EAAP 2010 - Session 15 - carole.moreno@toulouse.inra.fr

Searching for Genes of Interest in Sheep

Moreno C.,
Elsen JM., Legarra A., Rupp R., Bouix J., Barillet F., Palhiere I., Larroque H., Allain D., Francois D., Robert C., Tosser-Klopp G., Bodin L., Mulsant P.





SAGA - LGC

ALIMENTATION
AGRICULTURE
ENVIRONNEMENT

INRA

Plan

1) Sheep genome and its markers

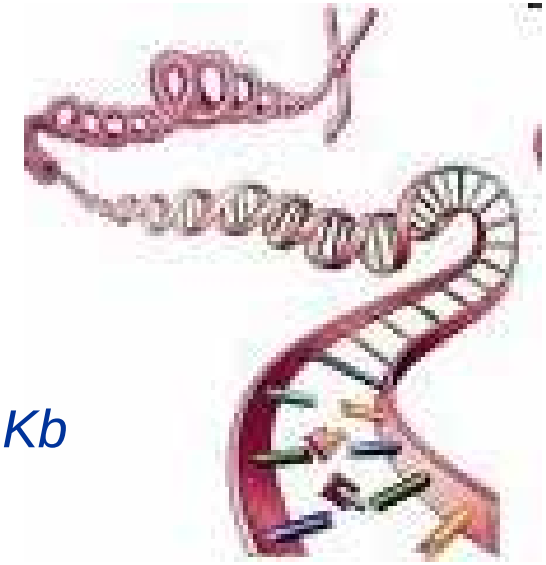
2) Detection of genes or QTL

3) Gene selection / genomic selection

The sheep genome:
general description

Genome

- 52+2 chromosomes
- 3 10^9 bases = 3 10^6 Kb
- 3 000 centimorgans (cM)



1 cM = 1% of recombination = 1000 Kb

- non-coding regions = 98 % genome
- coding regions = 2 % genome = 24 000 genes
- on average 15 genes /cM or 1 000 kB
- 1 gene ~ 1200 bases

Differences between microsatellite and SNP markers

Until now		Now
Microsatellite		**SNP** (single nucleotidic polymorphism)
Multiallelic marker		Bi allelic marker
In non-coding regions		Located in genes and non-coding regions *(can be a causal mutation)*
150 to 200 markers / panel	**X 300**	**50 000** markers/ chip
1 marker / 10 to 20 cM		15 markers / cM
Cost = 100 to 300 €	**X 1**	Cost= 100 to 200 €

