



X Simpósio Brasileiro de Melhoramento Animal Uberaba, MG – 18 a 23 de agosto de 2013

Genomic selection strategy in France: experiences in dairy cattle - how to make it beneficial for other breeds and countries?

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Abstract

In France, the use of molecular information for the prediction of breeding values in dairy cattle started in 2001. Then, a national consortium was established joining together a large research institute (INRA), the AI industry under the national federation of breeding companies and AI cooperatives (UNCEIA) and a genotyping laboratory (LABOGENA). This enabled the implantation of a large marker assisted selection program in the three main French dairy cattle breeds (Holstein, Normande, and Montbéliarde) for pre-selection of young bulls before progeny test. With the availability of high-throughput SNP chips, the French evaluation model was upgraded in 2008 with genome-wide information. In 2009, the first official genomic evaluations were made official, allowing for the use of young bulls without waiting for progeny-test results.

Genomic selection has drastically changed the practices in breeding companies and on farms. The quick and large adoption of the genomic tools was favored by (1) genomic predictions with high reliability, especially in the Holstein breed and by (2) continuously decreasing genotyping costs. Indeed, a European consortium (EuroGenomics) was created in 2009 to build a large reference population and benefit from cost saving due to larger chip consumption at the consortium level. In less than 4 years since the first official genomic breeding values, breeding companies and farmers have fully adopted the new technology. In France, more than 5,000 male and female selection candidates are being genotyped each month. Breeding schemes have been totally transformed on the male and female pathways. Progeny testing programs have been stopped, genomic and reproductive technologies have been associated. Up to 70% of the total AI are made with young bulls. More than 80% of the genotyped animals are females, about two third for herd management purposes using a low density chip.

For small populations, other strategies have been developed to implement genomic selection. In Brown Swiss, data and competences have been shared at an international level whereas French local dairy breeds and beef breeds are currently developing reference population and prediction methods based on multi-breed approaches.

Based on its experience in genomic selection in dairy cattle, INRA is now involved in a new type of collaboration with research partners in Brazil (Embrapa Gado de Leite), South Africa (ARC), India (BAIF) and Kazakhstan (KazAgroInnovation), trying to favor the development of accurate genomic evaluations in diversified populations and environments. Local genomic selection properly accounting for genotype by environment interactions should guarantee increased genetic gains serving local farmer interests.

Introduction

In France, molecular information is widely used in the management of livestock population under selection and contributes more and more to selection decisions. In cattle, small ruminants, poultry, aquaculture and horses, microsatellites or SNP markers are routinely used for parentage testing, genetic abnormalities detection, disease resistance testing, or for trait pre-selection based on QTL detection. However, in France, genomic selection, which refers to the use of markers distributed over their whole genome for the prediction of breeding values (Meuwissen et al., 2001) is only implemented in dairy cattle.

Compared with Brazil, France produces about the same volume of milk annually: 24,6 millions of tons in France and 22,4 millions of tons in Brazil (Source: International Dairy Federation). However, there are 3,664,000 dairy cows in France with an average yield of 6,674 kg/cow/year (versus 23,227,000 dairy cows with a yield of 1,382 kg/cow/year in Brazil). Eight dairy breeds are recorded and genetically evaluated in France. Among them, four breeds benefit from genomically enhanced breeding values (GEBV) as a tool for selection decision: two international breeds, Holstein and Brown Swiss and two regional breeds which contribute significantly to the total milk production in France: the Montbéliarde and Normande breeds (see table 1).

In this paper, we will focus on the three main breeds, Holstein, Montbéliarde and Normande, for which national reference populations are large enough. We will describe the development of genomic selection in France as well as its current implementation and use by breeding companies and farmers. We will conclude with lessons learnt from the French experiences in dairy cattle for genomic selection in other breeds and countries.

