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## The effect of genetic merit for fertility traits on pregnancy establishment in lactating dairy cows



### Key external stakeholders:

Dairy farmers, dairy industry, AI companies, veterinary practitioners, DAFM, universities

### Practical implications for stakeholders:

- Cows with good genetic merit for fertility traits have favourable fertility phenotypes. This indicates that it is possible to select for improved fertility performance.
- Calving pattern has a major economic effect on farm productivity and profitability, and hence it is vital that farmers continue to select for improved fertility sub-index within the EBI.

### Main results:

- After parturition, cows with good genetic merit for fertility traits (Fert+) have earlier resumption of cyclicity, better uterine health, greater body condition score (BCS) and more favourable blood indicators of bioenergetic status compared with cows with poor genetic merit for fertility traits (Fert-).
- Fert+ cows have greater circulating concentrations of progesterone during the luteal phase compared with Fert- cows. Greater circulating progesterone concentration is due a larger corpus luteum that produces more progesterone rather than differences in metabolic clearance rate.
- Uterine environment is affected by cow genetic merit for fertility traits. In endometrial tissue samples collected on day 7 and on day 13 of the oestrous cycle, global gene expression profiles indicated better energy status and reduced inflammation in Fert+ cows compared with Fert- cows. In addition, on day 13, Fert- cows had up-regulated expression of genes involved in prostaglandin  $F_{2\alpha}$  synthesis and secretion compared with Fert- cows.
- Collectively, the results indicate that Fert+ cows had to finely co-ordinate metabolism and gene expression profiles across multiple tissues and organs to achieve better fertility.

### Opportunity / Benefit:

The results of this research have:

- Demonstrated the potential benefit of intensively selecting on fertility traits as part of the long-term herd breeding goal.
- Identified fertility phenotypes under genetic control that may be explored in future studies with large numbers of animals to identify genetic markers to help accelerate the rate of genetic gain for fertility traits.

### Collaborating Institutions:

ICBF, UCD

**Teagasc project team:**

Dr Stephen Butler (Project Leader/PI)  
Dr Stephen Moore  
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**External collaborators**

Dr. Ross Evans (ICBF)  
Dr. Trudee Fair and Dr. Pat Lonergan (UCD)

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**1. Project background:**

The advent of AI has markedly improved the production potential of dairy cows in all systems of production and transformed the dairy industry in many countries. Unfortunately, for many years breeding objectives focused solely on milk production. This resulted in a major decline in genetic merit for fertility traits. In recent years, the underlying physiological mechanisms responsible for this decline have started to be unravelled. It is apparent that poor genetic merit for fertility traits is associated with multiple defects across a range of organs and tissues that are antagonistic to achieving satisfactory fertility performance. The objective of this project was to identify some of the physiological mechanisms under genetic control that are responsible for differences in fertility performance in lactating dairy cows with good and poor genetic merit for fertility traits.

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**2. Questions addressed by the project:**

- Does genetic merit for fertility traits affect fertility phenotypes in lactating dairy cows?
- Are differences in circulating progesterone concentrations primarily due to differences in luteal progesterone production or differences in hepatic progesterone clearance?
- Does genetic merit for fertility traits affect endometrial gene expression during the luteal phase?

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**3. The experimental studies:**

This project used a validated lactating Holstein cow genetic model with similar genetic merit for milk production traits but either good (Fert+) or poor (Fert-) genetic merit for fertility traits. Three separate but interlinked studies were conducted.

**Study 1:**

Twenty-six cows were enrolled in the study and data are reported for 15 Fert+ and 10 Fert- cows that completed the study. All cows received a total mixed ration diet during early lactation and were turned out to pasture in late spring. Dry matter intake was recorded daily from week -2 to 5 relative to parturition (week 0). Blood metabolites and metabolic hormones were measured from week -2 to 8 relative to parturition. Milk production, body condition score, and body weight until week 35 of lactation are reported. To monitor uterine health, vaginal mucus was scored weekly on a scale of 0 (no pus) to 3 ( $\geq 50\%$  pus) from parturition to week 8 and uterine polymorphonuclear neutrophil count was measured at week 3 and 6 postpartum.

