French genomic experience: genomics for all ruminant species

Eric Venot, Anne Barbat, Didier Boichard, Pascal Croiseau, Vincent Ducrocq,
Rachel Lefebvre, Florence Phocas, Marie-Pierre Sanchez, Thierry Tribout,
Aurélie Vinet, et al.

French genomic experience: genomics for all ruminant species

E. Venot[1], A. Barbat[1], D. Boichard[1], P. Croiseau[1], V. Ducrocq[1], R. Lefebvre[1], F. Phocas[1], M-P Sanchez[1], T. Tribout[1], A. Vinet[1], MN Fouilloux[2], A. Govignon-Gion[2], A. Launay[2], J. Promp[2], M. Barbat[3], A. Baur[3], C. Hoze[3], S. Fritz[3], R. Saintilan[3], C. Carillier[4], H. Larroque[4], A. Legarra[4], I. Palhière[4], C. Robert-Granié[4], R. Rupp[4], F. Tortereau[4], JM. Astruc[5], V. Clement[5], V. Loywyck[5], P. Boulesteix[6], S. Mattalia[2]

[1] *GABI, INRA, AgroParisTech, Université Paris-Saclay, 78350 Jouy-en-Josas, France*
eric.venot@jouy.inra.fr (Corresponding Author)
[2] *Institut de l'Elevage, GABI, domaine de Vilvert, 78350 Jouy-en-Josas, France*
[3] *Allice, GABI, domaine de Vilvert, 78350 Jouy-en-Josas, France*
[4] *GenPhySE, Université de Toulouse, INRA, INPT, ENVT, 31326 Castanet-Tolosan, France*
[5] *Institut de l'Elevage, 31326 Castanet Tolosan, France*
[6] *Institut de l'Elevage, 87060 Limoges, France*

Abstract

Genomic selection was implemented in France in 2009 for 3 French dairy cattle breeds and was then extended to 3 beef and 5 extra dairy cattle breeds. It was also implemented in the Lacaune dairy sheep breed in 2015, and will start in 2017 for the 2 main goat breeds and 3 other dairy sheep breeds. Major genes information will be used in meat sheep in the near future.

For each species and breed, the genomic methodology has been adapted to account for the specificities regarding genomic evaluation: size of the reference population, linkage disequilibrium, multi-breed evaluations, addition of foreign genetic and genomic information, cost and benefits compared across species.

A strong partnership between Research and Development organizations and industry made it possible to implement this technology in large populations as well as in small ones. This was facilitated through sharing of technological expertise and fast innovation transfer down to farm level.

Genomic tools allow selection for new traits that can be included in breeding goals. Use of genomic information is not limited to genomic evaluation: other new services of interest for breeders were developed, such as the determination of the animal status for specific major genes or genetic defects.

Keywords: genomic selection, ruminant, dairy, meat

Introduction

Considering its size (550,000 km^2), France presents a large landscape diversity and has managed to maintain a large panel of ruminant species and breeds adapted to these landscape specificities: 3 national dairy cattle breeds (Holstein (HOL), Montbéliarde (MON), Normande (NOR)) and 5 regional ones are nowadays under selection in France. The same can be found in dairy sheep mainly represented by the Lacaune breed (used for production of Roquefort cheese), followed by Manech (Red Faced and Black Faced), Basco-Béarnaise and Corsican breeds. The number of goat breeds is also large with 2 major breeds: Saanen and Alpine.

Meat breeds are also well represented in France with in cattle, 3 national (Charolaise (CHA), Limousine (LIM) and Blonde d'Aquitaine (BLA)) and 6 regional (Aubrac (AUB), Bazadaise (BAZ), Gasconne (GAS), Parthenaise (PAR), Rouge des prés (ROU) and Salers (SAL)) beef breeds. France is also one of the European leaders in sheep meat production relying on more than 20 specialized or hardy breeds.

France has managed to implement or will soon implement genomic selection for a large number of these breeds, thanks to a collaborative organization at national level.

The French genetic organization

The French genetic organization was originally built through the 1966 Livestock Law. This legislation defined the general framework for animal breeding operations (animal identification, performance recording, breed association, semen production, semen distribution, extension). It also designated the French National Institute for Agricultural Research (INRA) as the center operating the central database gathering all pedigree and phenotype data and running genetic evaluations and the French Livestock Institute (Idele) for EBV delivery. This legislation was updated in 2006 by suppressing most monopolistic situations but confirming the roles of INRA and Idele and creating an inter-professional association for genetic improvement of all ruminants (France Génétique Elevage – FGE), in charge of the coordination of the overall national system for all ruminants. FGE represents France at the International Committee of Animal Recording (ICAR). A common R&D effort is carried out by two joint private-public structures (UMT 3G and UMT GGPR) bringing together INRA, Idele and the French Federation of breeding companies (Allice).

