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Genetics markers in breeding

Modul no. 3: Animal Breeding

prof. Ing. Tomáš Urban, PhD.
Mendel University in Brno
Faculty of Agriscience

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

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Molecular genetics/genomics and breeding

The main importance of molecular breeding support

- Using real genetic variability of genetic markers

  -> **more accurate estimates** of genetic parameters and breeding values

  -> making breeding more efficient by increasing genetic gain and shortening the generation interval

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Molecular assistance for selection

- **MAS** – *marker assisted selection* (linkage 1 marker with 1 **QTL**)
  - Direct use of markers as selection criteria (CRC stress gene in pigs, BLAD in cattle)
  - Multiple markers -> markerBLUP to refine BV estimation
- **GAS** – *gene assisted selection* (**QTN** – quantitative trait nucleotide – using candidate genes)

- Genomic selection (**GS**) (**SNPs** equally across the genome)
- Using knowledge of the real genetic variability (mutations in or near genes) detectable by molecular genetic methods
- Their application in breeding in selection systems
- **GS** – incorporation of **genomic SNP markers into the genomic relationship matrix** and then into BLUP-AM equations (different variants) and **estimation of GEBV** (genomic EBV)
  - **More efficient breeding (reduces costs, refines PH estimates), shortens generation intervals**

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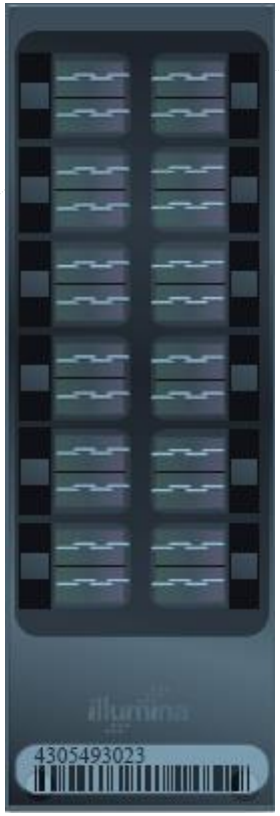
Molecular genetic markers

- **Detectable polymorphisms with a known position in the genome**
- **Type I** - coding genes, candidate genes (e.g. ESR, GH)
- **II. typ** - microsatellites (MS), short tandem repeats (STR)
- **III typ** – bialelic singlenucleotide polymorphism (**SNP**) in coding or, more commonly, non-coding intron or intergenic regions

PorcineSNP60 v2 BeadChip



More than 64,000 SNPs across the genome
Average distance between SNPs is less than 43.4 kb

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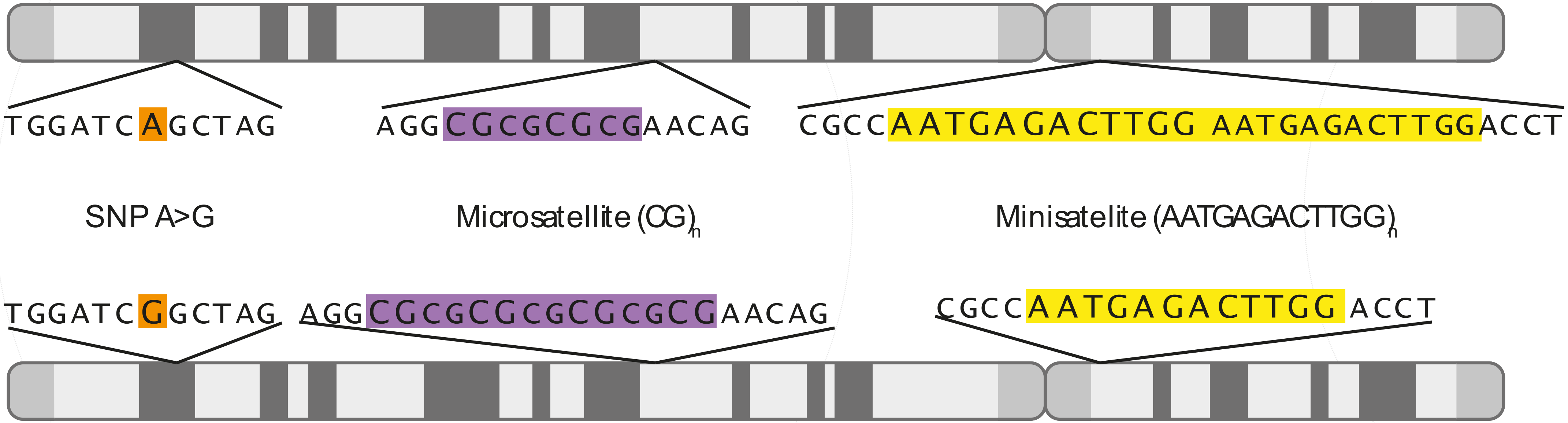