**Study 2**

A total of 28 cows were enrolled in an ovulation synchronisation protocol at  $61 \pm 13$  ( $\pm$ standard deviation) days postpartum, and data are presented for 13 Fert+ and 9 Fert- cows that remained in the study. Progesterone concentrations were determined from day 0 to day 9 (day 0 = day of oestrus) and on day 7, corpus luteum (CL) volume and blood flow area (BFA) were measured by B-mode and Doppler ultrasonography, respectively. Cows were administered PGF $2\alpha$  on day 7 in the p.m. and d 8 in the a.m. to regress the CL, and 2 controlled internal drug release devices were inserted per vaginam on d 8 in the a.m. Liver biopsies were collected on d 9 and hepatic mRNA abundance of genes involved in P4 catabolism was determined. On d 10, the controlled internal drug release inserts were removed and frequent blood samples were collected to measure the rate of decline in circulating P4.

**Study 3**

A total of 18 Fert+ and 17 Fert- cows were enrolled in the study. The oestrous cycle was synchronised using a progesterone-ovsynch synchronisation protocol. On day 7 after ovulation, the ovaries were examined by ultrasound. After ultrasonography of the largest follicle, a blood sample was collected simultaneous with follicular fluid aspiration. Amino acid and fatty acid composition of both follicular fluid and serum were determined using gas chromatography-mass spectrometry (GC/MS).

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**4. Main results:****Study 1**

Prepartum DMI was similar between genotypes, but Fert+ cows had significantly greater DMI than Fert- cows (19.7 vs. 16.8 kg of dry matter/d) during the postpartum period. Energy balance at wk 1 was

significantly greater in Fert+ cows than in Fert- cows [2.3 vs. -1.12 Unite Fourragere Lait (UFL)/d]. The Fert+ cows had significantly greater daily milk solids production (1.89 vs. 1.74 kg/d) and tended to have greater daily milk yield (24.2 vs. 22.3 kg/d). The Fert+ cows had significantly greater mean circulating insulin-like growth factor-I (102.62 vs. 56.85 ng/mL) and tended to have greater mean circulating insulin (3.25 vs. 2.62  $\mu$ U/mL) compared with Fert- cows from week -2 to 8 relative to parturition. Mean circulating concentrations of glucose (3.40 vs. 3.01 mmol/L) were significantly greater in Fert+ cows compared with Fert- cows from week -2 to 3 relative to parturition. The Fert+ cows maintained significantly greater mean body condition score throughout lactation compared with Fert- cows (2.98 vs. 2.74 units). Moreover, Fert+ cows had better uterine health compared with Fert- cows, as evidenced by lower weekly vaginal mucus scores from week 2 to 6 postpartum and, based on uterine cytology, smaller proportions were classified as having endometritis at week 3 (0.42 vs. 0.78) and 6 (0.25 vs. 0.75). Also, a significantly greater proportion of Fert+ cows had resumed cyclicity by week 6 postpartum (0.86 vs. 0.20) compared with Fert- cows. Hence, we report for the first time that genetic merit for fertility traits is associated with postpartum uterine health status. Superior uterine health and earlier resumption of cyclicity may be mediated through differences in DMI, energy balance, insulin, insulin-like growth factor-I, and body condition score profiles. Importantly, phenotypic improvement in fertility traits was achieved without antagonising milk production.

### **Study 2**

The Fert+ cows tended to have greater dry matter intake compared with Fert- cows (+0.79 kg of dry matter/d), but similar milk production (29.82 kg/d). After synchronised ovulation, the rate of increase in circulating concentrations of P4 was greater in Fert+ cows compared with Fert- cows. No effect of genotype on CL volume was detected, but BFA was 42% greater in Fert+ cows compared with Fert- cows. The Fert- cows had greater mRNA abundance of cytochrome P450, family 3, subfamily A (*CYP3A*) compared with Fert+ cows, but the mRNA abundance of aldo-keto reductase family 1, member C1 (*AKR1C1*), *AKR1C3*, *AKR1C4*, and cytochrome P450, family 2, subfamily C (*CYP2C*) were similar. The half-life and metabolic clearance rate of P4 were similar in Fert+ cows and Fert- cows.