Table 1 : Importance of the breeds under Genomic Selection in France

Breeds	Number of recorded cows	Percentage of the French population of recorded cows	Milk production per cow in 305 days (kg)	Implementation of Genomic Selection	
				First official genomic breeding values	Size of the reference population (proven bulls for milk production)
Holstein	1,387,730 ^a	67% ^a	9,135 ^a	June 2009	>25,000 ^b
Montbéliarde	415,552 ^a	17% ^a	7,209 ^a	June 2009	> 2,500
Normande	229,635 ^a	9% ^a	6,689 ^a	June 2009	> 2,000
Brown Swiss	17,235 ^a	< 1% ^a	7,170 ^a	April 2012 ^c	> 7,000 ^c

^a Milk recording results in 2012 (ICAR, http://www.waap.it/enquiry/France/FRA_index.htm)

^b EuroGenomics source

^c InterGenomics source

Principle of Genomic Selection

The principle of genomic selection is to estimate the effect of each marker in a reference population of both genotyped and phenotyped animals and then to use prediction equations based on these effects to get genomic breeding values for selection candidates: the genomic breeding values of a genotyped animal without performances is the (weighted) sum of the marker effects. Alternatively, these two steps can be performed using a BLUP approach (G-BLUP) based on genomic relationships, i.e., observed relationships measured from marker similarities (Van Raden, 2008). However, it is known that markers only explain a fraction of the additive genetic variance. It is therefore required to combine the genomic values with the polygenic information explaining the rest of this additive genetic variability, using single-step (Misztal et al., 2009, Christensen et al. 2010) or multi-step approaches involving blending (Van Raden, 2009) or a (BLUP) mixed model including a “residual” polygenic effect (Boichard et al, 2010, Liu et al. 2011).

The development of Genomic Selection in France: a bit of history

Until recently, DNA markers have only been used to search for quantitative trait loci (QTL) on the genome with the objective to use them in marker assisted selection (MAS). In the late 90's, INRA, responsible for national breeding values evaluations in France and UNCEIA, the national umbrella organization for breeding companies and AI cooperatives, on the behalf of 8 breeding companies, decided to collaborate on a national project. The initial project involved the systematic QTL detection using microsatellites markers, in the Holstein (HO), Montbéliarde (MO) and Normande (NO) breeds. The relevancy of QTL into breeding values estimation was tested in a first program of marker assisted selection from 2001 to 2007 called “MAS1” (Boichard et al., 2006). This was the first pre-selection tool of young bulls within family. From 2008, the availability of the Illumina Bovine SNP50 BeadChip allowed a fine mapping of the QTL and therefore a second generation of MAS (MAS2) based on Linkage disequilibrium analyses. From that point, reliabilities of the genomically

enhanced breeding values (GEBV) significantly increased compared with the reliability of the pedigree average. It was therefore possible to use GEBV as a pre-selection tool of young bulls. To keep increasing reliabilities, reference population were not only continuously increased, but genomes wide methodologies were also compared to fine tune the French approach to Genomic Selection (Croiseau et al., 2011).

Table 2 summarizes the steps towards genomic selection through the different research collaborative projects and their short-term implementation on the field. We can notice a progressive increase of the number of actors from the French livestock organization, involving additionally the genotyping laboratory, LABOGENA, and the beef and dairy cattle industry (financial support of APIS-GENE). In fact, the different partnerships did not only allow the accumulation of marker genotypes but also get the acquisition of experience in prediction methodologies with a first routine application in breeding schemes.

In France, Genomic Selection is the result of a continuous research on prediction methodologies, of development of laboratories and computing facilities, and of knowledge, jointly enhanced by the research and industry.

Table 2 : Steps towards genomic selection through the different collaborative research projects and their short-term implementation on the field