The dairy cattle pioneers: 20 years of collective investments

An ideal situation

Developments of genomic evaluation first focused on the 3 national dairy cattle breeds (HOL, MON, NOR) because of their favorable characteristics: a large number of progeny tested bulls, a high proportion of AI, the high cost of progeny test, a reduced genetic population size, a relatively low genotyping cost compared with the value of breeding animals… Moreover, the major breed (HOL) is used internationally and participates to Interbull international evaluations. This international status helped to build up a consortium with other countries to exchange genotypes and therefore increase reference population size: the *Eurogenomics* consortium gathered 7 organizations from 8 countries (initially – in 2009- Denmark, Finland, France, Germany, the Netherlands, the Flanders part of Belgium and Sweden, and later Spain and Poland). A similar international initiative for genotype exchange took also place later in the Brown Swiss breed through the *Intergenomics* consortium. Reference population sizes and expected reliability for candidates are presented in Table 1.

Table 1. Size of the male and female reference populations in dairy cattle breeds in 2016 and range of (trait dependent) expected reliability for young genotyped animals.

Breed	Number of Bulls	Number of Cows	Expected reliability for young Candidates
HOLSTEIN & RED	33 000		[0.55-0.70]
BROWN SWISS	6 000		[0.45-0.70]
MONTBELIARDE	2 800	31 000	[0.55-0.70]
NORMANDE	2 400	16 000	[0.55-0.65]
ABONDANCE	350	1 900	[0.35-0.55]
TARENTAISE	300	1 300	[0.30-0.50]
VOSGIENNE	60	1 100	[0.20-0.50]

National genomic selection of dairy cattle

The current approach (an extension of Boichard et al, 2012) consists in a genomic evaluation which combines the advantages of QTL-detection and genomic selection (GS): for each trait, a QTL detection is first applied using a Bayesian method (Bayes Cπ). Haplotypes of 4 markers are then defined for each of the 3000 main QTL. It is expected that haplotypes trace better the transmission of QTL between generations. A residual polygenic component is added to estimate the sum of the remaining (tiny) QTL, through a *genomic* relationship matrix based on about 8000 SNP of the low density chip. In practice, a completely equivalent model is used where haplotype and SNP effects are estimated together.

Official genomic selection started in 2009 for HOL, MON and NOR breeds, in 2013 for BSW and in 2016 for regional breeds (ABO, TAR, VOS). Genomic evaluations of females became official in 2011. National evaluations are run 6 times per year (including haplotype and SNP effects re-estimation) and weekly for all animals with new genotype (without haplotype and SNP effects re-estimation). Since 2013, most genotypes are obtained with the EuroG10k chip and imputed to the 50k chip. Nevertheless, all AI bulls are (re)genotyped with the 50k chip to maintain a high imputation accuracy.

Practical implications

Genomic selection was quickly implemented in the 3 national dairy cattle breeds and quickly had large impacts on selection schemes of these breeds. No new young bull entered progeny test after 2010. With GS, GEBV of any genotyped animal are available at the latest 3 months after birth with already high reliability for all kinds of traits (between 0.6 and 0.7 for production or functional traits). Bulls are selected and used on a large scale as soon as they reach sexual maturity. Regular genetic evaluations are also performed, so EBV of these bulls based on progeny performances are still available (and compared with initial GEBV) but with a much higher reliability, because of the much larger number of progeny per bull.

Dairy breeders quickly adopted this technology: since 2011, the number of genotyped calves increased by more than 25% per year, reaching 140,000 in 2016. Breeders also quickly changed their practices and now mainly use young genomic bulls: in 2015, 68%, 67% and 90% of the AI corresponded to young bulls with no daughter information yet, in HOL, MON, and NOR, respectively.

Relying on similar levels of reliability across all traits, breed organizations can now apply more balanced selection between production and functional traits in their selection goals: e.g., from 2001 to 2012, the economic weights for fertility and udder health increased respectively from 13% to 22% and from 13% to 18% in the Holstein total merit index, whereas the one for milk production decreased from 50% to 35%.

GS also induced the use of a larger panel of bulls, in particular sires of sons, for a better maintenance of genetic diversity. In the Montbeliarde breed, the proportion of AI done with the 5 most used bulls each year decreased from 32% to 14% between 2007 and 2015.

