# Analysis of quantitative trait loci affecting female fertility and twinning rate in Israeli Holsteins

G. Glick, M. Golik, A. Shirak, E. Ezra, Y. Zeron, E. Seroussi, M. Ron, and J. I. Weller Institute of Animal Sciences, A. R. O., The Volcani Center, Bet Dagan, Israel



## Genetic analysis of female fertility in Israel

- > Female fertility is computed as the inverse of the number of inseminations to conception at each parity.
- > For cows that were inseminated, but did not conceive the number of inseminations to conception is predicted.
- Parities 1 through 5 are analyzed.

# Analysis of twinning rate in Israel

- Twinning rate is scored as a dichotomous trait, but analyzed by a linear model
- Results of parties 1 through 5 are included in the analysis.
- Twining rate increases with increase in parity.

## Genetic analysis of female fertility and twinning rate in Israel

- Both traits were analyzed by the multitrait animal model.
- > Each parity is considered a separate trait.
- > A REML analysis was applied to a subset of data for each trait to determine if this model was appropriate and to estimate variance components.
- > A further REML analysis was performed to estimate genetic correlations between twinning rate and female fertility.

#### Heritabilities (on the diagonal) genetic correlations (above the diagonal), and environmental correlations (below the diagonal) for twinning rate by parity, 66,210 cows with records

Parity	1	2	3	4	5
1	0.013	0.805	0.793	0.784	0.774
2	0.031	0.022	0.876	0.927	0.957
3	0.023	0.051	0.024	0.957	0.945
4	0.027	0.053	0.049	0.026	0.977
5	0.019	0.045	0.051	0.061	0.031

Heritabilities (on the diagonal) genetic correlations (above the diagonal), and environmental correlations (below the diagonal) for twinning rate and female fertility by parity, 53,765 cows with records

Trait		Twinning rate			Female fertility		
	Parity	1	2	3	1	2	3
Twinning rate	1	0.012	0.890	0.925	-0.278	-0.159	-0.127
	2	0.029	0.022	0.816	-0.270	-0.366	-0.284
	3	0.014	0.041	0.021	-0.369	-0.195	-0.113
Fertility	1	-0.014	-0.025	-0.015	0.018	0.874	0.861
	2	-0.002	-0.027	-0.015	0.048	0.016	0.971
	3	0.001	-0.014	-0.038	0.043	0.053	0.018

## **Conclusions from the REML analysis**

- > Heritabilities ranged between 1 and 2% for both traits for all parities.
- > Heritabilities tended to increase slightly by parity for both traits.
- Genetic correlations among parities ranged from 0.9 to 0.75, but environmental correlations were all close to zero.
- > Genetic correlations between fertility and twinning rate were negative for all combinations of the first three parities.



## Genetic trends

- Annual genetic trends were computed as the regression of the cows' breeding values on their
- Genetic trends were positive for both traits.

## Genome scan of the Israeli Holstein population by the BovineSNP50 BeadChip, preliminary results

- > The chips are sold in batches of 288 units.
- > We therefore decided to analyze 576 bulls in the first stage.
- > All bulls in the selected samples have reliabilities > 50% for all traits included in the Israeli breeding index.

## Results on the first 576 bulls genotyped

- > Of 31,104,576 possible genotypes (576 bulls X 54,001 SNPs) genotypes were determined for 30,631,040 (98.5%).
- There were 27,114,367 genotypes with "call rates" > 0.7 (87.2%)
- > SNPs were deleted from further analysis if:
  - 1. Frequency of the more common allele > 0.95.
- 2. Less than 288 bulls had valid genotypes.
- > This left 40,744 valid SNPs as compared to 38,416 in the US analysis.
- > Of these there were 1160 SNPs without assignment to the physical map (2.8%).
- > A total of 494 SNPs were assigned to the X chromosome (1.2%).
- > We determined deviation from the predicted Hardy-Weinberg for the remaining markers.
- There were 783 SNPs with deviations > 0.10 between the expected and observed frequencies of heterozygotes.

#### Linkage disequilibrium analysis

Significant linkage disequilibrium (LD) between SNP genotypes of the bulls and QTL for the traits analyzed was tested by the following regression model:

## $BV_i = S + BY + BY^2 + e_i$

Where  $BV_i$  = breeding value of bull i, S = SNP genotype, BY is the birth year, and  $e_i$ is the random residual.

Heterozygotes were scored as 1 and homozygotes as either 0 or 2.

## **Determination of significance**

- > Because of the huge number of comparisons, normal significance levels of 0.01 or even 0.001 will be obtained many times purely be chance.
- Therefore significance was determined by the false discovery rate. For a given nominal significance rate the FDR is defined as:

## Expected number of significant effects Observed number of significant effects

## FDR for the 50 SNPs with the lowest nominal probability values

Trait	F- value	Nominal probability	Expected number of effects	FDR		
Fertility	30.1	6.2 x10 <sup>-8</sup>	0.0025	5.05x10 <sup>-5</sup>		
Twining rate	25.6	5.7x10 <sup>-7</sup>	0.0232	4.65x10 <sup>-4</sup>		
Thus, virtually all of these effects can be considered real effects.						

#### SNPs with significant effects on both traits

Independence of distribution of significant effects for the two traits were tested by  $\chi^2$ 

		Twinnir		
		Significant	N. S.	Total
Fertility	Significant	126 (77)	2054 (2103)	2180
	N. S.	1274 (1323)	36129 (36080)	37403
	Total	1400	38183	39583

Expected values are given in parentheses.

- > There were 64% more SNPs with significant effects on both traits than expected.
- >  $\chi^2$  = 34.0, which is significant at p<0.001.
- There were 18 SNPs with significant effects for both traits at p<0.0001.</p>
- > For all 18 of these SNPs, the effect for fertility was in the opposite direction to the effect on twinning rate!

## Conclusions

- > The observed negative genetic correlation between conception rate and twinning rate is due to specific quantitative trait loci with effects in opposite directions on twinning rate and female fertility.
- > Apparently genetic propensity for multiple ovulation has a negative effect on conception rate.



These results are part of the SABRE research project that has been cofinanced by the European Commission, within the 6th Framework Programme, contract No. FOOD-CT-2006-016250. This poster represents the views of the Authors, not the European Commission. The Commission is not liable for any use that may be made of the information. For further information on the SABRE project please visit www.sabre-eu.eu.

CUTTING EDGE GENOMICS FOR SUSTAINABL

- birth dates.
- Genetic trends were:

0.0294% for conception rate 0.0529% for twinning rate