Purpose of the research project?	QTL detection	Proof of concept: Marker assisted selection (MAS1, first generation)	QTL fine mapping + MAS2 (2 nd generation)	From MAS2 to genomic selection (GMAS)
Who?	INRA + UNCEIA (on behalf of breeding companies)	INRA + UNCEIA + LABOGENA (genotyping lab)	INRA + APIS GENE (including UNCEIA and other livestock breeding organizations) + LABOGENA	INRA + APIS GENE (including UNCEIA and other livestock breeding organizations) + LABOGENA + CTIG (computing centre)
When?	1996 - 1999	2001 - 2007	2006 - 2008	2009 - 2011
How?	Breed	MO, NO, HO	MO, NO, HO	MO, NO, HO
	Genotypes	1560 genotyped sires	> 60,000 genotyped animals: male and female	3200 sires
	Markers	169 microsatellites	45 microsatellites	>50,000 SNP
	Achievement	Detection of 3 to 5 QTL by trait for 25 traits	MAS Breeding values for 8 traits, 5 QTL /traits	MAS breeding values for 25 traits, 30-40 QTL /traits with a reliability increase of 20% to 30% compared with parent average.
Impact on breeding schemes:		Within family pre-selection of the candidates before testing	From 2008, pre-selection tool of bull and bull dam candidates	From 2010, selection tool of bull candidates without progeny testing

“The French approach” to genomic evaluation

In France, the genomic estimation of breeding values is currently a combination of a Marker Assisted (MAS) approach and a genome wide approach. It is called the G-MAS approach (Boichard et al., 2010). Another specificity is that it relies on the use haplotypes (window of 4-6 markers) instead of single markers. The G-MAS approach involves a preliminary step which aims at identifying the informative haplotypes in two ways:

- a QTL detection based on Linkage Disequilibrium and Linkage Analysis (LDLA) using haplotypes of consecutives SNP (Druet et al., 2008, Meuwissen and Goddard, 2001);
- a SNP pre-selection using a Elastic-Net (EN) approach (Croiseau et al., 2011). The EN includes as specific cases the LASSO and the Ridge Regression estimation methods.

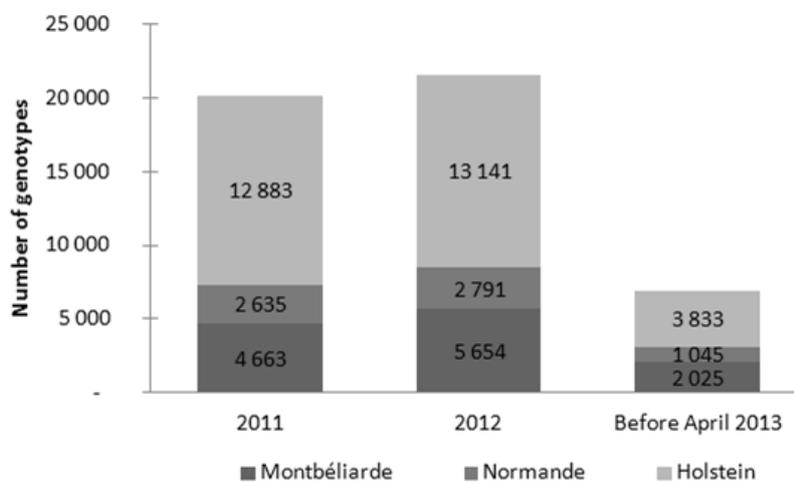
Genomic evaluations are then performed again in a two-step approach. The first step is the computation of phenotypes (Daughter Yield Deviation, DYD or De-regressed Proofs, DRP) from the most recent and most complete classical evaluation (step 1). In a second step, haplotypic and residual polygenic effects are jointly estimated in a BLUP-based evaluation (step 2). The total breeding value of each animal is the sum of all QTL effects and the residual polygenic component where the variance explained by QTL and SNP is assumed to be between 40 and 60% depending on traits. We can note that this multi-step approach does not require any blending methodology.

The implementation of Genomic Selection in France: a success story for the AI industry and farmers

Since October 2008, genomic evaluations (coming from MAS2 and then GMAS approaches) have been provided for the selection candidates, male and female. Actually, GEBV of such category are not available for dairy farmers but only for the breeding companies having participated to the setting up of the Holstein or Montbéliarde or Normande reference populations. From June 2009, GEBV have been officially published for the young bulls marketed by the associated breeding companies. And in January 2011, the service for genomic evaluations was officially opened to all users for the genomic evaluations of females. Males and females are now monthly evaluated for about 35 traits, with the same level of genomic reliability for both sexes. Since then, VALOGENE, a daughter company of UNCEIA has been responsible for the data management of the genotypes. VALOGENE is therefore responsible for the data flow from farm to INRA (where the data are stored and where GEBV are computed) going through the genotyping step. VALOGENE is finally in charge of the GEBV release to the dedicated client (e.g., breeding companies for candidates, association of dairy breeders for females, among other users...).

