# FRANCE,
## GENETIC SELECTION
## & TECHNOLOGY-DRIVEN INNOVATION

**THE KEY FIGURE:**

Already over

# 750 000

genotyping tests
completed for genomic
selection purposes

# The genomic selection
## revolution is underway

The fact that France has successfully integrated genomics science into its selection programmes is a major technological leap forward. The size of the reference breed populations coupled with decade-long optimization of the scientific methods used enables robustly reliable genomics evaluations on every trait conventionally evaluated on progeny.

The value of this genotyping dataset can be further exploited to generate greater genetic progress, broader range of genetic offer and even sharper indexing of the functional traits. Genomics-enhanced evaluation therefore opens up new perspectives, including in terms of selecting for functional traits.

These new assets on offer to livestock farmers are the culmination of work co-led by all the actors in the French national genetic improvement chain coordinated by France Génétique Elevage.
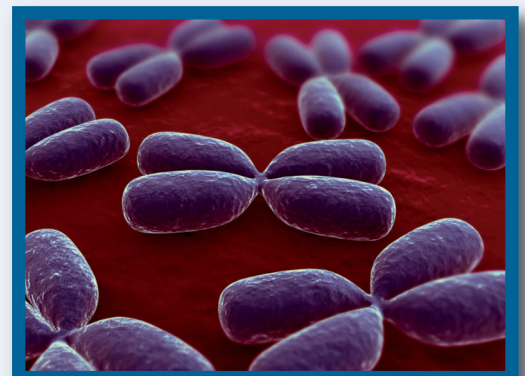
# 1

## A technology-driven revolution



In addition to data used in conventional evaluations (pedigree and performances), **genomic selection exploits the added value of information garnered through DNA analysis** via new DNA mapping-based genotyping technologies.

Genomic selection does not involve any genetic modification: neither the animals evaluated nor their genetic potential become modified. **Genomics 'simply' offers a powerful new tool for assessing the genetic quality of livestock.**

These breakthroughs have now made it possible to evaluate a breeder sire even before it has reached maturity, without having to wait for its progeny to start producing.

**The net result is that genomic selection enables to increase greatly annual genetic gain.** Furthermore, indexing on functional traits (such as fertility, mastitis resistance, calving ease) is now much sharper than before.

Genomic selection has been the biggest technology-driven breakthrough to happen in genetic improvement over the last 40 years.
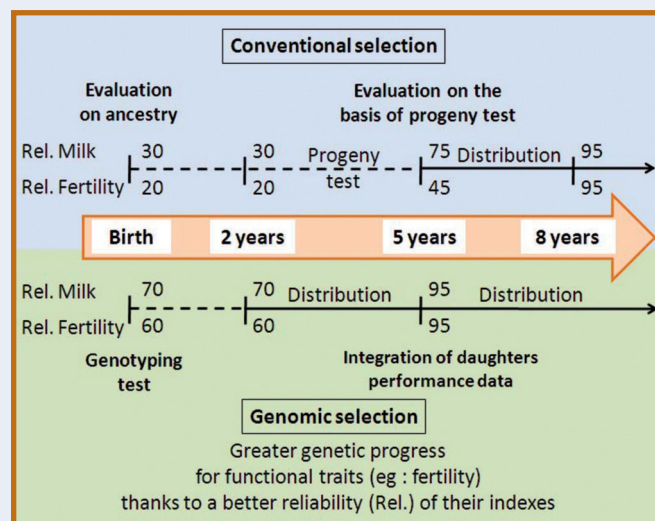


# 2

## Size the decisive factor for breed reference populations



The pivotal first step in the genomic evaluation of sires in a given breed is to build up a reference population - a purebred set of fully genotyped and progeny-tested breed animals.

**This population serves as a basis for analyzing genotype-performance relationships.** Mathematical modelling has established statistical relationships between genotype profiles and the indexes calculated after progeny testing.

**The robustness of these formulae for predicting genetic values from genotypes hinges on the number of animals making up the reference population.** The larger the reference population, the sharper the statistical correlations.

