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Genomics: A Paradigm Shift in Animal Breeding

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Modern Genomic Technologies

- Short introduction to Genomics
- Some Applications of Genomics
- Looking into the future & conclusions

All living things contain DNA

Animals

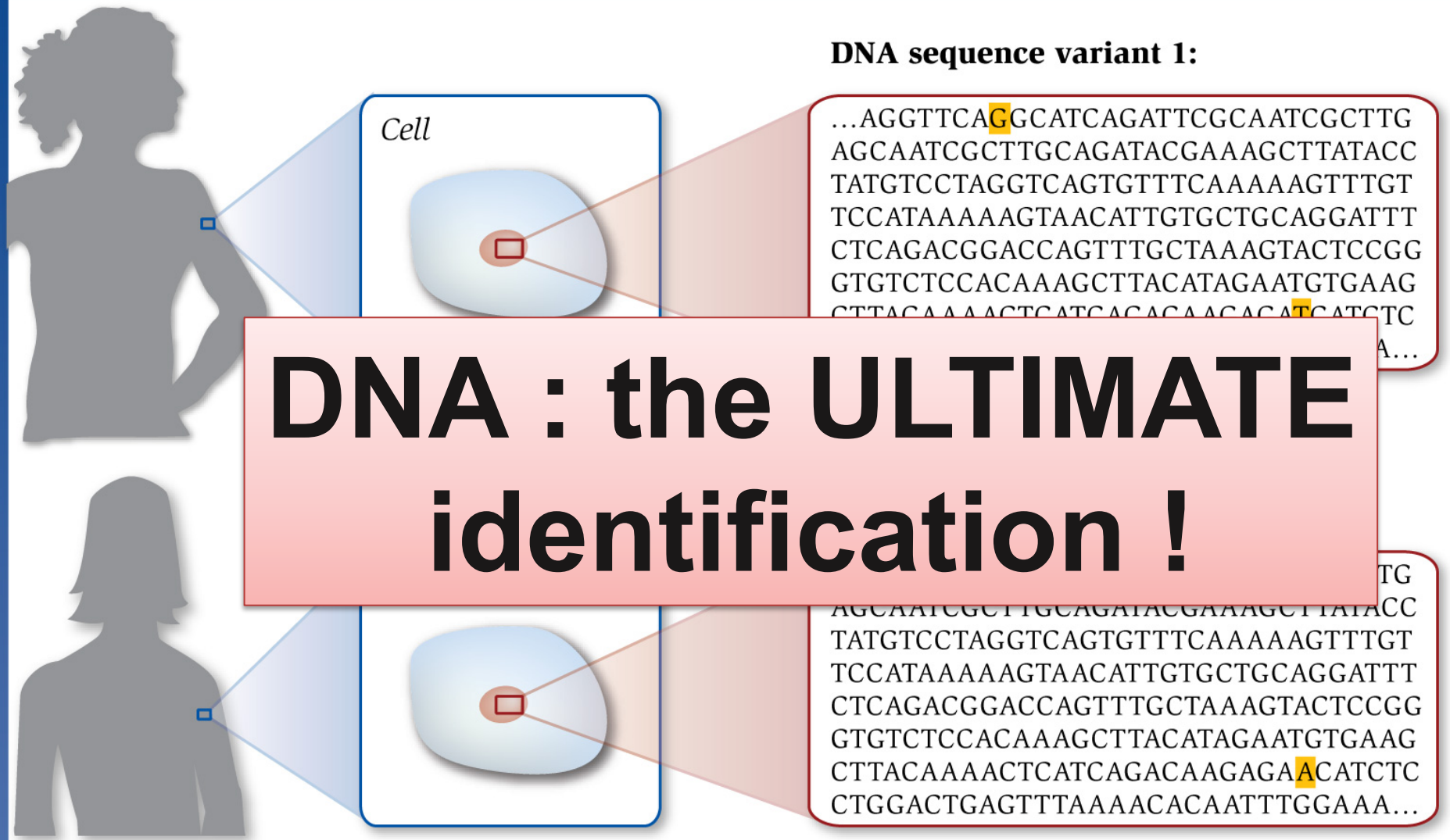
Plants

Bacteria

Humans

- DNA from every organism looks essentially the same.