TGGATCAGCTAG

AGGCGCGCGCGAACAG

CGCCAATGAGACTTGG AATGAGACTTGGACCT

SNP A>G

Microsatellite (CG)$_n$

Minisatelite (AATGAGACTTGG)$_n$

TGGATCGGCTAG

AGGCGCGCGCGCGCGAACAG

CGCCAATGAGACTTGG ACCT

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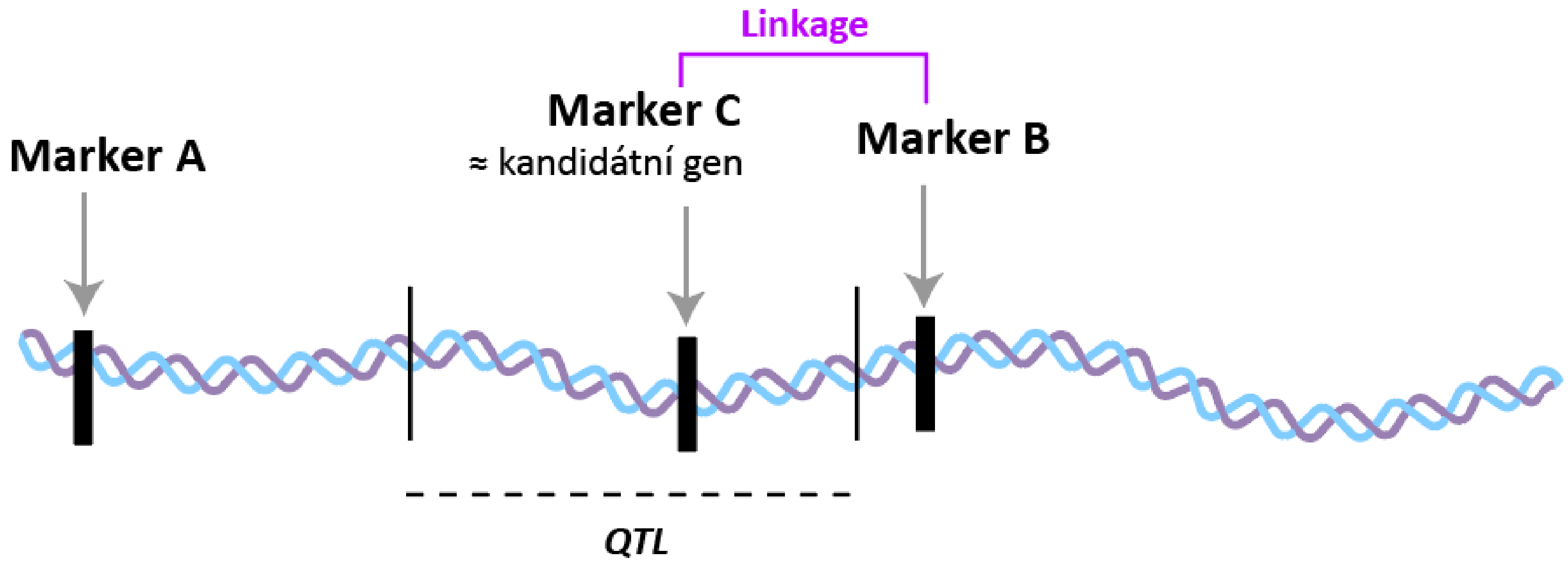
Genetic marker (**GM**)**:** a polymorphic sequence whose variants exhibit mendelian inheritance and may be associated with trait variation important for breeding (or mapping), although it may not have a direct biological effect

Marker: **direct** (causative polymorphism in the gene) and **indirect** (in linkage with unknown causative gene - LD linkage disequilibrium)



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Genetic marker as a candidate gene

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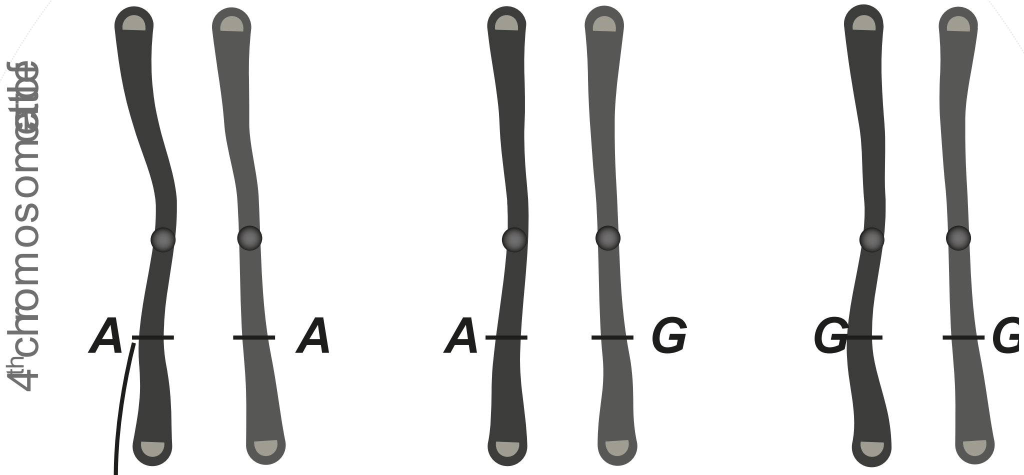
Animal 1