Plan

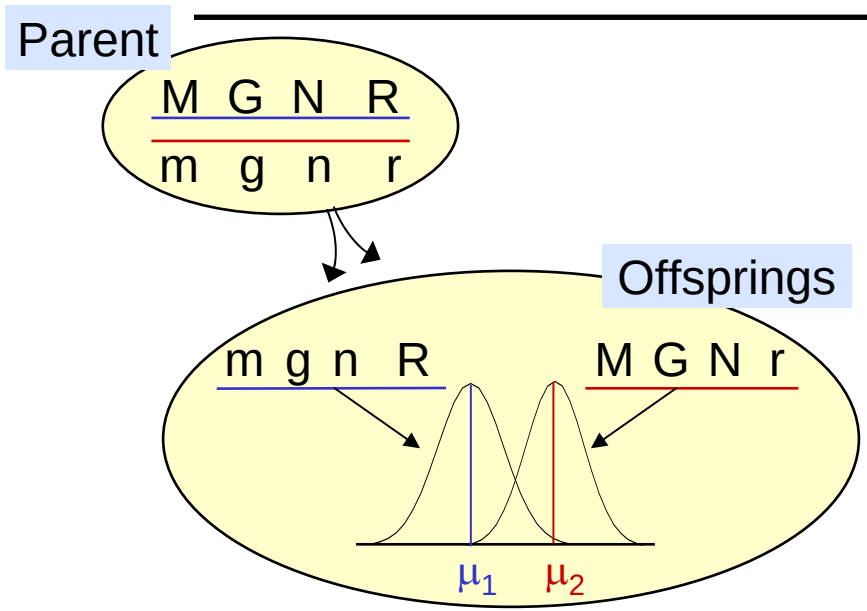
✓ 1) Sheep genome and its markers

2) Detection of genes or QTL

3) Gene selection/ genomic selection

QTL detection methods: LD LA

LA: Linkage Analysis

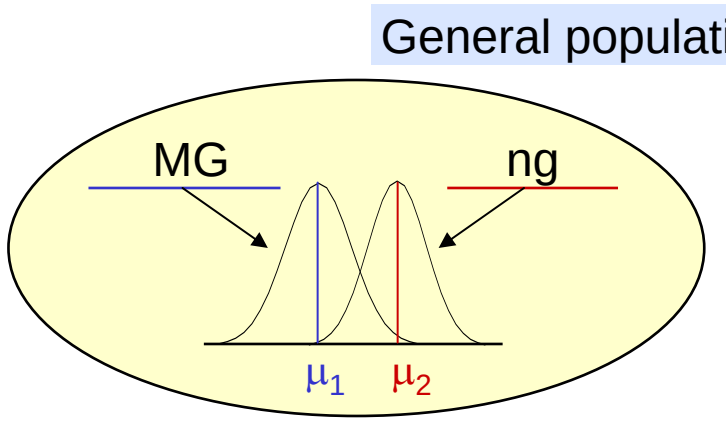


Actual transmission between relatives
↘ QTL detection is sure

Large genomic segments transmitted
↘ low location accuracy (5 – 15 cM)

Lower location with microsat. than with SNP

LD: Linkage Desequilibrium



Association between markers and QTL
↘ QTL detection is not sure

Small genomic segments historically preserved
↘ fine location accuracy (0.5 - 2 cM)

Impossible with microsat.

Steps after the QTL detection

- Fine gene location:
  positional candidate genes
  Genotyping new animals (different families, breeds…)
- Expression gene study:
  functional candidate genes
  Transcriptomic study on few extreme animals
- Search of candidate genes in data bases
  Using known sequence and comparative genomics
- Sequencing to identify new SNP

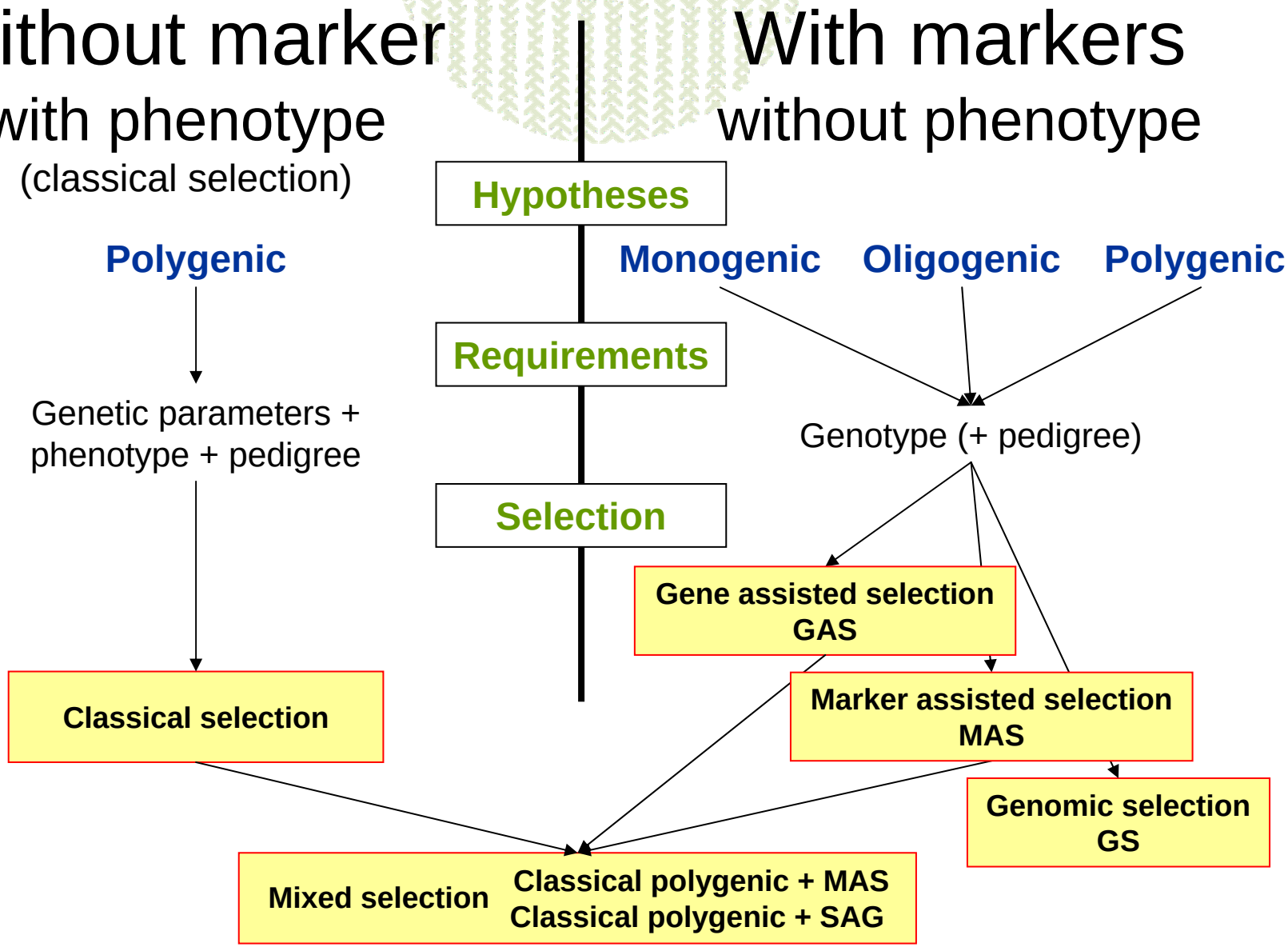
Detection of the causal mutation in a gene or a regulatory region