Each individual has a unique DNA sequence



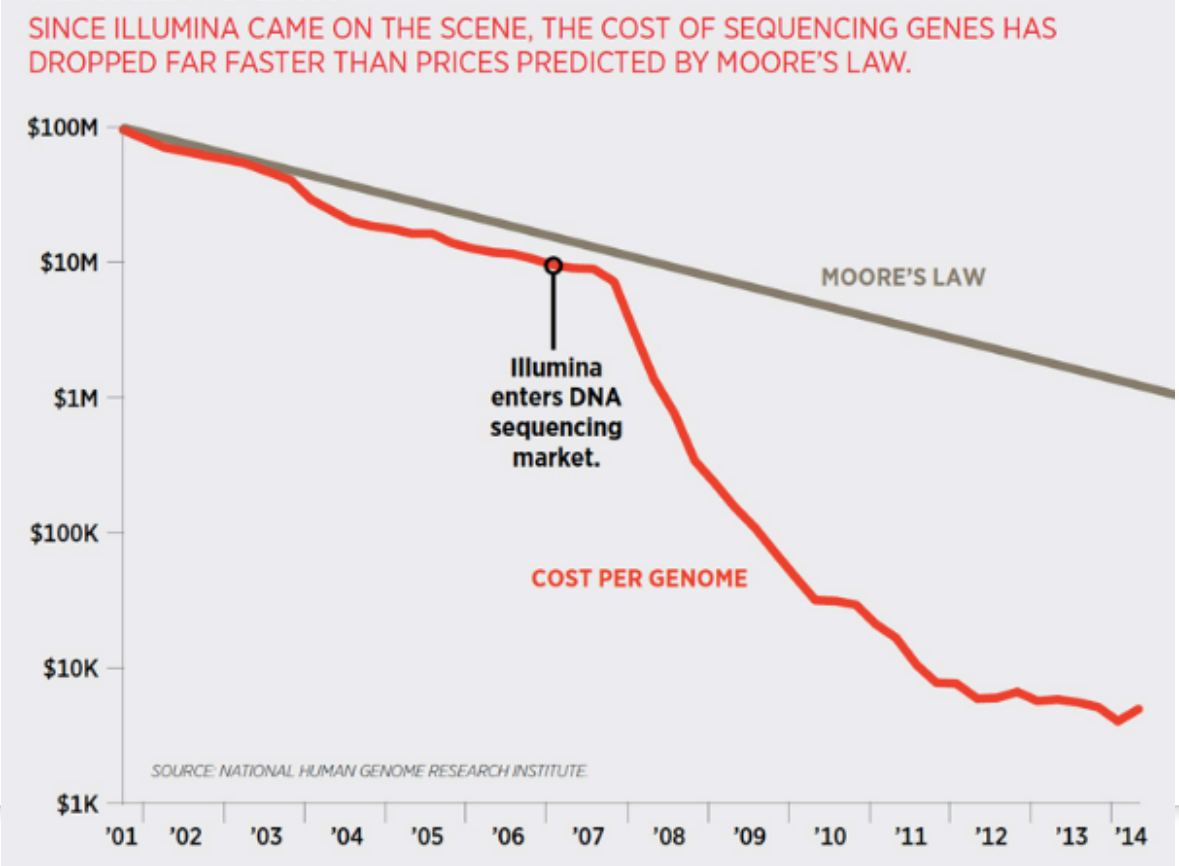
DNA : the ULTIMATE identification !

National Human Genome Research Institute

SNP : **S**ingle **N**ucleotide **P**olymorsphism

From the Human Genome Project to High-Throughput Livestock Genomes Genotyping and Sequencing

- The race to sequence the first human genome, and, subsequently, the race to enable routine re-sequencing has resulted in a 100 million fold decrease in DNA sequencing prices since 1990