Once these predictive formulae have been established and verified, they can be employed to estimate a series of genetic indexes for a young animal using its genotype data.

This means that the genomic evaluation can only focus on the progeny-tested traits. The reference population still has to be renewed every year by progeny testing new animals in order to continually optimize the predictive formulae.

**The genomic evaluation can therefore only be efficient if it gets a regular input of dense (size of the reference population) fresh (population re-updating) information.**

## 3
# France still among
# the world leaders



**France was one of the first countries in the world to gain official international validation from Interbull on its genomics evaluation protocols.**

This position at the leading edge of genomic selection has been built up through long-term close cooperation between members of the France Génétique Elevage network.

Currently this cooperation brings together the national federation of selection-industry businesses (UNCEIA), the selection businesses themselves, the Institut de l'Elevage [French national Livestock Institute], and the INRA [French national institute for agronomics research] which delivers the basic research component.

From as early as 2001, the breed selection programmes for the Holstein, Montbéliard and Normande have been constantly optimized (candidate bulls screening ahead of on-station testing, etc.) to integrate genomics breakthroughs as soon as they are confirmed.

Since 2008, capitalizing on this policy of continuously integrating technological innovations, the selection programmes have been using use genomics data at every phase of the selection chain: choice of bull parents, males shortlisted for the testing station, selection of the bulls for planned mating...

In June 2009, this next-generation genetics data was unlocked for all breeders via official published release of the first Holstein, Montbéliard and Normande bull genomics indexes.

**Every trait traditionally evaluated on progeny now has its own genomics evaluation,** from dairy productivity (milk quantity and quality) to animal morphology and on to functional traits (traits liable to cut production costs, such as cow fertility, mastitis resistance, and so on).

## 4
# Consolidated assets
# and new perspectives



With experience built in and new output from large-scale scientific research programmes, the other dairy and beef cattle breeds, as well as sheep and goat breeds, are soon to reap the benefits of the genomics revolution.

**Genomics-based evaluations are set to be extended to encompass criteria** that conventional selection programmes are incapable to integrate, **such as milk composition components** with positive (or negative) effects on human health (fatty acids, etc.), **disease resistance, meat quality** (tenderness, marbling, flavour, and more).

The critical prerequisite for developing robust predictive formulae is to work with a reference population comprising fully genotyped animals on which these specific traits have also been measured.

That is the main purpose of 2 programmes led by the INRA, the UNCEIA, the Institut de l'Elevage and selection-industry businesses.
› Phénofinlait (advanced compositional analysis of the milk from 20,000 genotyped cows, goats and sheep)
› Qualvigène (meat quality analysis on over 3,000 young bulls genotyped).

As with the Holstein, Montbéliarde and Normande breeds, **the next generation of breed sires will not be marketed until their genomics-enhanced evaluations gained proven reliability, international acceptance and recognition.**

These are the basic condition to achieve our quality expectation.

# FROM SOURCE ANIMAL TO A GENOMIC INDEX SET: THE PHASES IN 10 IMAGES
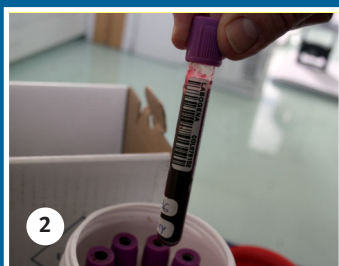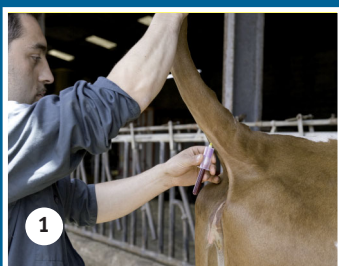




## SAMPLING:

99% of tissue samples are on plasma (1). Each sample is barcoded to ensure full end-to-end process traceability (2).

Each test tube holds 6 ml of blood plasma instead of the 4 ml used for conventional analyses, so that the control genetic material can be preserved long-term.

## DNA EXTRACTION:

LABOGENA, the French national animal genetics analysis lab, takes 5 days to complete the full battery of sample analysis protocols (3).