Application of Genomic Selection in breeding schemes

GEBV were first used for the selection of young bulls and bull mothers. In fact, more than 20,000 young candidates have been yearly genotyped for the 3 breeds (see graph 1). Initially, only 40% of the candidates were females (Boichard et al, 2010). In 2011 and later, at most 40% of the candidates were males, with about 7,500 candidates genotyped yearly, mainly with 54,000 markers (Valogene statistics).



Graph 1 : Number of animals (males and females) genotyped for breeding schemes since 2011 (Source: Valogene)

Such a large implementation of genomic selection was made possible by the dramatic increase of the reliability of the breeding values for very young animals. Compared with the reliability of parent average estimates, the reliability of GEBV has increased by 30 to 40% depending on traits to be only slightly lower than after progeny testing. In June 2010, according to traits and animals, reliabilities ranged from 0.50 to 0.60 in Normande and Montbéliarde breeds, and from 0.60 to 0.70 in Holstein (Boichard et al., 2010). In fact, the Holstein breed benefits from a larger reference population, which has been significantly increased - from 4,000 genotyped proven bulls to 16,000 – thanks to the creation in 2009 of the EuroGenomics consortium. It initially involved the participation of breeding organizations - including AI industry, Holstein breeder associations and computing center- from 7 countries: France, the Netherlands, Belgium, the Nordic countries (Sweden, Finland, Denmark) and Germany. Nowadays, the EuroGenomics consortium also includes Spain and Poland and the

reference population exceeds 25,000 proven bulls. These organizations actually decided to set up the largest bull reference population in the world based on Interbull breeding values as phenotypes. As a result, the GEBV reliability immediately increased by an extra 10% for all traits in all countries (Lund et al., 2010). This especially accelerated the changes into breeding schemes, moving away from progeny testing.

Based on the same genomic tools (GEBV and available chips among Low Density or denser:50k), breeding companies have developed different strategies aiming at optimizing breeding schemes. On the male pathway, one of the most drastic changes was the end of organized progeny testing programs starting in 2009, hence strongly reducing the generation interval and cutting selection costs. Because of the long experience with MAS, this change occurred more drastically than in the rest of Europe. On the female pathway, the benefit of genomic and reproductive technologies can be combined. Based on GEBV, genetically superior females can be identified with a higher confidence so that breeding companies can better target bull dams and contract fewer of them as cow donors for Embryo Transfer program (on farm). They can also produce more calves based on repeated OPU-IVF sessions (on farm and in female stations). In the interest of the genetic progress, France is the largest countries in Europe involved in embryo production, with emphasis on in vivo production (see table 2). To go further, embryo production can be combined with embryo biotechnologies to even decrease the generation interval. This trend started in 2012 with 169 sexed embryos genotyped in France.

Table 3 : Comparison (embryo volume and techniques) between the 4 largest countries in Europe regarding embryo production (28th AETE Annual meeting)

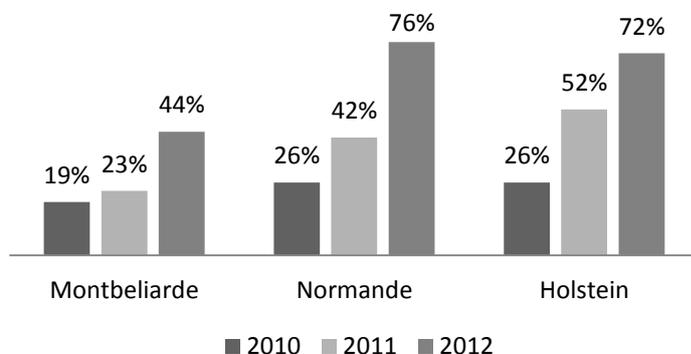
	Italy	Germany	The Netherlands	France
In vivo embryo production (transferable)	-	14,780	27,609	29,966
In vitro embryo production (transferable) – from OPU	423	3814	3217	524
Total transferred embryos (and percentage of the European production)	13,451 (11%)	16,295 (13%)	24,275 (20%)	29,747 (24%)