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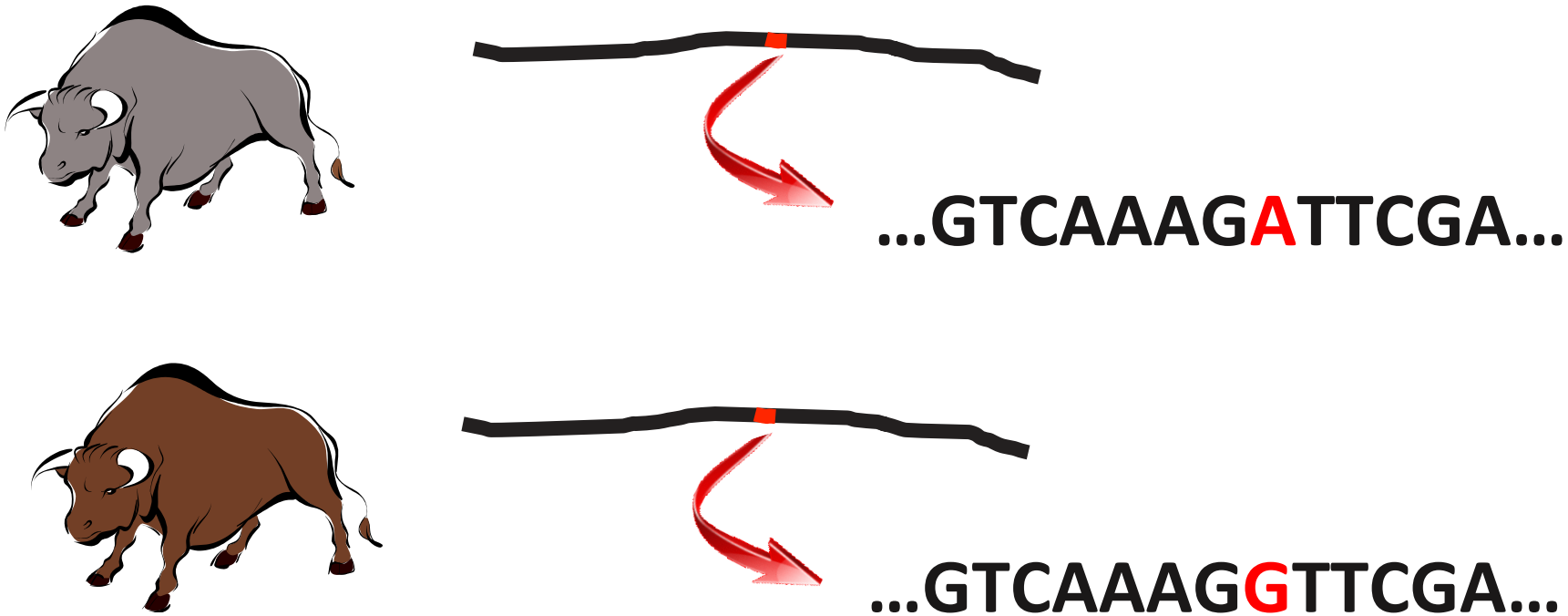
From the Human Genome Project to High-Throughput Livestock Genomes Genotyping and Sequencing

- Reference genomes for many Animal and Plant Species have been generated over the past decade
- Sequencing and re-sequencing of economically important livestock and plant species has resulted in the discovery of millions upon millions of SNPs

The AgriGenomic Era …

- Sequencing of livestock genomes has discovered millions of Single Nucleotide Polymorphism (SNP) markers



Even if the mutations themselves do not directly affect the phenotype, they can track for the variability of causal mutations in their vicinity.

