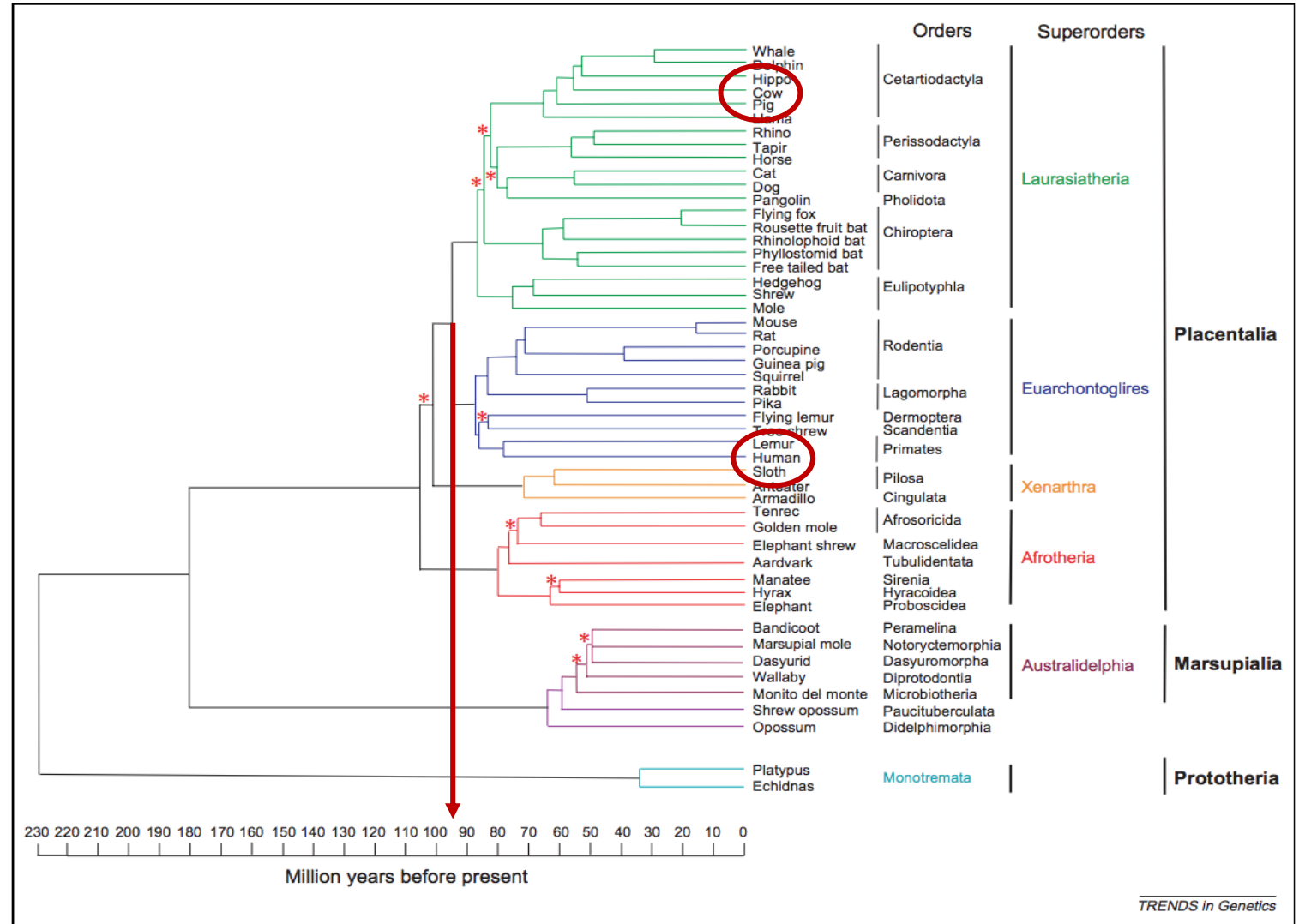 analysis of complex traits

Research question (This talk):

Can prior information from studies on human height be used to

select relevant stature genes/variants in cattle?

MATERIALS & METHODS: COMMON GENES IN HUMANS AND CATTLE

- Separation > 90M years

- Common variants not likely

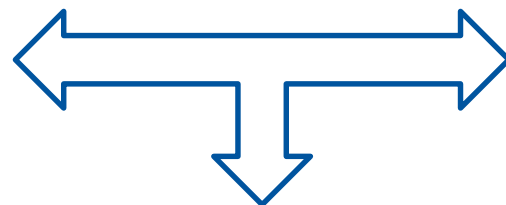- Comparison = **at gene level**

➢ **~ 13k** orthologs

OVERLAP OF HUMAN HEIGHT AND CATTLE STATURE GENES

Bouwman et al., 2018
(Meta-GWAS, cattle stature)

Yengo et al., 2018
(Meta-GWAS, human height)

Potential cattle stature genes ⟷ Potential Human height genes

Overlap of cattle stature & human height genes

✓ More than expected by chance?

