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SEARCH FOR NEW MUTATIONS IN CATTLE BY SYSTEMATIC WHOLE GENOME RESEQUENCING

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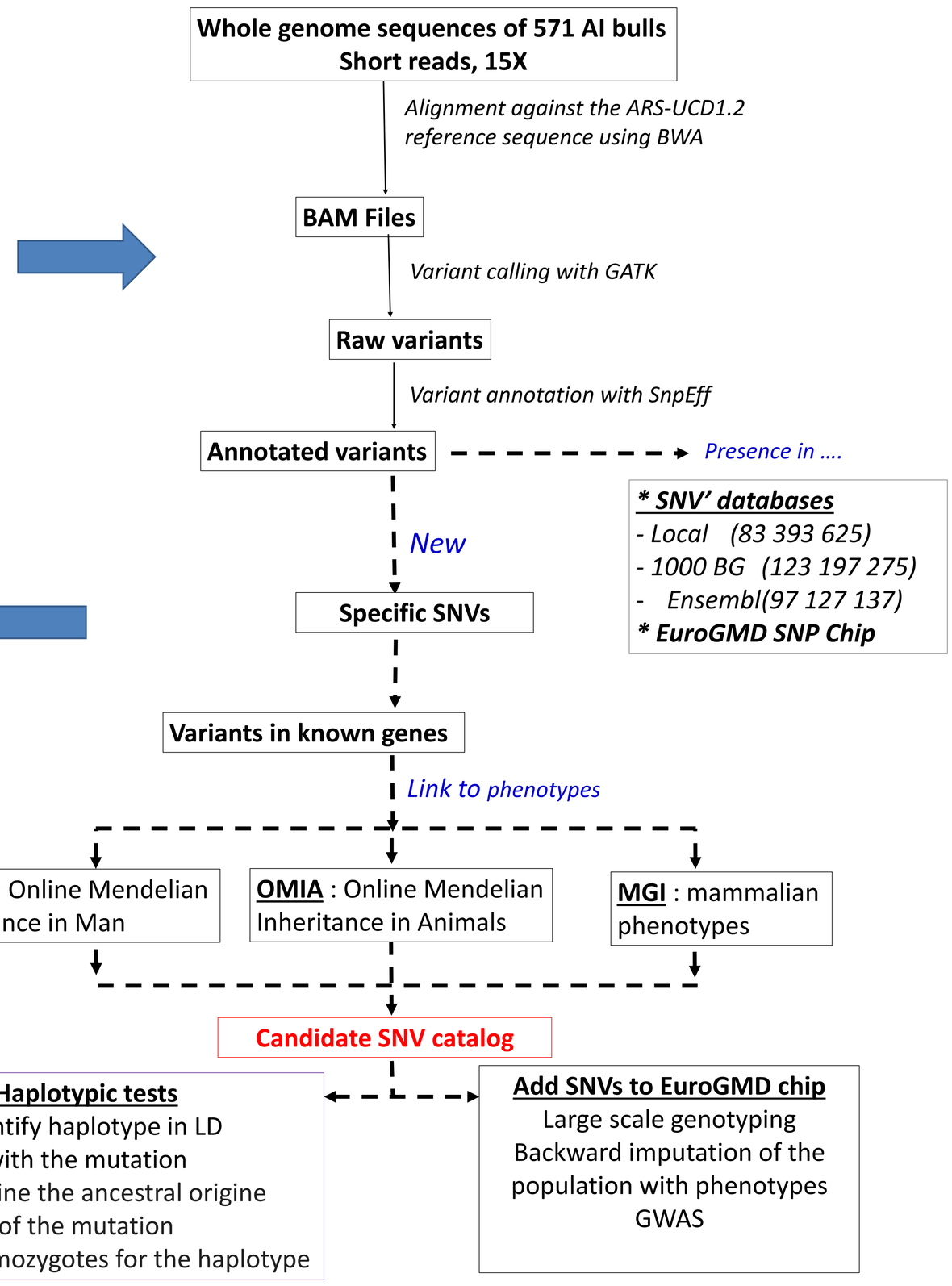
Introduction

Systematic whole genome sequencing of artificial insemination bulls presents strong advantages:

- Discovery of all genetic variants, including the rarest ones
- Improvement of imputation up to the sequence level, especially in medium size populations
- Identification of candidate variants of QTL
- Early identification of new potential genetic defects and their carriers before wide spreading in the population

As part of the SeqOccIn project, 571 AI bulls from 14 dairy and beef breeds were sequenced (Illumina NovaSeq technology). We present the strategy used to reduce false positives, with some of the results

Strategy to select potentially causal novel mutations



General results

- ***Total # of variants*** : 34 252 085
  - SNP : 28 931 309
  - InDels : 5 320 77
- ***Novel candidate variants***: 1 548
- ***Novel variants added into the EuroGMD chip*** : 1 342

Two examples of putative genetic defects

- ***ACAN: Bulldog defect, already known in Dexter***
- ***ITGB4 : Junctional epidermolysis bullosa***

Based on the severity and the certainty of these predictions, three AI bulls were culled

Several others are monitored with chip results (detection and phenotyping of homozygotes)

Study of some candidate variants on milk production

Within-sire regression coefficients

Variant	Breed	Milk	Fat	Protein	Fat%	Prot%	Haplotype frequency
PRLR	BrownSwiss	ns	**	*	***	**	2.5%
DGAT1	Abondance	***	**	ns	***	***	4.3%
SLC25A13		ns	ns	ns	*	ns	7.6%
FTO	Normande	ns	ns	ns	ns	ns	0.3%
SLC25A21	Montbeliarde	***	***	***	ns	ns	4.4%
BCO2		ns	**	ns	***	**	5.6%
MATN3	Holstein	ns	**	ns	***	**	4.2%
HPS3		*	ns	ns	**	**	6.3%

Conclusion

- All AI bulls have a large impact in their population and are worth sequencing to fully characterize their genome
- New variants can be studied by genotyping with the chip widely used in genomic selection, by annotation, and by imputation in the population
- Here, we present a strategy to detect and characterize these new variants, while minimizing false positives
- 1 548 new variants with a strong annotation and an anticipated effect on phenotypes (abnormality or QTL)
- Large scale effect confirmation and identification of individuals of interest through SNP chip genotypes
- These variants will help to
  - anticipate the emergence of genetic defects
  - To improve accuracy and persistence of genomic predictions

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