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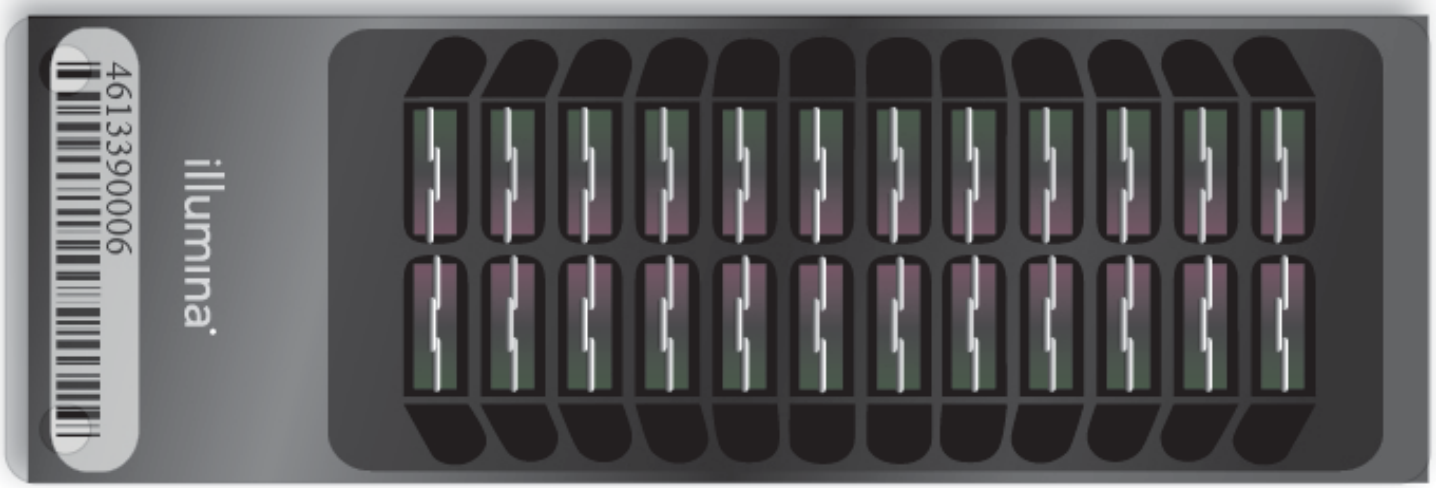
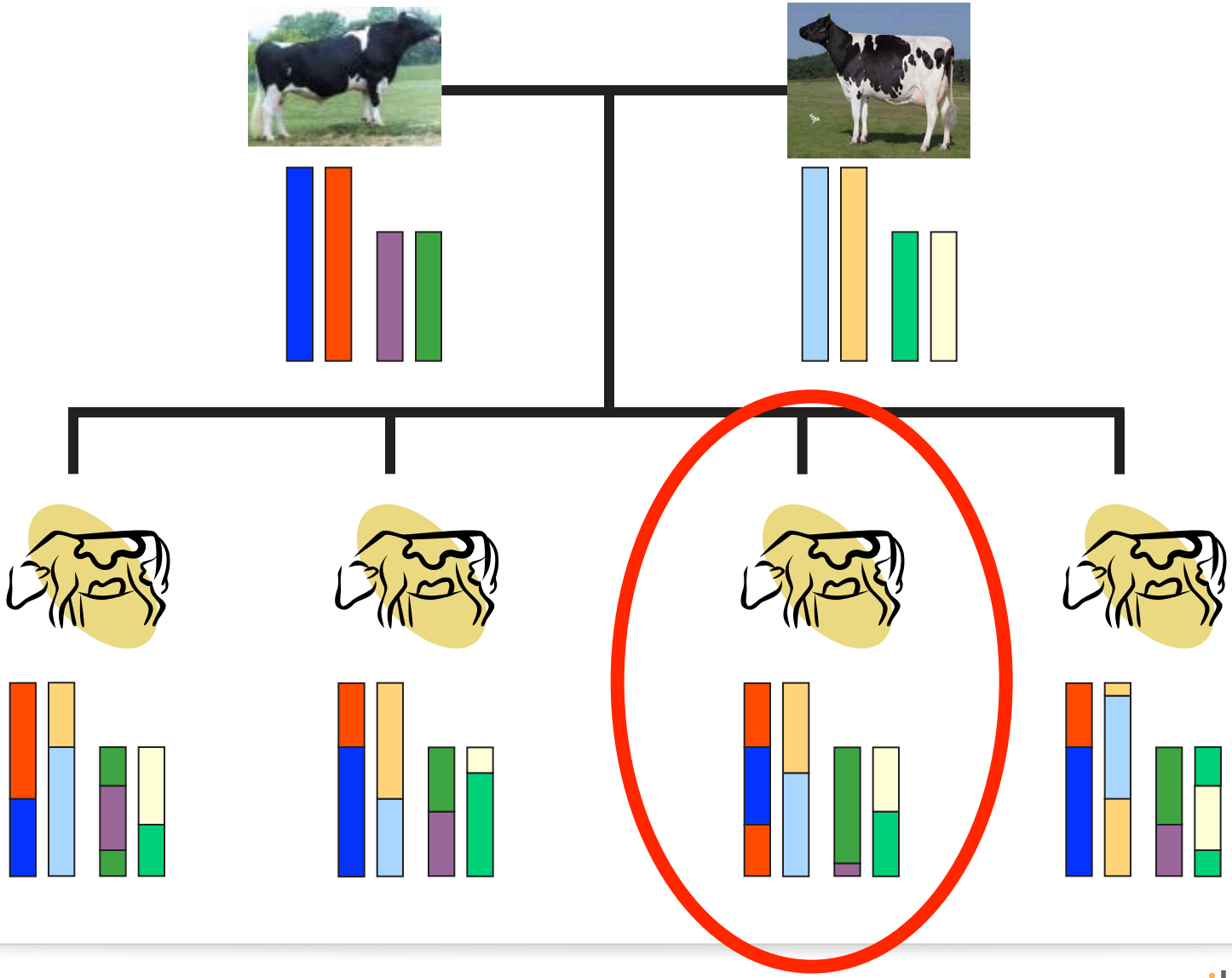
From the Human Genome Project to High-Throughput Livestock Genomes Genotyping and Sequencing

- These single nucleotide polymorphisms are being deployed in massively parallel fashion on DNA microarrays
- DNA microarrays are enabling genome-wide association studies to identify genotype-phenotype correlations for both simple and, more important, complex traits.