In fact, genomic selection did not only impact the design of the breeding schemes but also the marketing strategies of the breeding companies. In order to reduce the risk due to reliability levels slightly lower than for proven bulls and to consider inbreeding issues, farmers are advised to consider groups of bulls with similar characteristics rather than “bet” on single bulls. Young bulls are therefore marketed under the form of “package” promoting a profile (e.g., profitability, durability, productivity...). New “brand” have also been promoted combining genomic testing and sexing semen technology.

Application of Genomic Selection at the farm level

Use of genomically tested bulls

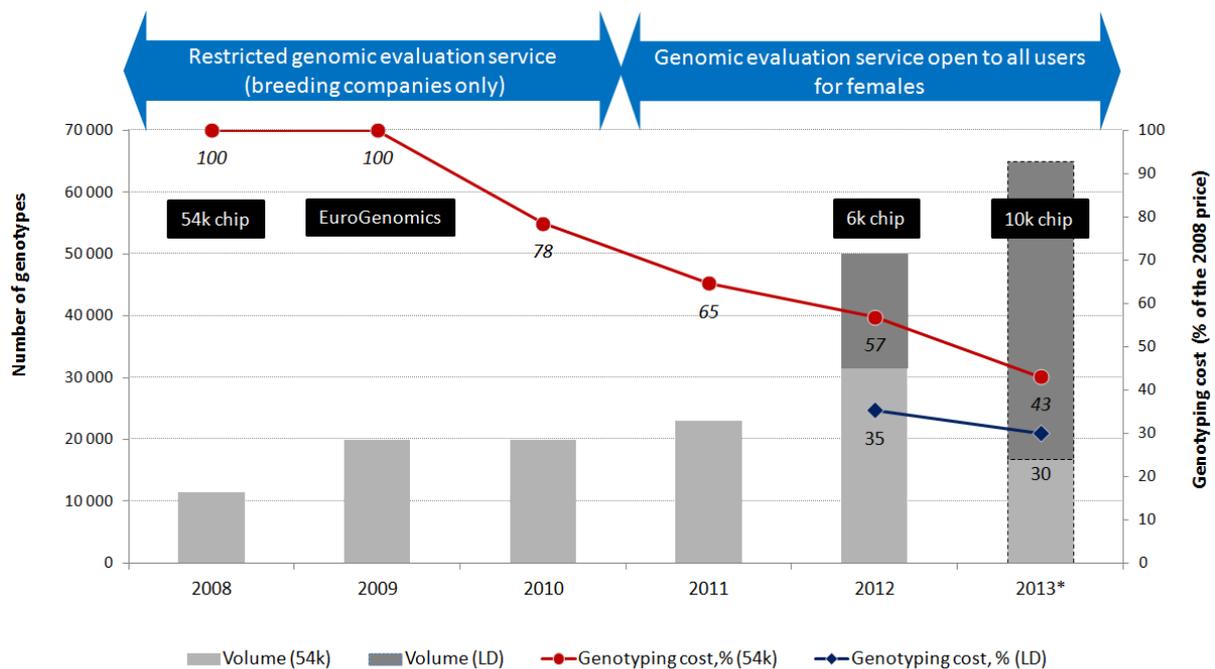
Dairy farmers can now choose between different bull categories for AI: the young bulls which are genomically tested (without the contribution of any daughters or few of them) or the proven bulls which are progeny tested. Since young bulls have been marketed for the first time in 2009, the number of such AI has quickly increased: it now represents the majority of the AI activity in the Normande and Holstein breeds (see graph 3) which is not the case in Montbéliarde.