### **Study 3**

The most pronounced effect of genotype was noted in the serum, where the abundance of total polyunsaturated fatty acids and n-6 polyunsaturated fatty acids was greater in Fert+ cows, and the abundance of total saturated fatty acids was greater in Fert- cows. The abundance of nine fatty acids (arachidic acid, heneicosanoic acid, myristic acid, behenic acid, myristoleic acid, heptadecenoic acid, cis-11-eicosanoic acid, nervonic acid and g-linolenic acid) in follicular fluid was affected by genotype. Concentrations of cysteine, leucine, ornithine, proline and tyrosine in follicular fluid, and asparagine, creatinine, cysteine, methionine, proline and valine in serum, were also affected by genotype. Receiver operating characteristic curve analysis indicated that the follicular fluid and serum fatty acids and follicular fluid amino acids that were significantly affected by genotype were highly predictive of fertility genotype.

## **5. Opportunity/Benefit:**

- Improvements to fertility traits were achieved without antagonising milk production.
- Genetic merit for fertility traits was associated with postpartum uterine health status. Superior uterine health and earlier resumption of cyclicity may be mediated through differences in DMI, energy balance, insulin, insulin-like growth factor-I, and body condition score profiles.
- Greater circulating concentrations of P4 were primarily due to greater CL P4 synthetic capacity rather than differences in P4 clearance in this lactating cow genetic model of fertility.
- Cows with a high EBI fertility sub-index had a faster recovery from uterine infection and resume ovarian cyclicity earlier after calving. As a result, the need for veterinary intervention can be reduced and fertility improved by selecting sires with a high fertility sub-index to generate replacement heifers with superior genetics for fertility traits. In addition, improved reproductive performance will facilitate better synchronisation between pasture supply and demand and earlier calving will increase the proportion of cows that complete a full lactation, thereby increasing milk production from pasture.
- Changes to the fatty acid and amino acid metabolome in serum and follicular fluid reflect the physiological status of dairy cows, with favourable and unfavourable consequences for their health and fertility. We identified changes to fatty acids and amino acids in follicular fluid and serum that may explain, at least in part, the differences in reproductive performance reported in this genetic model. These biomarkers were highly predictive of the fertility genotype of the dairy cows used in the study. High throughput assay diagnostics for these biomarkers may provide useful screening tools in dairy cattle.

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## 6. Dissemination:

### Main publications:

Moore, S. G., T. Fair, P. Lonergan, and S. T. Butler. 2014a. Genetic merit for fertility traits in Holstein cows: IV. Transition period, uterine health, and resumption of cyclicity. *Journal of Dairy Science* 97:2740-2752.

Moore, S. G., A. O'Gorman, L. Brennan, T. Fair, and S. T. Butler. 2015. Follicular fluid and serum metabolites in Holstein cows are predictive of genetic merit for fertility. *Reproduction, Fertility and Development*.

Moore, S. G., S. Scully, J. A. Browne, T. Fair, and S. T. Butler. 2014b. Genetic merit for fertility traits in Holstein cows: V. Factors affecting circulating progesterone concentrations. *Journal of Dairy Science* 97(9):5543-5557.

### Popular publications:

Moore, S. G. and S. T. Butler (2013). The effect of genetic merit for fertility traits on uterine health in dairy cows. *Moorepark '13 Open Day*, page 79 to 80.

Moore, S. G. and S. T. Butler (2013). Genetic merit for fertility affects uterine health. *TResearch* 8(4):24-25

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## 7. Compiled by: Dr. Stephen Butler

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