Animal 2

Animal 3



SNP position on chromosome 4

4:g.93262101 A>G

SNP LEP
ID: rs436985239

alela A

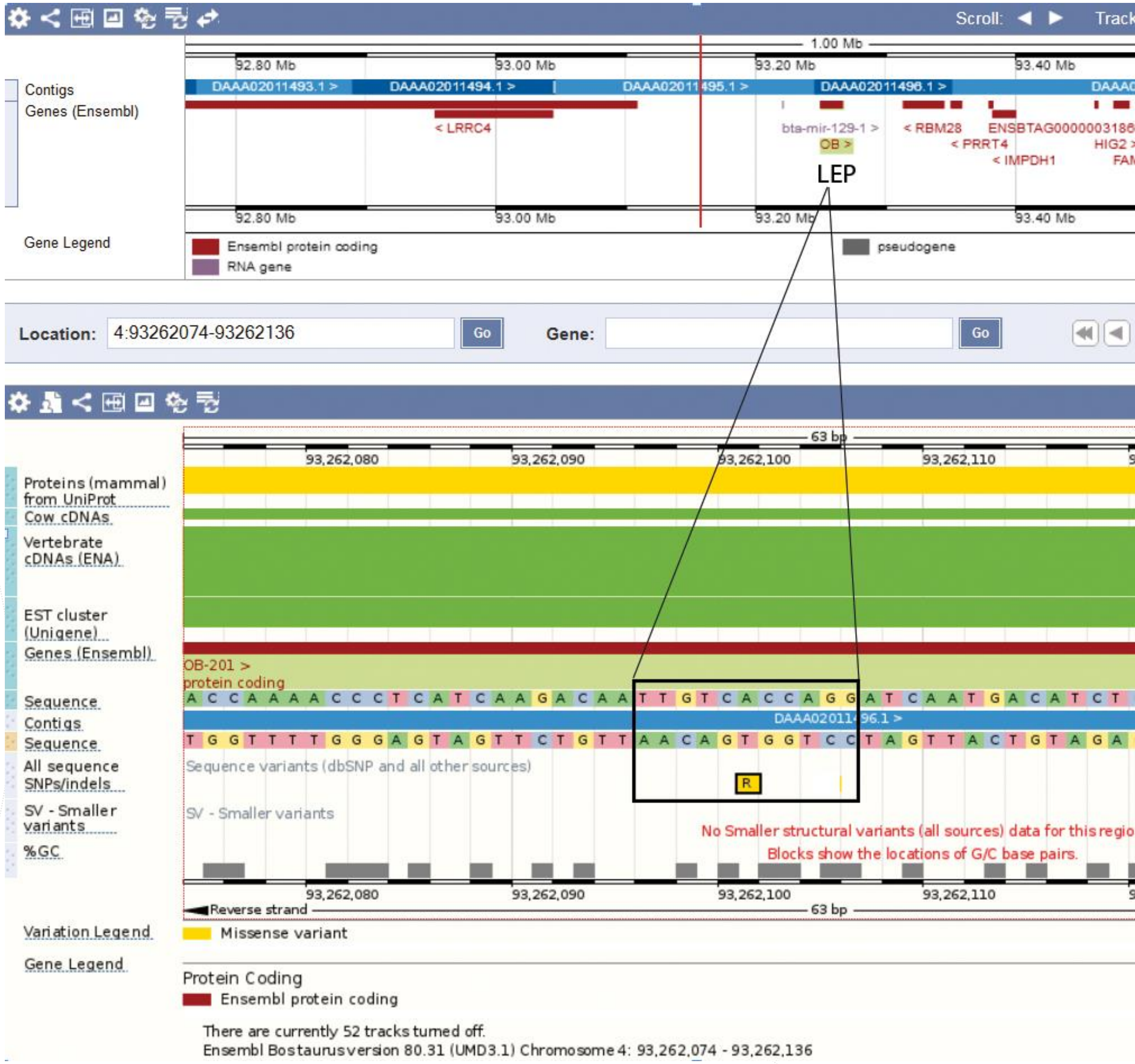
TTGTC A CCAGGA
AACAG T GGTCCT

alela G

TTGTC G CCAGGA
AACAG C GGTCCT

Amino acid substitution in the protein leptin in cattle

Thr40 → Ala



Location: 4:93262074-93262136

Gene:

Sequence: A C C A A A A C C C T C A T C A A G A C A A T T G T C A C C A G G A T C A A T G A C A T C T

Sequence: T G G T T T T G G G A G T A G T T C T G T T A A C A G T G G T C C T A G T T A C T G T A G A

Sequence variants (dbSNP and all other sources)

SV - Smaller variants

No Smaller structural variants (all sources) data for this regio

Blocks show the locations of G/C base pairs.