Graph 2 Percentage of the AI using young bull semen among the 3 breeds over the last 3 complete year in France

Genomically testing females

Genomic selection has also impacted the dairy farmers' practices by providing them with new tools for herd management and more appropriate mating. The genomic evaluation service for females has been opened in 2011. During the first year, less than 2,000 females have been genotyped versus 25,000 in 2012, and 40,000 to be expected in 2013 (Source: Valogene). This large success is mainly explained by the reduction of the genotyping costs at the farm level (see graph 3). Except for bull dam selection, low density (LD) chips (with 6 to 10,000 SNP) are used for females at a lower cost than the 50k chip. However, the use of low density genotypes requires the use of a particular methodology (called imputation) to predict the missing genotypes compared with the 50k SNP panel. In fact, different kinds of SNP panel were initially used within EuroGenomics which made the development of an imputation method (Druet et al., 2010) essential at the time of the first genotype exchanges for setting up the international reference population. The use of imputation was stimulated by the EuroGenomics needs and quickly extended to such broader use, e.g., massive genotyping for females. Now EuroGenomics is customizing the Illumina LD chip (called EuroG10k) to provide the dairy farmers more services regarding mating plan based on the detection of genetic defects, e.g., impacting fertility.



Graph 3 : Decrease of the genotyping costs explained by the increase of the volume of genotypes in France (and at the EuroGenomics level for joint purchase of chip) and the availability of lower density chip (6k, 10k customized by EuroGenomics) – Source: Valogene

Alternatives strategies for Genomic Selection

In Brown Swiss: an international approach

Genomically enhanced breeding values were made available for Brown Swiss animals thanks to the initiative in 2009 of the European Federation of Brown Swiss breeders. Quickly joined by the USA, seven countries in total decided (1) to first share more 7,000 progeny tested bulls genotyped with the Illumina Bovine SNP50 BeadChip (Croiseau et al., 2012) and then (2) to develop a common method for genomic predictions. This initiative was called InterGenomics. Since April 2012, the international organization for international evaluation in dairy cattle, Interbull, released the first genomic evaluations in the Brown Swiss breed for 3 to 15 traits in a country. This strategy was found to be attractive for small population.

In other local dairy breeds and beef breeds: Multi-breed approaches

Because of too small reference populations, local dairy breeds as well as beef breeds in France do not have access to genomic selection. To avoid a multiplication of too small and inefficient initiatives, breeder associations, breeding companies and AI cooperatives whatever the breed have decided to join their forces into a new research project aiming at developing a multi-breed genomic selection (GEMBAL project financed by the

French Research Agency). The three main dairy breeds first contribute to benefit from large data set and to be able to compare within and multi-breed approaches. In fact, data will be pooled into multi-breed reference populations, in dairy and in beef or in a unique one. The set up of the reference populations was optimized considering the costs for genotyping (type of chip and number of animals) and how informative are the data. It was therefore decided to genotype a reduced number of animals in each breed with more than 800,000 SNP markers and then, the rest of the phenotyped animals with an LD chip. Hence, one of the challenges is to develop an adapted imputation method to infer missing genotypes, then to develop a genomic prediction model, using QTL detection and linkage disequilibrium information across breeds. This strategy should be beneficial for many small populations at the same time and beyond the dairy and beef orientations.

Lessons from the French experiences of genomic selection

Importance of recording:

Phenotypes are as important as genotypes to set up a reference population and define the prediction equations. Genomic Selection in France was only made possible because of the extensive recording program and the participation to Interbull for setting up an international reference population. In France, phenotypes are collected for 70% of the dairy population and then evaluated for production (5 traits), type (23 to 28 traits), fertility (5 traits), udder health (2 traits), longevity, calving, and stillbirth. Even if formal progeny testing have been removed from Holstein, Montbéliarde and Normande, phenotyping is still necessary to update the prediction equations and being able to record for new traits. The recording organizations responsible for collection, quality control, data base management and storage were therefore maintained.