The analytical chain is computer-controlled and automated end-to-end. Phase 1 is DNA extraction (4), and the process requires fifteen times more material than conventional analyses.
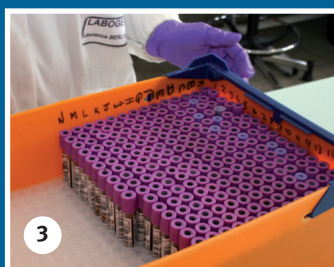








## DNA PREPARATION:

The extracted DNA is recovered then distributed by a TECAN liquid handling robot into 96-well microplates, i.e. DNA from 96 different animals (5).

The robot dispenser system then adds the reagents necessary for DNA denaturation (separation of double-helix) (6). Each microwell plate is then placed in a lab stirrer to mix the reagents with the DNA.

## READING OF GENETIC MARKERS:

After centrifugation (7), a final incubation step (24 hours at 37°C), and DNA fragmentation, the samples are dispensed onto a microarray (8).

Adding fluorescent reagents then makes it possible to scan and read the genetic markers of each DNA sample.
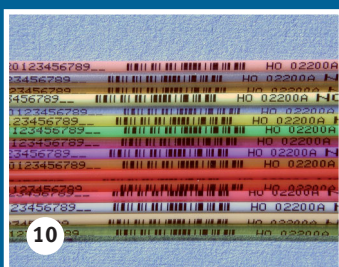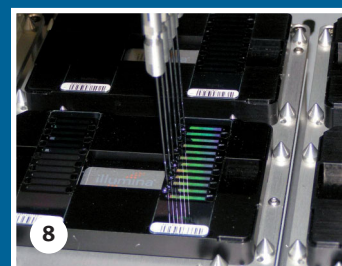








## ANALYSIS AND INDEXING:

The results are forwarded on to the INRA via the French national genetics information system (9). Genetic indexing is coordinated under INRA leadership, with support from UNCEIA and Institut de l'Elevage geneticists.

The selection business that supplied the samples then uses these results to select which bulls to continue siring (10).

## A FULLY-OPTIMIZED METHOD

The French genomics-enhanced evaluation method has been comprehensively optimized through ultra-accurate progeny tests and major investment in methodological input.

The reliability of these genomic indexes stems from the hugely robust size of the reference populations: 1,250 Normande-breed bulls, 1,500 Montbéliard-breed bulls and 18,300 Holstein-breed bulls, all within the framework of the pan-European EuroGenomics project.

Since 2009, impelled by an UNCEIA-led initiative, Europe's leading Holstein breed selection businesses joined forces to pool the reference population datasets (the EuroGenomics project).

Counting over 18,000 fully genotyped and progeny-tested purebred Holstein bulls (and 19 millions daughters!), this vast one-of-its kind reference population has been built on the best genetic material that Europe and North America can provide.

Although each country still works with its own evaluation methods, the EuroGenomics project partners now co-use a pooled reference population. Compared to genomics evaluation based on a national-scale reference population the gain in accuracy is 10%.
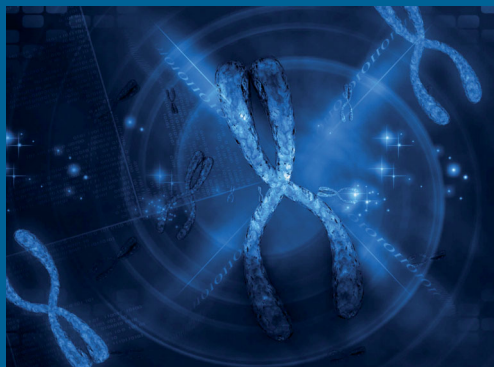


## 5
# A broader offer
# for greater sustainability



**Thanks to integration of genomics-based technologies, French genetic selection programmes are now able to offer an extended range of high-performance sires** with sharper indexes on functional traits. These sires open up new perspectives for farmers in terms of improved genetic gains on traits that are pivotal to livestock system sustainability.

First, there was the conventional offer of progeny-tested bulls. Now, there is also a new offer of genomically-selected bulls in all three core French dairy breeds.