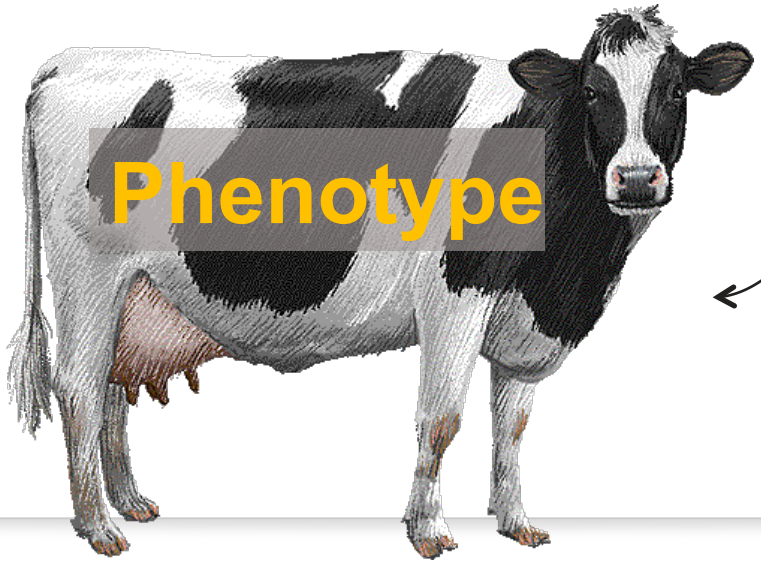


Transmission of Genetic Information




Genotype


Environment


Phenotype

Expectations from Genomics - Academic

- Genome structure and function
- Understand the history of life
- Simple phenotypes & genetic disorders
- Genetic control for complex phenotypes
- Biomedical models
  - Growth
  - Development
  - Health
  - Reproduction

Immense pressure exists to speed up the discovery process and close the "genotype / phenotype" gap.

Commercial Expectations from Genomics

- **Increased efficiency** of animal breeding
- Better insights into reproduction, growth, nutrition, health and animal welfare
- **Increased quality and security** of Animal products

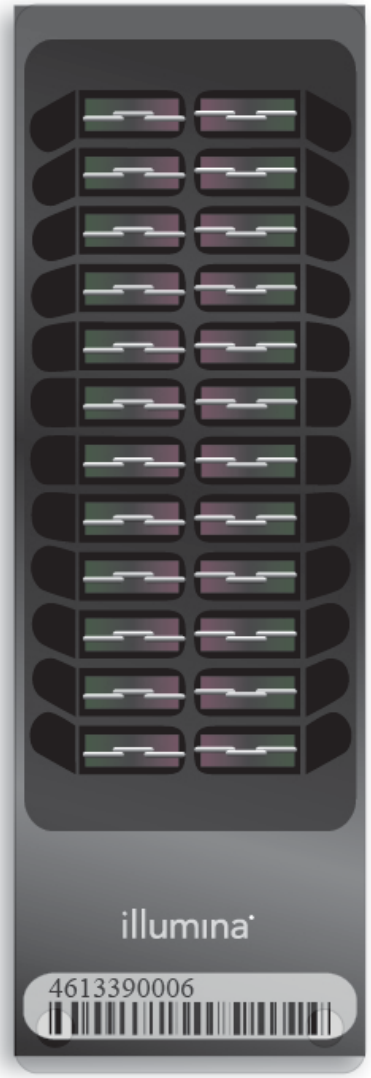
Genomics is providing the tools needed to refine and more rapidly achieve breeding goals.