Causal mutations affecting production traits

Gene	Affected trait(s)
PrP	Scrapie resistance
BMPR1B	Ovulation rate
GDF9	
BMP15	
GDF8	Muscle mass
αs1-casein	Casein content
β-lactoglobulin	Cheese-making properties; milk yield
ASIP	White dominant color
TYRP1	Light fleece color
Hairless (hr)	Hypotrichosis

Plan

- ✓ 1) Sheep genome and its markers
- ✓ 2) Detection of genes or QTL
- 3) Gene selection/ genomic selection


Without marker
with phenotype
(classical selection)
With markers
without phenotype
Hypotheses
Polygenic
Monogenic
Oligogenic
Polygenic
Requirements
Genetic parameters +
phenotype + pedigree
Genotype (+ pedigree)
Selection
Gene assisted selection
GAS
Classical selection
Marker assisted selection
MAS
Genomic selection
GS
Mixed selection
Classical polygenic + MAS
Classical polygenic + SAG

Mixed selections (classical + MAS / GAS) nice opportunities for sheep

On the same trait (i.e. milk yield + casein content)

- classical requirements needed
- genotyping of some markers only

On different traits (i.e. milk yield + PrP)

- classical requirements needed
- genotyping of some markers only
- no phenotype required for the trait selected by MAS or SAG

- No need to identify the causal mutation
- Problems with:
  - . no fully additive alleles (e.g. BMP15, GDF9)
  - . gene fixation and genetic variability (e.g. PrP)
  - . breakdown of disease resistance with one gene involved

Principle of genomic Selection

1/ Training population A+A'

- Phenotyped and genotyped animals (50K SNP chip)
- Prediction equations of marker effects are calculated using population A and verify using the population A'

2/ Application to the selected population B

- No phenotypes are needed, only genotyping
- Same accuracy for young males and females, particularly interesting when progeny testing is necessary

Genomic selection in sheep?

- Difficulties to perform genomic selection
  - Large training population (>1000 animals under progeny test)
  - Genotyping cost (>100€ or more / animal)

- Possible use:
  - Large selected population (dairy sheep breeds,…)
  - Very expensive selection criteria (e.g. disease resistant traits)

Conclusions

- 50K SNP chip
  revolution to detect genes and perform genomic selection
- 600K SNP chip and 3K SNP chip are in progress
  → new opportunity for selection
  (selection of several breeds simultaneously, genotype imputation …)
- But a bigger revolution is preparing: direct sequencing
- Future selection:
  - genomic selection for the biggest breeds and genes
  - mixed gene and polygenic selection for the other breeds

Thank you for your attention