



GENOMIC VARIATION AND GENE EDITING

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Who Is Genus?



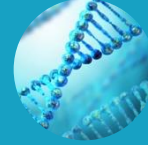
Pork



Dairy



Beef



R&D



World-leading animal genetics company

70+ countries

More than **2,700** employees;
R&D/IntelliGen team of nearly **400 employees**

60+ year history

Genus' global porcine and bovine businesses
(PIC and ABS) partner with **over 50,000 farmers globally**

***Relationships with leading research institutions
around the world***



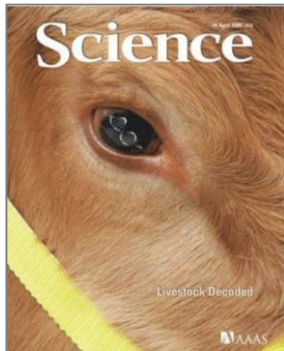
**QUESTION: COULD GENETIC CHANGES
INTRODUCED BY GENE EDITING HAVE ARISEN
NATURALLY?**

**UNDERSTANDING GENOMIC VARIATION HELPS TO
ANSWER THIS QUESTION**

PROGRESS IN UNDERSTANDING GENOMIC VARIATION

Accumulating genomic knowledge helps to uncover existing variations within and across populations

Cow Genome



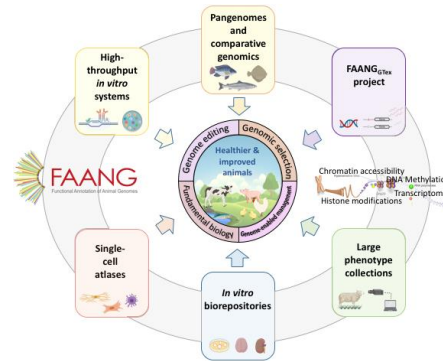
2007

Pig Genome



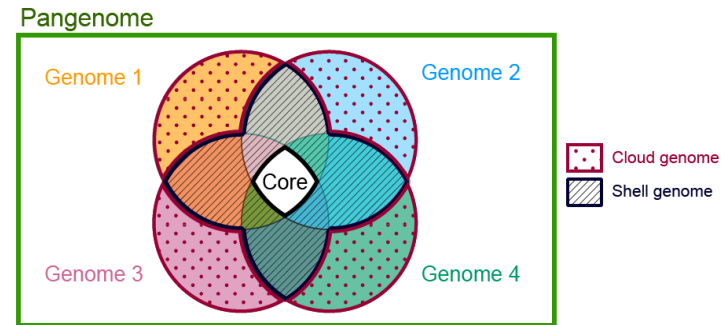
2009

Functional annotation of cattle and pig genomes



2018

Start of pangenomes



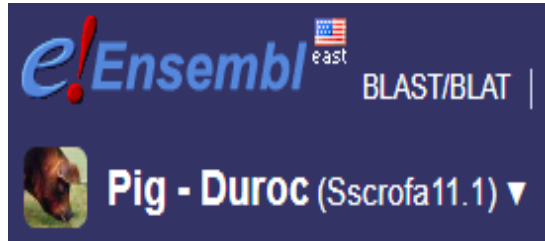
~2020



2025



IS THERE MORE INFORMATION TO CAPTURE?



Ensembl variant database:
total SNPs: 63,845,700



Functional SNP based on gene annotation:

stop gain/lost: 8,092
synonymous: 287,606
missense: 227,894



European Variant Archive:
total SNPs 72,607,645



Genus Whole Genome Sequence data
(7000 samples):
Total SNPs: 101,012,026

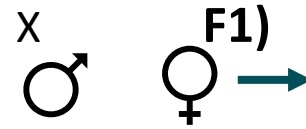
SNPs not present in public databases: 37,021,234
stop gain/lost: 14,394
synonymous: 284,502
missense: 217,793

DE NOVO VARIANTS IN EXISTING POPULATIONS

De novo variant - a genetic alteration that is present for the first time in one family member

Evaluated level of naturally occurring *de novo* variants in pigs through **normal reproduction cycles**

- Whole Genome Sequencing of 13 litters in trios (



F1 animals

Total “*de novo*” variants - 1367
(88-134 variants per individual)

Indels - 394
(24-43 indels per individual)