Implementation of genomic selection in beef cattle breeds

The general situation of beef cattle breeds was less favorable than the main dairy breeds one: first, large reference populations are more difficult to constitute due to the low use of AI bulls in beef herds and the limited amount of information (own performance or offspring ones) available for most of the natural service bulls. To circumvent these difficulties, a research project was set up between 2010 and 2014 to study a multi-breed genomic evaluation with the use of high-density chip (including around 777,000 SNPs). However, only very few QTLs were found to be common across beef breeds and no benefit was found to develop multi-breed GS (Gunia et al., 2014). Nevertheless, the animals genotyped in the context of this research program constituted valuable initial within breed reference populations, allowing within breed GS implementation.

Table 2 presents the size of the reference population available in December 2016 for the groups of traits evaluated. Genomic evaluations for some beef cattle traits predict breeding values for both direct and maternal genetic effects. Reference populations for the latter effects are constituted by genotyped dams and genotyped grandsires, and are therefore smaller than reference populations for direct genetic effects. The current reference populations are rather large for direct genetic effects for birth and weaning traits, but they are more limited for maternal effects and for carcass traits, especially if we focus on the reference animals with accurate phenotypes (in brackets in Table 2).

Eventually, a gain in reliability through genomic evaluation exists but is quite limited at the moment: e.g., +0.10 for birth traits of young Charolais calves or +0.06 for Growth Total Merit Index.

Table 2. Size of beef cattle reference population (between brackets: number of animals with deregressed EBV reliability greater than 0.7)) (December 2016)

Type of genetic effect	Traits	Charolaise	Limousine	Blonde d'Aquitaine
Direct	Birth	16 571 (1816)	7 047 (2 766)	6 791 (1 319)
	Weaning	15064 (1376)	6 302 (2 373)	4 193 (770)
	Carcass	2 336 (426)	1 756 (233)	786 (138)
Maternal	Birth	6250 (598)	3 385 (1003)	3 255 (258)
	Weaning	5081 (383)	2 458 (370)	2 327 (188)

The genomic evaluation method used for beef cattle is a two-step approach. The direct genomic breeding values are estimated using the Bayes-C methodology. Then polygenic and genomic results are blended following the method of VanRaden et al. (2009). Genomic evaluations became official in 2015 for the 3 main French cattle breeds (Tribout et al., 2016). It is performed twice a year with complete marker effects re-estimation, and weekly without re-estimation.

Developments and implementation of Genomic Selection for small ruminants

The situation is even less favorable for small ruminants, due to a high genotyping cost compared to the animal value, a limited potential gain in generation interval which is already short and AI specificities (use of fresh semen and AI demand highly concentrated in time). Different cases can be distinguished between dairy and meat sheep, or goats.

Genomic developments in sheep occurred up to now mainly in the largest dairy breed, the Lacaune breed. The OvineSNP50 Illumina chip has been available since 2009. A Single Step GBLUP (with phantom parent groups) approach was tested to take into account all information available (Baloche et al., 2014): reliability gains obtained varied between 0.10 and 0.20 depending on the trait.

A specific experimental study was then set up in 2011 to balance pros and cons of GS in Lacaune breed: in the classic progeny test process, a one-third selection intensity was applied on half of the ram candidates based on genomic results and a comparison of Total Merit Index (TMI) was performed after the 2 years of progeny testing: TMI of rams selected based on GS results was found higher than classical TMI by +0.5 TMI standard deviation (Barillet et al., 2014). In addition, an economic study showed that applying this one-third extra selection intensity led to 15% extra genetic gain without extra cost, the genotyping cost being balanced by the reduction in the number of rams kept in AI center (Buisson et al, 2014). Following these results, progeny test was ended in 2015 in Lacaune breed and replaced by GS. Extension of GS to other dairy sheep breeds is foreseen in 2017. Because they are well related, a multi-breed evaluation may circumvent smaller reference population sizes (Legarra et al, 2014). The size of the reference populations (progeny-tested rams that have been genotyped so far) is near 5,500 for the Lacaune, 2,100 for the Red Faced Manech, 600 for the Basco-Béarnaise, 500 for the Black Faced Manech and 225 for the Corsican breed.

With limited AI use and progeny testing and no expected positive profitability, no GS is planned in the close future for meat sheep breeds. However, genotyping can be used for new services of interest for breeders, such as determination of the animal's status on specific major genes or genetic defects (e.g., hyperprolificacy), or for parentage verification and assignment. Research is going on to include major genes in genetic evaluation.