Cattle Genetic Diversity Study

Gautier *et al*., 2010

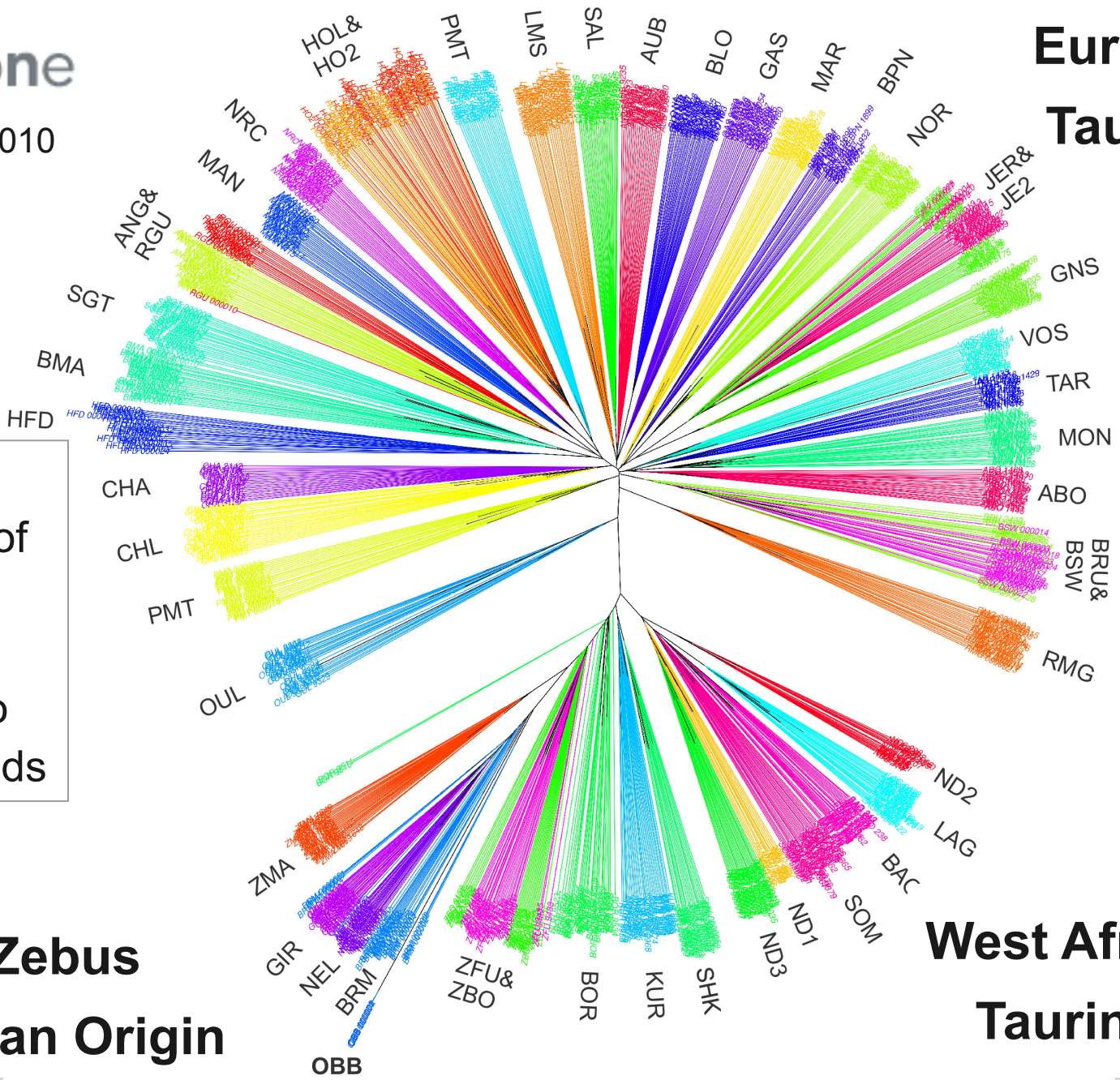
Insights into the Genetic History of French Cattle from Dense SNP Data on 47 Worldwide Breeds

- **47 populations** from different parts of the world
- **1121 animals**
- Genotyped with BovineSNP50
- **44706 SNPs**
- Detailed analysis of genetic structure at both the individual and population levels.



PLoS one

Gautier *et al*., 2010



European Taurines

Clear partitioning of the cattle genetic diversity into distinct breeds

Zebus Indian Origin

OBB

West African Taurines

Population Genomics

- The study of variation at genome-wide level and at population-level
- New paradigm for connecting DNA to phenotype referred as **selection signature** analysis
- Identification of target of selection (natural/artificial)
  - Independent of the phenotype (initially)
  - **Within populations** or **case-control populations**
  - **Fixed** as well as **segregating** traits
  - **Weak** or **strong** selection (question of time…)

Parentage verification & Traceability : *moving from microsatellites to SNPs*

- International Society for Animal Genetics (**ISAG**) is supporting transition from microsatellites to SNPs
  - Released a **list of 200 SNPs to be used in Bovine parentage** verification
    - 100 SNPs as core panel
    - 100 SNPs as additional panel
  - Organized regular comparison tests for SNP genotyping to ensure a standard in SNP Parentage genotyping
- Genotyping laboratories : accreditation by ICAR

- The 200 SNPs are part of the BovineLD content (>8000 SNPs) widely used as based content SNP chip for genomic selection worldwide

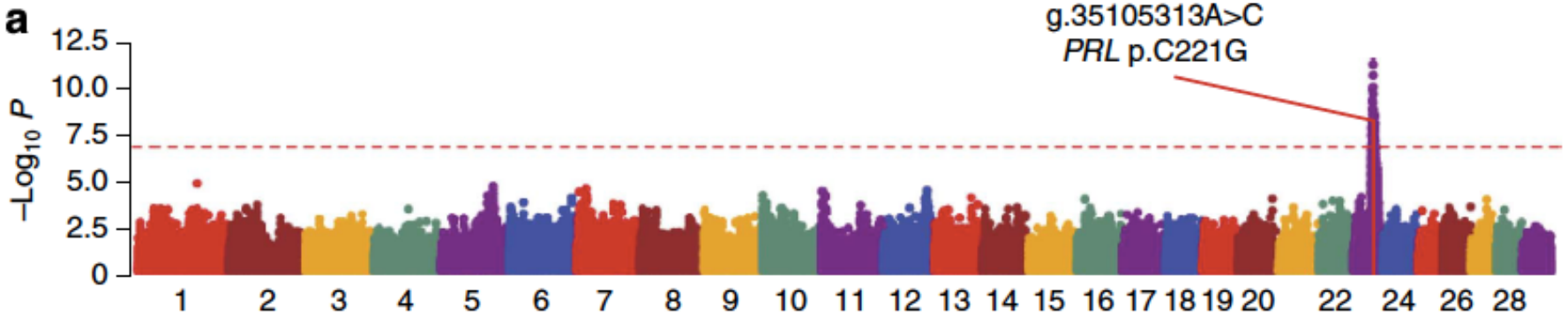
Finding Genes of Interest and Causal mutations

