All cows are worth to be genotyped !

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Genomic Evaluation Properties

- Early evaluation
- As accurate for females as for males => big change of paradigm !
- Similar accuracy for all « conventional » traits (ie for all traits with progeny test evaluations)
- Much larger panel (x3-4) of young genomically evaluated bulls than of progeny tested bulls

=> Within herd selection can be strongly enhanced, and possibly to a customized breeding objective !

Two complementary interests of large scale female genotyping : at the farmer and the population levels

- For the population:
  - Genotyped females are the reference population of the future, because the number of progeny evaluated bulls will decrease
  - For many traits, 1 progeny tested bull is equivalent to 3-6 females with phenotype, depending on h^2
  - Only possibility for new traits: few bulls will be progeny evaluated for a completely new trait
  - Major opportunity for breeds of limited size *(eg : the male reference population is around 2500 in Montbéliarde or Normande breeds, and less than 500 in the other French breeds)*

Two complementary interests of large scale female genotyping : at the farmer and the population levels

- For the population (2):
  - Broader screening of the population at a reasonable cost: one can more easily afford to genotype an original animal
  - Due to the much larger genotyping volume, the cost of genotyping will decrease for everybody, including for the breeding scheme

=> Strong interest to encourage / find the most appropriate conditions for mass female genotyping

Within herd selection

- For the first time, a clear increase of dam-cow’s pathway potential contribution to genetic gain
- A real opportunity to **customize** the genetic trend at the farm level, through the choice of bulls, but also through female selection
- The **issue**: selection **intensity** is strongly limited by the low natural prolificacy (~0.4 female calf / year),
- Nearly all young females are needed for replacement
- Embryo Transfer is expensive and will not generalize

Within herd selection

- The solution in the present conditions: Sexed Semen
- One can expect a strong increase of this technique in the near future, in parallel of genotyping
- Replacement made from the top 50% of the herd, based on genomic evaluation and on a breeding goal defined by the farmer
- Other females bred for other purposes (crossbreeding, sales…)

The question of the cost and profitability

- It is often argued that genotyping is not profitable
- Generalized female genotyping without sexing is likely not profitable (based on genetic gain arguments), unless at a very low price, due to low selection intensity and poor use of the information
- Sexing alone is profitable, in spite of its high cost. It is presently limited by technical and social constraints, not by a low return => not further developed here

Review of the literature

Study	Country	Genotyping cost	Compared to selection on pedigree	Replacement rate	Economic value of 1 TMI σg	Gain due to female genotyping
Chesnais 2011	Canada	CAN$47	NO	10 to 40%	CAN$159	CAN $70
Pryce and Hayes	Australia	AU$50	NO	15 to 30 %	AU$80	AU$41
Pryce and Hayes	Australia	AU$50	YES	15 to 30 %	AU$80	negative
Weigel et al 2012	USA	$40	YES	10 to 90%	$396	huge
Pryce (ICAR 2012)	Ireland	29 €	NO	select top 50%	62 €	46 €
Pryce (ICAR 2012)	Ireland	29 €	YES	select top 50%	62 €	-31€

Simple example, assuming sexing and no female selection on pedigree

- Additional genetic gain
  - p=0.5 => i=0.8
  - R^2=0.7 => R=0.85
  - σ = 100€
  - T=5 years (probably less)

  => Yearly additional ΔG~7€ per expression

- The number of expressions depends on
  - the trait (1 lactation / year, 1 « longevity » / cow)
  - the gene flow: individual (w=1), progeny (w=0.5), …
  - the time horizon
  - the discounting rate

Illustration with a simple example, assuming sexing and no female selection on pedigree

- Result are highly dependent on the time horizon
- I assumed no additional heifer culling after genomic evaluation
  => the immediate effect is zero, but this is a too conservative assumption
- Genomic evaluation is used only for the choice of the 50% matings for replacement
- The present superiority must be attributed to the previous genotypings, not to that of the present year

Illustration with a simple example, assuming sexing and no female selection on pedigree

Horizon	Expressions	Expected gain
1-2	0	0
4	3	19
5	6	36
6	8	48
…		↗

Discouting rate = 4%

Genotyping cost

- Already strongly decreased with use of LD chip, with very limited loss of efficiency
- Will continue to decrease with low sampling cost and large volumes
- An good target is 30€ and an upper bound target is 45€
- When using both genotyping and sexing, accounting only for genotyping cost and additional genetic gain on a steady state scheme, genotyping is profitable at a 5 years time horizon

Is it fair to compare with pedigree index ?

- I would say No :
- Sire selection is already accounted for on the other pathways
- The remaining variability in pedigree index is rather small within herd
- Constraints on genetic variability limit the available selection intensity
- I did not consider the possibility of additional selection after genotyping

Additional interests

- Additional genetic gain is only a part of the return of genotyping
- Other consequences should be added to the benefit
- Some consequences are immediate
- For many farmers, they could be of more interest

List of Additional interests

- Much more accurate mating plan, based on GEBV with $R^2=0.7$ for all traits
- Information on major genes and genetic abnormalities
- Parentage checking (or even assignation) at marginal cost
- More customized breeding objective
- Possible additional bull dams discovery
- Computation of true parentage coefficients
- True inbreeding coefficients
- New generation mating plans which optimize genomic information (inbreeding minimization, QTL complementation, non additive effects…)

The example of EuroGenomics

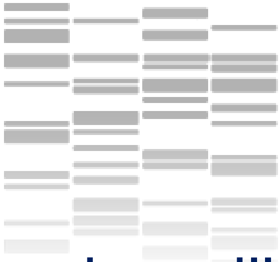
- Strategy based on a custom chip (presently EuroG10K)
- Add-On developed by INRA, Unceia, Labogena, Univ Liège, VIT, Aarhus Univ
- including
  - Additional markers for general or targeted imputation
  - 140 published mutations (for research or for release), in duplicate
  - **An increasing number of candidate mutations**, derived from research projects (association studies and sequencing)

  => A cheap and efficient way to first validate and quickly disseminate results for better predictions
- Regular updates of the chip – v2 available in october

Large scale genotyping

- Illustration with the first month of use of the EuroG10k last spring
- No homozygous found in 3849 Holstein, 909 Normand and 2931 Montbéliard for HH1, HH3, HH4, MH2
=> statistical confirmation/«validation» of causative mutations
- Information available at marginal cost

QTL	Gene	Polymorphism	HOL	MON	NOR
HH1	APAF1	p.Q579X	**3,5%**	0,0%	0,0%
HH3	SMC2	p.F1135S	**6,7%**	0,0%	0,0%
HH4	GART	p.N290T	**8,0%**	0,0%	0,0%
MH2	SLC37A2	p.R12X	0,0%	**12,1%**	0,0%



Conclusion

- Genotyping will generalize in dairy production, in association with sexed semen
- Synergy between within herd selection, within herd management, reference population set-up and replacement
- SNP chips will continue to be enriched with causative variants
- New tools will be developed to make the best use of this information
- A rich resource for research (gene hunting, gene validation, non additive effects, G x E, …) => Female genotyping and phenotyping is the source for the future innovations