Competition and collaboration:

Genomic selection is seen as a revolution with its drastic and fast changes. It has impacted the methodological approaches and the data management of the scientists responsible for breeding values estimations as well as it has changed the technical and marketing practices of the breeding companies.

Moreover, genomic selection has had significant consequences on the relationships between all actors of the breeding improvement, at the both national and international levels:

- *in between breeding companies:* genomic evaluations provide more transparent tools to compare bulls from one breeding companies to another whatever the country of origin. The number of sires is larger with shorter carriers. At the national level for example, an increased competition between AI cooperatives led to larger unions of AI cooperatives into bigger companies.
- *in between breeding companies and farmers:* genomic selection has increased the role of the female pathway in the breeding improvement.
- *in between genetic evaluation centers from different countries:* because of the reduction of generation interval and the associated cost saving, pressure is put on the frequency of the GEBV. The efficiency of the service provided to farmers and to the breeding companies has become of high relevancy in an international context where genotypes are standardized data that are easier to exchange than phenotypes.
- *in between breeds and countries:* having access or not to genomic technologies might increase the gaps between breeds and between countries.

Nevertheless, under such a pressure, collaborations involving the share of data and competences have become more than necessary to benefit from scale effect and develop innovative methodologies that have to be shortly implemented on the field with confidence. France provides example of intense and long-term collaborations between dairy farmers, the AI industry and research explaining how fast and broadly genomic selection has been adopted. There are also different examples of international consortia involving different levels of collaboration (the North-American and the EuroGenomics consortia for international reference population in Holstein and InterGenomics in Brown Swiss). They have all accelerated the on-going changes and participated to transfer technology from one breed to another or from one country to another.

Conclusions and perspectives for other breeds and countries

In Holstein, Montbéliarde, Normande and Brown Swiss breeds, genomic selection in France has been quickly developed and implemented to benefit from a larger genetic progress. This is the result of a joint impulse of the research and the dairy and beef industry in a competitive international context. In a few years, dairy farmers and

breeding companies have largely adopted new tools for new practices regarding breeding improvement, herd management, and inbreeding. Even genomic evaluations for new traits are under development.

From the French experiences, it seems that genomic selection first requires adapted and affordable tools (chip and accurate genomic prediction). But genomic technologies also depend on human, genotyping and computing facilities. With genomic selection, genetic gain is expected to be fast. This is only true if on-going recording system already exists. Because of the large investments (money and possibly time) required by genomic selection, all stakeholders including the livestock keepers, small scale farmers, scientists, policy makers should be involved in its development.

It is to be feared that the gap between countries and breeds may increase due to differences in access to genomic selection. However, such technology would be the opportunity to develop innovative breeding programs based on traits representing facing the specific challenges of, e.g., tropical areas: drought, heat, poor quality forage, lack of supplemental micro nutrients, internal and external parasites, disease...

At the national and international levels, there are already examples of beneficial collaboration between breeds, between countries within a breed. At INRA, a project called GENOSOUTH (launched in 2012) has been especially designed for the development of collaborations with Brazil (EMBRAPA Gado de Leite), India (BAIF), Kazakhstan (KazAgroinnovation), and South Africa (ARC Irene). GENOSOUTH is aiming at technology transfer and capacity building on genomic selection. In the short-term, the project is focused on methodological and applied aspects of genomic selection in Holstein cattle accounting for the local conditions. Local genomic selection properly accounting for genotype by environment interactions should guarantee increased genetic gains serving local farmer interests. On the longer-term, this project can be seen as a first step before genomic selection in other breeds or crossbreds involving local (e.g., *bos indicus*) dairy or beef cattle.

Partnerships

Genomic methodologies have been developed in the framework of the mixed unity of technology (UMT 3G) associating INRA G²B (Domaine de Vilvert, 78 352 Jouy-en-Josas, France), UNCEIA (MNE, 149 rue de Bercy 75012 Paris) and the French Livestock Institute, IDELE (MNE, 149 rue de Bercy 75012 Paris), with the collaboration of LABOGENA (the genotyping lab), CTIG (the computation centre of the Animal Genetics department of INRA) and INRA SAGA (31326 Castanet-Tolosan) and benefiting from the funding of the French Research Agency.