Following a long period dominated by the sons of just a handful of stud sires, the wide panel of Holstein sires now available **offer much broader genetic diversity.** Their profiles are adapted to a range of objectives: improved milk production, improved morphology, or improved functional traits.

This range, put together with high-ISU-index (all-round composite index) breed sires, also includes bulls boasting other sought-after criteria (redding, naturally polled...).

The Montbéliard and Normande breeds have also been range-extended and rejuvenated to offer recent-pedigree sires and sires presenting profiles that showcase the hybrid vigour of their breed mix (good all-round value set, lifespan, mastitis resistance).

# 6

## Large-scale selection of a major sheep gene

The National Genetic Improvement Plan for Scrapie-Resistant Sheep, encompassing provides to all French sheep breeds a unique case-illustration of very-large-scale selection for a major gene : **PrP gene that confers varying degrees of scrapie resistance.**

The scheme coordinated the genotyping of over 670,000 sheep in the space of 6 years, with the onus on eliminating breeder rams carrying the PrP gene susceptibility alleles (VRQ and AHQ) and disseminating those carrying the resistance alleles (ARR).

**The results command attention.** Since 2008, there is not a single ram from any farm in the sheep meat breed selection population that possesses the VRQ scrapie hypersensitivity allele. Furthermore, over 95% of them are scrapie-resistant (ARR/ARR genotype).

**DEVELOPMENT OF RESISTANCE TO SCRAPIE THANKS TO LARGE-SCALE GENOMIC SELECTION**



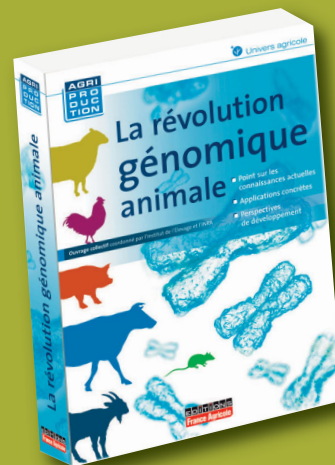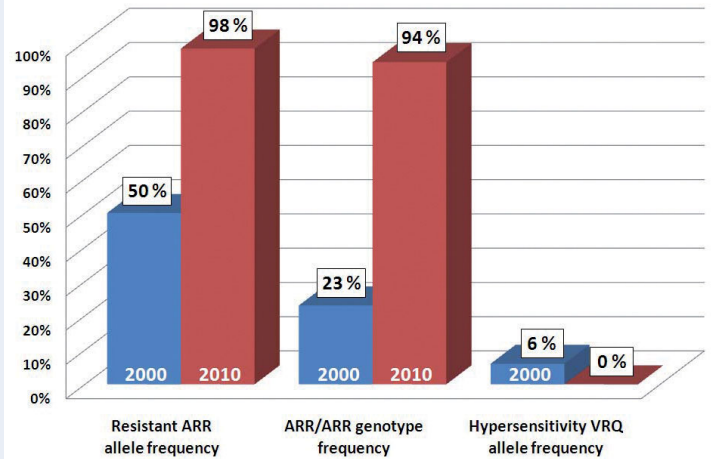| | Resistant ARR allele frequency | ARR/ARR genotype frequency | Hypersensitivity VRQ allele frequency |
|---|---|---|---|
| 2000 | 50 % | 23 % | 6 % |
| 2010 | 98 % | 94 % | 0 % |

**The scale of the selection programmes and the results achieved over the last 40 years have secured France a position among the leading nations worldwide.** Successful integration of genomics-based technologies has taken the French genetic selection offer to new levels of quality and diversity.

With traits geared to either productivity objectives or breedability objectives, this offer holds unprecedented capacity to efficiently meet the needs of breeders in France and worldwide.

**For further information, please contact France Génétique Elevage.**



**THE LIVESTOCK GENOMICS REVOLUTION**

This collaborative reference work coordinated by the Institut de l'Elevage [French national livestock institute] and the INRA [French national agronomics research institute] overviews current state-of-the-art in genomics science and investigates the applications for livestock selection, 161 pages.