In French dairy goats, 825 bucks (471 Alpine and 354 Saanen) and 1945 females have been genotyped with the Illumina goat SNP50 Bead-Chip available since 2011. The study of the reference populations structure showed that linkage disequilibrium and inbreeding levels and relationship between reference and candidate populations of the two breeds were not ideal to maximize genomic evaluation accuracy (Carillier et al., 2014). Two-step genomic evaluations did not improve accuracy compared to classical evaluations for milk production traits, udder type traits and somatic cells score.

When using single step GBLUP based on female performances, the prediction quality using multi-breed or within-breed model was similar. Genomic breeding value accuracy of candidates exceeds parent average accuracy from 10% for protein yield in Alpine breed to 14% for protein content in Saanen breed. Clearly, single step GBLUP provides opportunities for efficient genomic selection in French goats. Its routine implementation is planned for 2018. Accuracy could be slightly improved by integrating major genes such as the αs1-casein (Carillier et al., 2016).

Conclusion

Genomic selection has generated a considerable technological revolution during these last years in France. It started with the national dairy cattle breeds and was quickly extended to other breeds or species: it has already had a huge impact on the organization of breeding schemes, with the end of progeny test and the fast and steady increase of the use of young "genomic" bulls for higher genetic gain on a variety of traits. All these quick developments were made possible by the existing efficient collective partnership between industry partners and national Research and Development organizations. GS is now in place in 11 cattle and 1 sheep breeds. In the very near future, it will be extended to 4 extra sheep breeds and 2 goat breeds.

However, it is not the end of the story yet! It is even only the beginning of the genomic revolution: organizational reforms, maintenance and enlargement reference population, integration of new phenotypes, use of sequence information… are all new exciting challenges to come.

List of References

Baloche G., Legarra A., Larroque H., Astruc J.M., Robert-Granié C. and Barillet F. (2014) Assessment of genomic selection efficiency in French Lacaune dairy sheep. J Dairy Sci, 97, 1107.

Barillet, F., Baloche, G., Buisson, D., Lagriffoul, G., Aguerre, X., Boulenc, P., Fidele, F., Frégeat, G., Giral-Viala, B., Guibert, P., Panis, P., Soulas, C., Larroque, H., Legarra, A., Astruc, J.-M. (2014). Genomic selection in French dairy sheep: main results and design to implement genomic breeding schemes. 39th. ICAR Biennal Session, Berlin,

Boichard D., Guillaume F., Baur A., Croiseau P., Rossignol M.N., Boscher M.Y., Druet T., Genestout L., Colleau J.J., Journaux L., Ducrocq V., Fritz S. 2012. Genomic Selection in French Dairy Cattle. Anim Prod Sci, 52, 115-120.

Buisson, D., et al. (2014) Genomic breeding schemes in French Lacaune and Manech dairy sheep: design and expected genetic gain. 10thWCGALP, Vancouver, Canada

Carillier C., Larroque H., Robert-Granié C (2014) Comparison of joint and purebred genomic evaluation in the French multi-breed dairy goat population. Genet Sel Evol, 46: 67.

Carillier C., Larroque H., Robert-Granié C (2016) Including αs1 casein gene information in genomic evaluations of French dairy goats. Genet Sel Evol, 48: 54.

Gunia M., Saintilan R., Venot E., Hozé C., Fouilloux M.N., Phocas F. (2014). Genomic prediction in French Charolais beef cattle using high-density single nucleotide polymorphism markers. J. Anim. Sci. 92, 3258-3269

Legarra A, Baloche G, Barillet F, et al. (2014) Within-and across-breed genomic predictions and genomic relationships for Western Pyrenees dairy sheep breed Latxa, Manech and Basco-Béarnaise. J Dairy Sci, 97: 3200–3212.

Tribout T., Barbat M., Saintilan R., Fouilloux M.N., Venot E., Phocas F. 2015. Mise en place d'évaluations génomiques nationales dans les populations bovines allaitantes françaises Charolaise, Limousine et Blonde d'Aquitaine. Renc. Rech. Rum., 22

VanRaden P.M., Van Tassel C.P., Wiggans G.R., Sonstegard T.S., Schnabel R.D., Taylor J.F., Schenkel F.S., 2009. Reliability of genomic predictions for North American Holstein bulls. J. Dairy Sci., 92: 16-24.

Comment citer ce document :
Venot, E. (Auteur de correspondance), Barbat, A., Boichard, D., Croiseau, P., Ducrocq, V.,
Lefebvre, R., Phocas, F., Sanchez, M. P., Tribout, T., Vinet, A., Fouilloux, M.-N., Govignon Gion,