✓ ~40% overlap

✓ Fisher's exact test (p-value = 3.2e-10)

ENRICHMENT FOR GWAS HITS IN CANDIDATE VS CONTROL GENES

Potential Human height genes
(Yengo et al. (2018)

Cattle orthologs (**Candidate** genes)

lead SNPs for stature
(within & 100kb either side of the genes)

>>>>>?

Control cattle genes

Random cattle genes
✓ Similar patter of gene-length

1,000 replicates

lead SNPs for stature

VARIANCE FOR STATURE EXPLAINED BY CANDIDATE VS CONTROL SNPs (1)

Most sign. SNPs from "human height" genes vs Most sign. SNPs from random genes

Potential Human height genes
(Yengo et al. (2018)

⬇

Cattle <u>orthologs</u>

⬇

lead SNPs for stature (MAF > 0.01)
(within & 100kb either side of the genes)

⬇

% G. variance for stature

Random cattle genes
✓ Similar patter of gene-length

⬇ 1,000 replicates

lead SNPs for stature (MAF > 0.01)
✓ Similar patter of allele frequency

⬇

% G. variance for stature

>>>>>?

Random SNPs from "human height" genes vs Random SNPs in random genes

Potential Human height genes
(Yengo et al. (2018)

⇩

Cattle <u>orthologs</u>

⇩

5 random SNPs per gene (MAF > 0.01)
- No cattle prior information

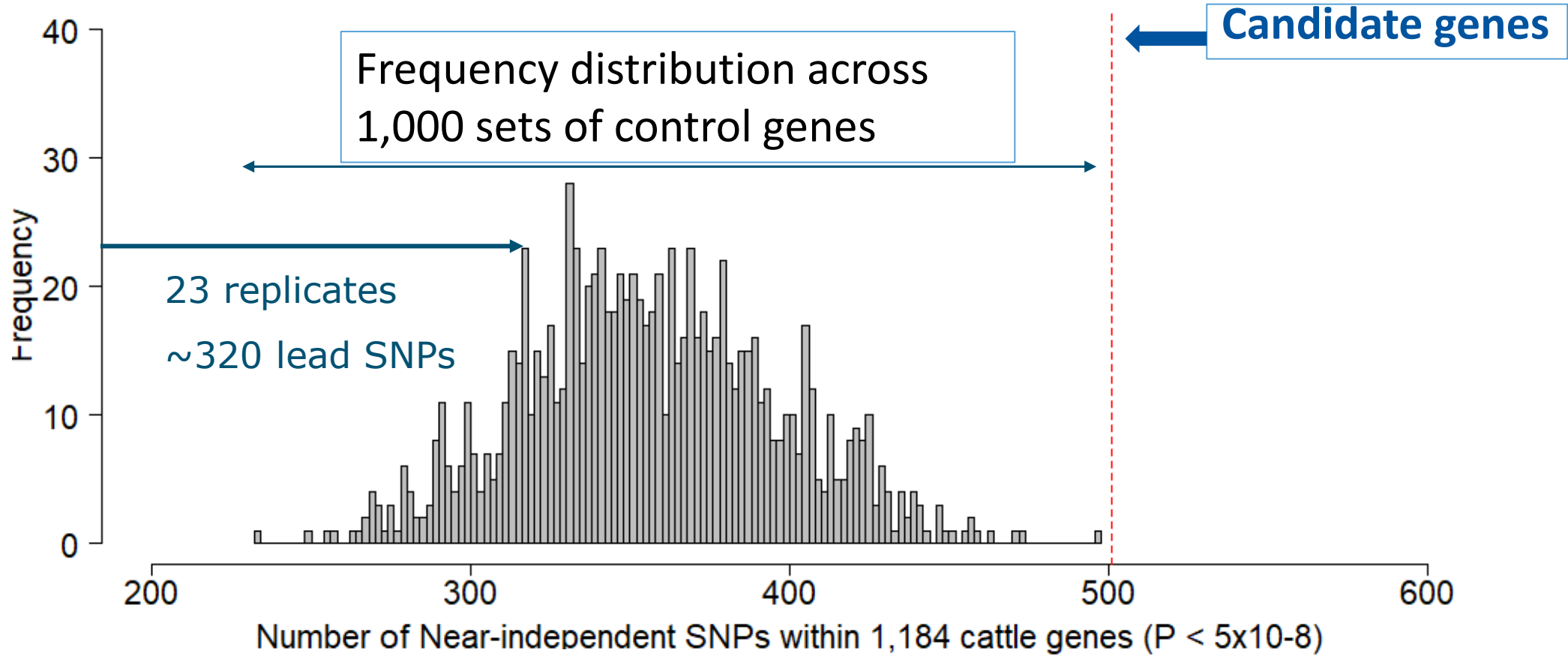⇩

% G. variance for stature

random cattle SNPs (MAF > 0.01)
✓ Similar patter of allele frequency

1,000 replicates

⇩
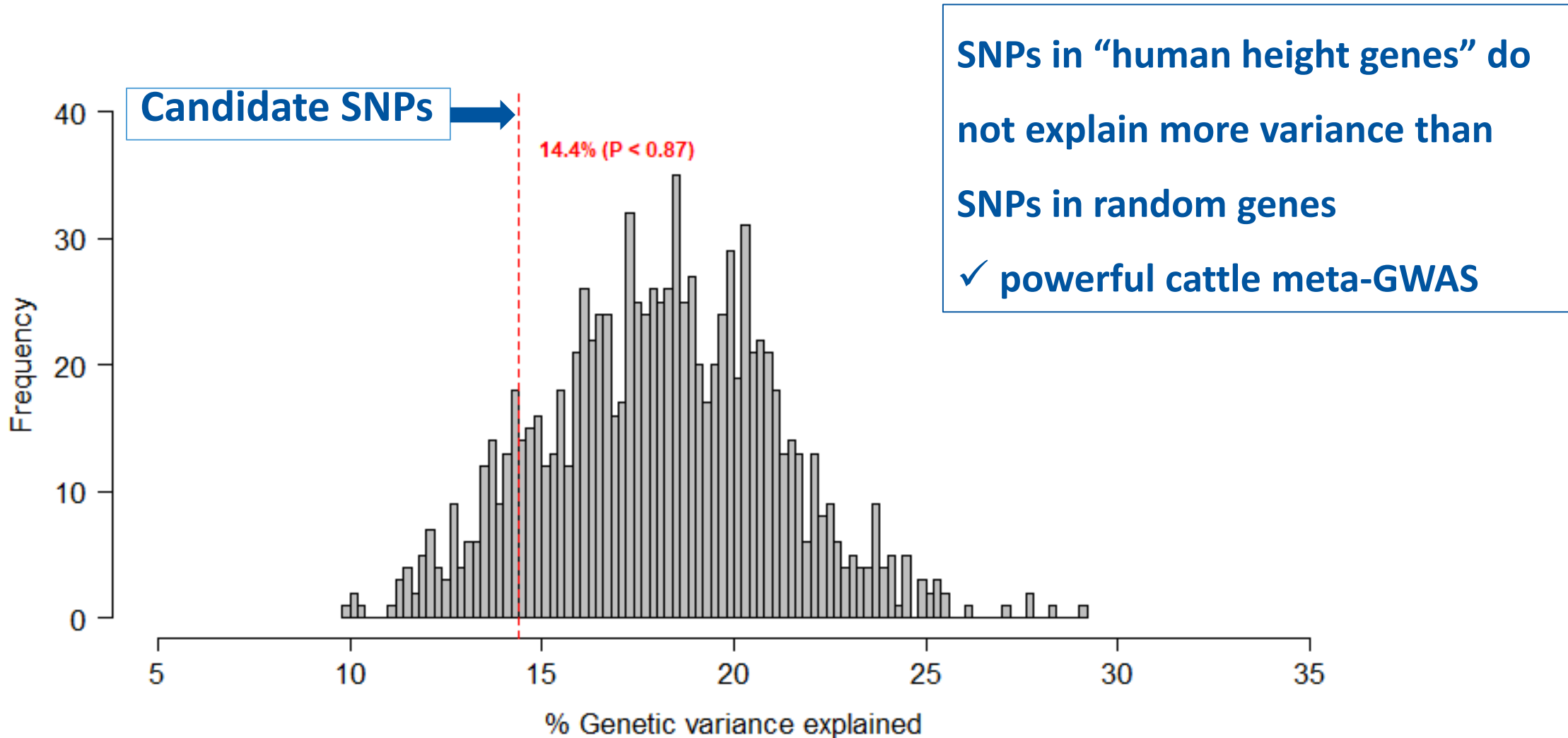
% G. variance for stature

>>>>>?