- Senepol breed of Cattle
- A dominant genetic syndrome discovered
- Rapidly propagated through the population through widespread use of semen representing a bull and his son.
- A collection of unusual phenotypes including
  - lactation failure
  - excessively ‘hairy’ pelage
  - thermoregulatory dysfunction

Photograph showing coat differences between wild-type and mutant half-sibs, with muddy coat due to wallowing behaviour typical of affected animals.

Mapping the ‘hairy’ mutation

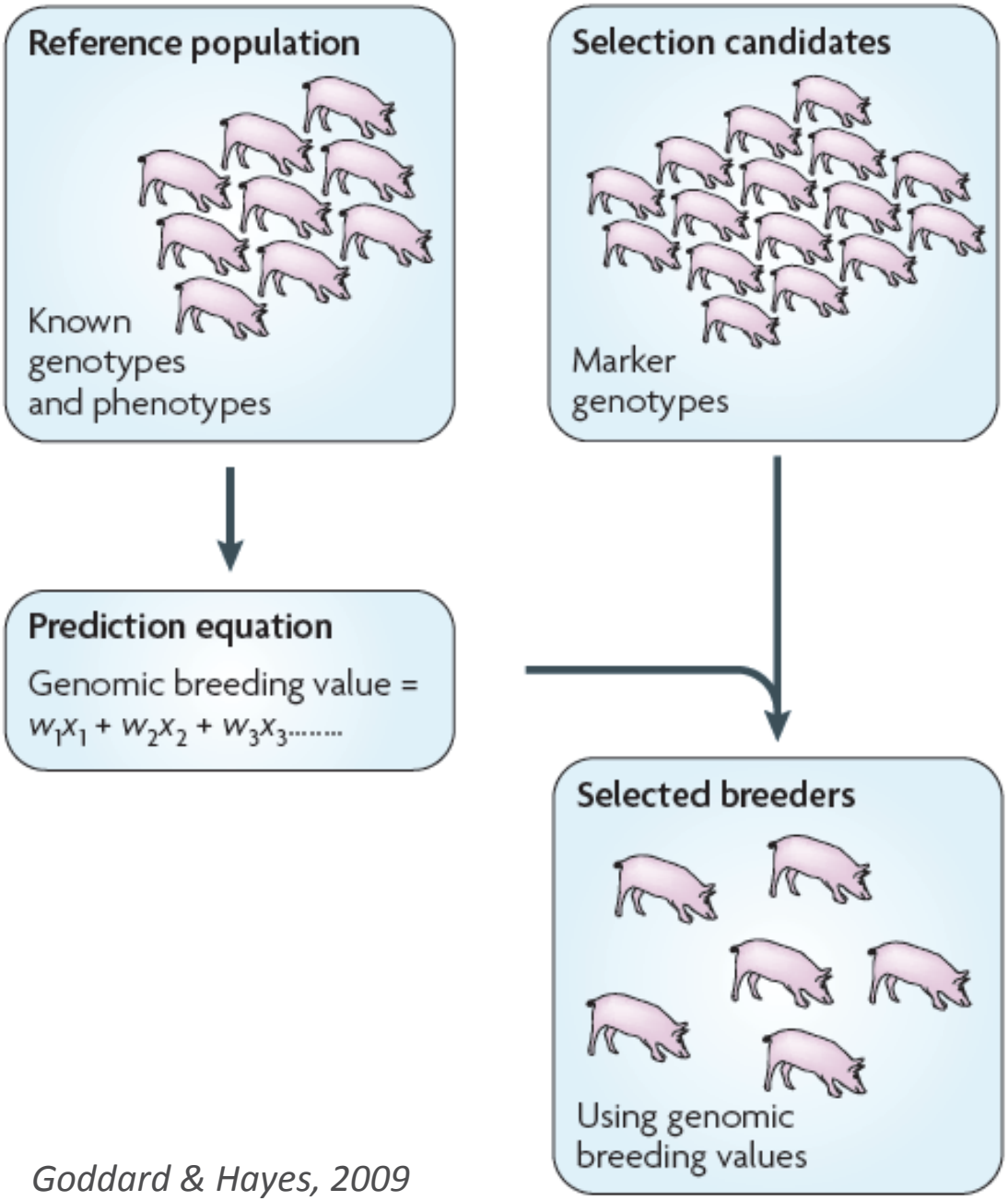
- Genome-wide transmission disequilibrium testing (GWAS)
- 22 nuclear trios and 55 half-sib offspring of the two founder sires
- 628 278 SNPs (ILMN Beadchips)