De novo variants in genes - 740

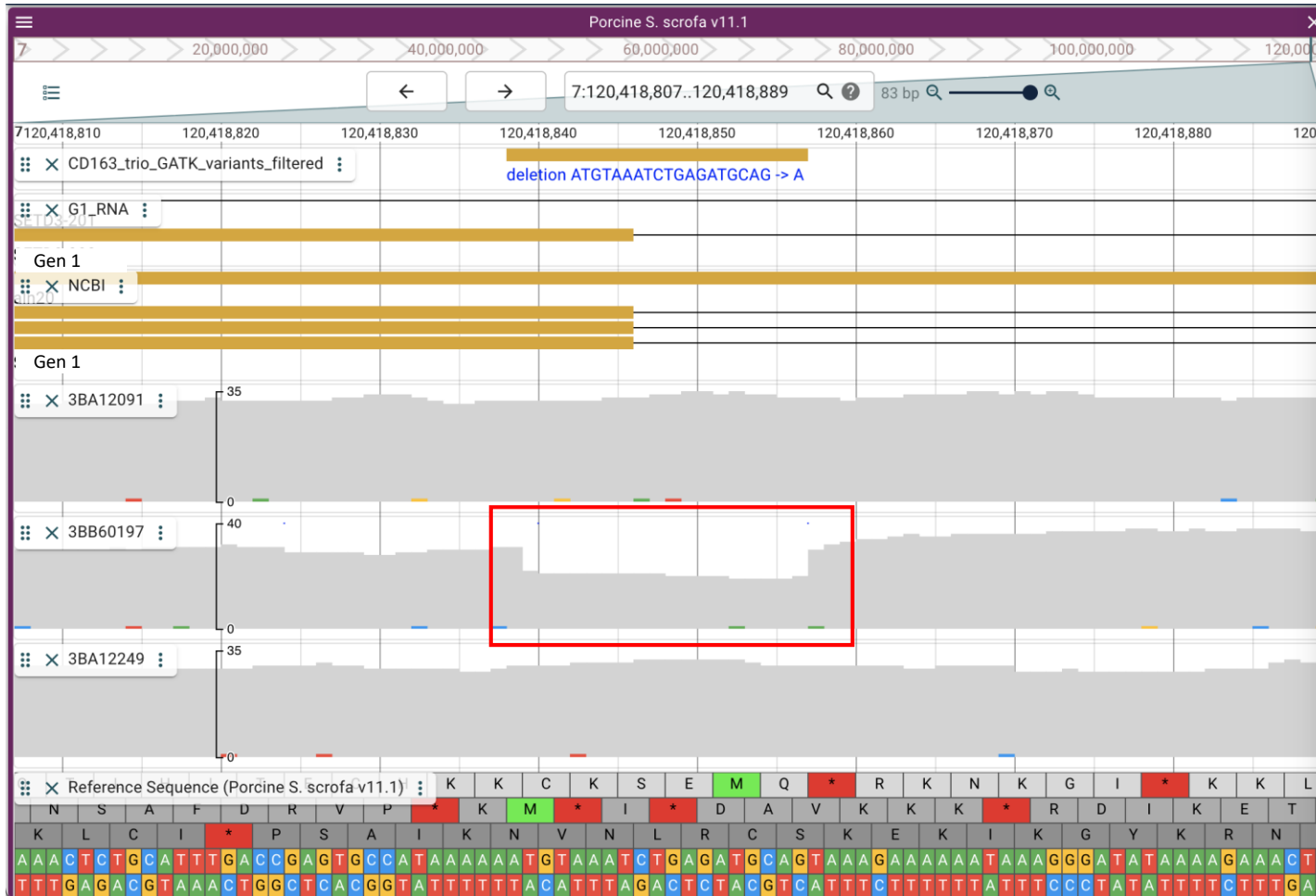
In coding regions - 37

Missense - 2

De novo variants defined as:

- Not present in either parent
- Heterozygous (0/1) in F1 offspring
- Criteria used: allele frequency >0.2 with depth of alternative allele coverage ≥20X coverage

UNDERSTANDING FUNCTIONAL CONSEQUENCES OF “*DE NOVO*” VARIANTS CAN HELP WITH BREEDING FOR DESIRED TRAITS



Example: Deletion of a partial exon in gene Gen1

- Gen1 is a methyl transferase implicated in the replication of all enteroviruses
- A mouse line deficient in Gen1 expression was shown to be resistant to enterovirus infection

GENE EDITING CAN HELP HARNESS NATURALLY OCCURRING VARIATIONS FOR ANIMAL HEALTH AND WELL BEING

Nature creates millions of genetic variants every reproductive cycle. Traditional breeding relies and makes use of a range of genetic changes if phenotypes are observed

Many genomic variants are lost during breeding

- **observable phenotype may not be present**
- **phenotype is not easy to detect without specific studies**

If variants are found, it will require many years to incorporate into population. The process may lead to a potential loss of genetic gain in other important traits

Gene editing can reproduce useful variation in elite germplasm quickly by introducing naturally occurring variants.

In many cases, genetic changes that can be introduced by gene editing have already occurred or will occur naturally

Thanks!