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ENRICHMENT FOR GWAS HITS IN CANDIDATE VS CONTROL CATTLE GENES

**Candidate genes more enriched for stature GWAS hits than random sets of genes**

VARIANCE FOR STATURE EXPLAINED BY CANDIDATE VS CONTROL SNPs (1)

Most sign. SNPs from "human height" gene vs Most sign. SNPs from random genes

Candidate SNPs

14.4% (P < 0.87)

SNPs in "human height genes" do not explain more variance than SNPs in random genes

✓ powerful cattle meta-GWAS

VARIANCE FOR STATURE EXPLAINED BY CANDIDATE VS CONTROL SNPs (2)

Random SNPs from "human height" genes vs Random SNPs in random genes

Candidate SNPs

14.4% (P < 0.09)
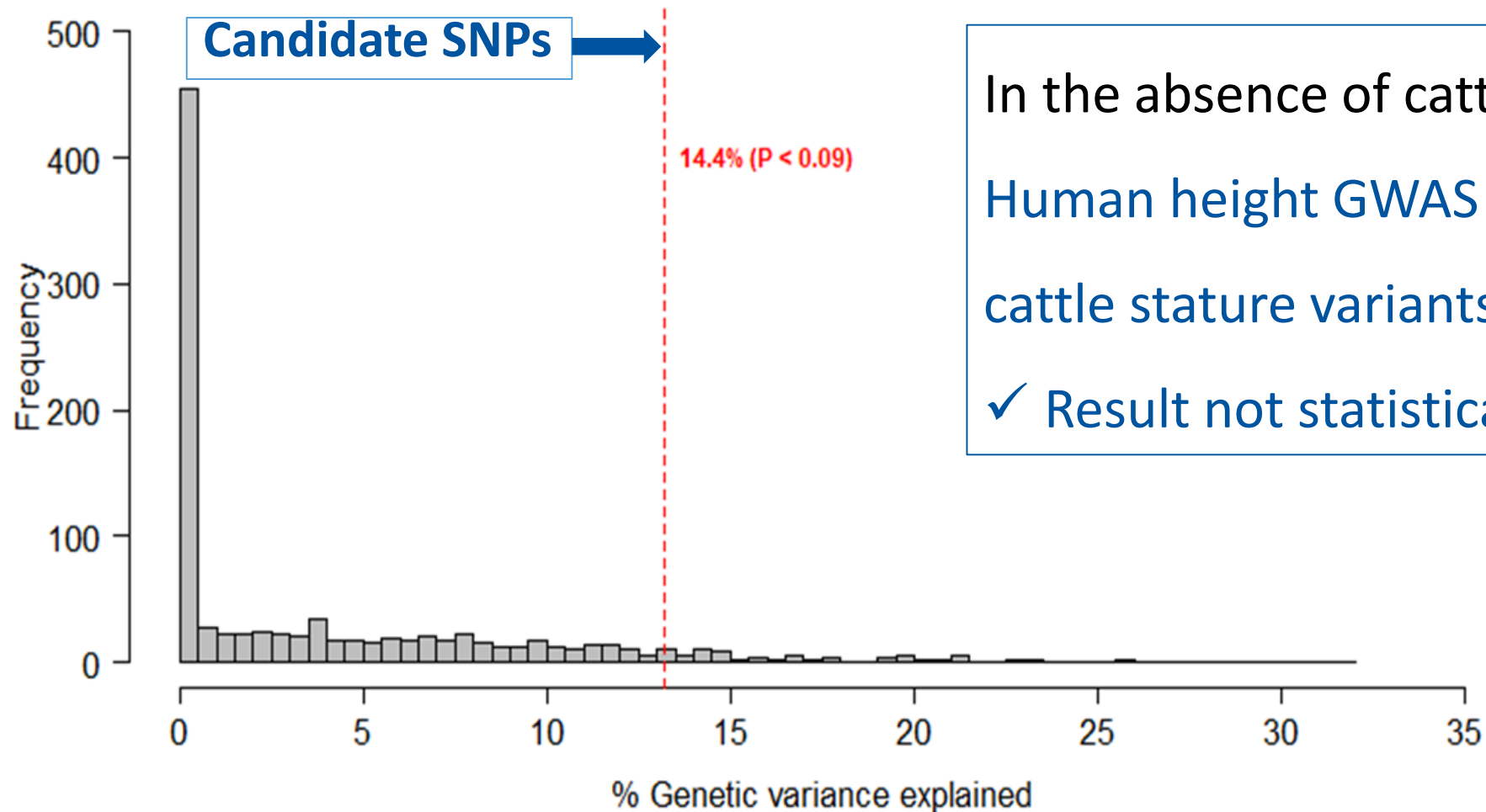
In the absence of cattle prior information:

Human height GWAS can help to prioritize cattle stature variants

✓ Result not statistically significant

CONCLUSIONS

- Human height GWAS result can be used to prioritize cattle stature genes

- Adding human GWAS information ↑ increased variance explained

Potential to utilize powerful meta-GWAS studies in humans for analysis of complex traits in livestock species

  ✓ Highly heritable trait

- In cases where **cattle prior information is not available**:

  ✓ Prior information from human GWAS can be useful

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