Genomic Selection
A definition

Genomic selection in plant breeding:
from theory to practice
Jean-Luc Jannink, Aaron J. Lorenz and Hiroyoshi Iwata
Advance Access publication date 15 February 2010

We intuitively believe that the dramatic drop in the cost of DNA marker information we have experienced should have immediate benefits in accelerating the delivery of crop varieties with improved yield, quality and biotic and abiotic stress tolerance. But these traits are complex and affected by many genes, each with small effect. Traditional marker-assisted selection has been ineffective for such traits. The introduction of genomic selection (GS), however, has shifted that paradigm. Rather than seeking to identify individual loci significantly associated with a trait, ***GS uses all marker data as predictors of performance and consequently delivers more accurate predictions.*** Selection can be based on GS predictions, potentially leading to more rapid and lower cost gains from breeding. The objectives of this article are to review essential aspects of GS and summarize the important take-home messages from recent theoretical, simulation and empirical studies.We then look forward and consider research needs surrounding methodological questions and the implications of GS for long-term selection



Goddard & Hayes, 2009

TOWARDS GENOMIC SELECTION IN ANIMAL BREEDING

Genomic Selection requirements

The accuracy of GEBV depends on :

- The size of the reference population used to derive prediction equations
- The heritability of the trait
- The extent of relationships between selection candidates and the reference population.

A Paradigm Change for Breeding

- Genetic evaluation can be performed as soon as DNA is available
- Allows accurate selection in both genders early in life
- Direct consequences *(Schaeffer, 2006)*
  - Genetic progress could be doubled
  - Potential to reduce costs for proving bulls by > 90%

Technology with the largest impact on dairy genetics since the introduction of artificial insemination

Opportunities for Developing Countries

- In developed countries
  - Phenotypes and pedigrees recorded for more than 100 years
  - Progeny testing implmented for nearly 50 years
- Developing countries
  - Limited by the absence of programs that record phenotypes on pedigrees animals
  - Lack of evaluation or national testing programs to assess the genetic valus of germplasms
- Genomic approaches could help identifying
  - Critical populations for preservation
  - Local well-adapted breeds to be utilized (combination of selection and cross-breeding)

Application of Genomics

- Parentage verification & Traceability
- Population Genomics
  - Structure of the population(s)
  - Characterization of the Animal Genetic Resources
  - Signatures of selection
- Genomic breeding (Genomic selection)
  - Improve animal production and conserve the indigenous animal genetic resources (Introgression)
  - Maximize heterozygosity (genome-wide heterozygosity)
  - Minimize inbreeding
  - Assess the originality of an animal compare to a specific population
  - Control the presence of unfavorable variants
  - **Genomic Selection**
- **Animal health** : pathogen identification, characterization, diagnostic

Critical points to consider for Genomics

- **It is NOT a magic tool** !
- **No genomics without pertinent and accurate phenotypes !**
- The “Trash In – Trash Out” principle applies also for Genomics
- It is impossible, today, to predict the weather with 100% accuracy even with all the scientific improvements. **Likewise genomic selection is not an exact science but it is a powerful new tool for predicting results !**

The potential advantages of a genome-wide selection scheme are too great to ignore (Larry Schaeffer C.G.I.L.)

2020-2025 Ag Predictions*

- Genomic selection will surpass conventional methods as the dominant breeding paradigm
  - Economic values will be associated with specific haplotypes
  - Genomics-assisted breeding will be holistic
- All economically impactful agricultural species, subspecies and their pathogens will be sequenced
- Animal pharmacogenomics, metagenomics and epigenetic analysis will be a reality
- Tens of thousands of related genomes will be sequenced to sample genetic diversity within and between germplasm pools
- Labeling based on genetics will be a marketing tool
  - Superior product quality, enhanced benefits, absence of specific allergens or negative components

* Opinions expressed in this slide are just that – opinions. They do not represent a guarantee, nor do they represent the opinions of the Company as a whole, but rather just the presenter.

Thank you for your attention !

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