Genomic implementation have been allowed by the cattle industry contribution, i.e., by the French breeding companies (DYNAM'IS, EVOLUTION, GENE DIFFUSION, GNA, JURA BETAÏL, UMOTEST, MIDATEST) their national umbrella, UNCEIA, VALOGENE and APIS-GENE.

The EuroGenomics consortium also contributed in the development of reliable methods and tools supporting genomic selection in Holstein with benefits in other breeds.

References

- Boichard D, Fritz S, Rossignol MN, Guillaume F, Colleau JJ, Druet T (2006) Implementation of marker-assisted selection: practical lessons from dairy cattle. In 'Proceedings of the 8th world congress of genetics applied to livestock production, Belo Horizonte, Brazil'. Comm. n° 22-11.
- Christensen O, Lund M (2010) Genomic prediction when some animals are not genotyped. *Genet Sel Evol*, 42:2
- Croiseau P, Legarra A, Guillaume F, Fritz S, Baur A, Colombani C, Robert-Granié C, Boichard D, Ducrocq V. (2011) Fine tuning genomic evaluations in dairy cattle through SNP pre-selection with the Elastic-Net algorithm *Genet. Res.* 93:409-417
- Croiseau P., F. Guillaume, and S. Fritz (2012) Comparison of Genomic Selection Approaches in Brown Swiss within Intergenomics, *Interbull Bulletin* n° 46. Cork, Ireland, May 28 - 31, 201
- Druet, T., S. Fritz, M. Boussaha, S. Ben Jemma, F. Guillaume, D. Derbala, D. Zelenika, D. Lechner, C. Charon, D. Boichard, I. G. Gut, A. Eggen, and M. Gautier (2008). Fine Mapping of Quantitative Trait Loci Affecting Female Fertility in Dairy Cattle on BTA03 Using a Dense Single Nucleotide Polymorphism Map. *Genetics* 178: 2227-2235.
- Druet, T., C. Schrooten, A.P.W. de Roos (2010) Imputation of genotypes from different single nucleotide polymorphism panels in dairy cattle, *J Dairy Sci* 93:5443–5454.

- Liu, Z., FR Seefried, F. Reinhardt, S. Rensing., G. Thaller and R. Reents (2011) Impacts of both reference population size and inclusion of a residual polygenic effect on the accuracy of genomic prediction, *Genet Sel Evol*, 43:19
- Lund M., APW de Roos, A. de Vries, T. Druet, V. Ducrocq, S. Fritz, F. Guillaume, B. Guldbrandtsen, Z. Liu, R. Reents, C. Schrooten, F. Seefried and G. Su (2011) A common reference population from four European Holstein populations increases reliability of genomic predictions, *Genet Sel Evol*, 43:43
- Meuwissen T. H. E., Hayes B. J., Goddard M. E. (2001) Prediction of total genetic value using genome-wide dense marker maps. *Genetics* 157:1819–1829.
- Misztal I, Legarra A, Aguilar I (2009) Computing procedures for genetic evaluation including phenotypic, full pedigree, and genomic information. *J Dairy Sci* 2009,92:4648-4655.
- Phocas, F. (2010): Multi-breed Genomics of Beef and Dairy Cattle, GEMBAL ANR funded project: [http://www.agence-nationale-recherche.fr/en/anr-funded-project/?tx_lwmsuivibilan_pi2\[CODE\]=ANR-10-GENM-0014](http://www.agence-nationale-recherche.fr/en/anr-funded-project/?tx_lwmsuivibilan_pi2[CODE]=ANR-10-GENM-0014)
- Van Raden, P (2008) Efficient methods to compute genomic predictions, *J Dairy Sci* 91:4414 - 4423.
- Van Raden, P., C. Van Tassell, G. Wiggans, T. Sonstegard, R. Schnabel, J. Taylor, and F. Schenkel (2009) Invited review: reliability of genomic predictions for North American Holstein bulls. *J Dairy Sci* 92:16-24.