Missense variant

Protein Coding

Ensembl protein coding

There are currently 52 tracks turned off.
Ensembl Bostaurus version 80.31 (UMD3.1) Chromosome 4: 93,262,074 - 93,262,136

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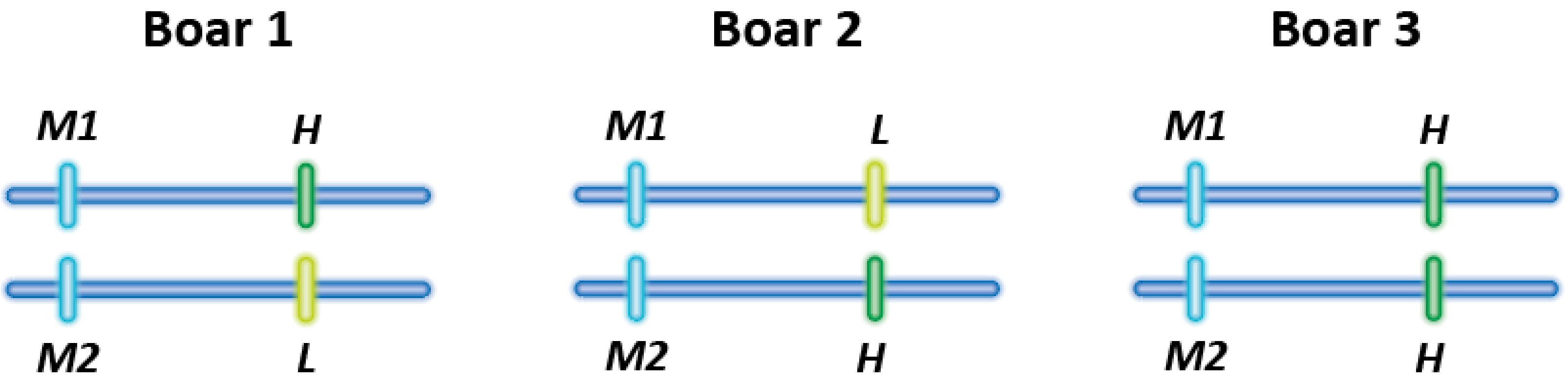
Relationship between marker and QTL

- QTL - quantitative trait locus (a region in the genome detected by association analysis assessing the relationship between variation in a genetic marker and variation in a performance trait
- The association between marker and QTL depend on distance between marker and target traits.
- Marker (***M***) may not be causative, but may be linked to the causative locus QTL (***H***), which we do not know (has 2 alleles; ***H*** - associated with higher performance, ***L*** - with lower performance) - possibility of recombination



M1 marker allele is associated with high performance

M1 marker allele is associated with low performance

Marker alleles are not associated with QTL

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Marker assisted selection (MAS)

- MAS in livestock selection programmes allows to increase the accuracy of selection for specific DNA variations that are associated with measurable differences in economically important traits.
- The rate of genetic improvement achieved by MAS can be significantly higher than that achieved by selection based on EPD values for traits that have low heritability values in populations or are determined *post mortem*.
- MAS therefore has the potential to significantly increase the efficiency of animal breeding.

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Phases of MAS

- in **the detection phase**, DNA polymorphisms are used as direct or linked markers to detect specific allele frequencies within segregating QTL populations. During this phase, QTL-associated markers are identified and QTL allele effect sizes and QTL locations in the genome can be estimated.
- In **the evaluation phase**, linked markers are tested in target populations to determine whether QTL segregate within the population.
- And in **the implementation phase**, predictive linked markers within families are used in the population and direct markers are used across families to create a genotype database. These data are combined with pedigree and phenotypic information during genetic evaluation to predict individual genetic values.

MAS and its applications

The use of MAS for direct selection of an individual by genotype of a genetic marker/gene for simple traits - monogenic (most often monogenic diseases) is appropriate.

- e.g. CRC stress gene in pigs, BLAD disease gene in cattle

Little usage - For markers associated with quantitative traits, the use of MAS is smaller, with less effect - there are not as many candidate genes described, and more importantly, not many traits with simple genetic determinism. For these traits, it is necessary to include genome-wide SNP markers and to do so in a genomic selection system.

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Thank you for your attention!

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Tomáš Urban
urban@mendelu.cz

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