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## Relationships among maternal environment, fetal development, follicle numbers and fertility in cattle



### Key external stakeholders:

Reproductive biologists, geneticists, animal breeding organisations, dairy farmers.

### Practical implications for stakeholders:

- Improved understanding of the links between in utero development, ovarian organogenesis, postnatal follicle numbers and fertility performance in lactating dairy cows.

### Main results:

The key results were:

- Greater milk yield (after accounting for differences in genetic merit) around the time of conception and during gestation was associated with reduced survival and milk yield and greater SCC in the progeny.
- Restricting maternal nutrition during the first 110 days of gestation results in the birth of calves with reduced numbers of ovarian follicles.
- The number of follicles on the ovaries was positively associated with fertility in dairy cattle.

### Opportunity / Benefit:

The number of ovarian follicles may be a useful index of fertility in lactating dairy cows. An opportunity exists to develop a rapid low-cost screening test to assess ovarian follicle numbers. Subsequent research would be necessary to validate the relationship with phenotypic fertility performance, determine heritability, and assess whether there is value in incorporating the trait into the national breeding objective.

### Collaborating Institutions:

Teagasc, UCD, Michigan State University

**Teagasc project team:** Dr. Stephen Butler  
Dr. Donagh Berry

**External collaborators:** Prof. Alex Evans, Prof. Pat Lonergan and Dr. Francesca Mossa (all UCD)  
Prof James Ireland (MSU)

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### 1. Project background:

An emerging area of developmental biology is the study of the foetal origins of adult disease. The hypothesis proposes that some diseases originate through adaptations that the foetus makes when it is undernourished, which permanently alter the structure and function of the body. This hypothesis is frequently referred to as the 'Barker hypothesis' after David Barker who first suggested it.

Dairy cows have been selected for an increase in milk production, but there has been a concomitant decrease in fertility and increased susceptibility to some diseases. In order to have a 365 day calving interval, cows must conceive during the period of their peak lactation. This period of peak metabolic burden is coincident with follicle growth, ovulation, fertilization, early embryonic development and early fetal development. According to the Barker Hypothesis, animals conceived and developing in this nutritionally stressed maternal environment have compromised development that could affect them for the rest of their lives.

Previous research established that peak numbers of follicles in ovarian follicular waves of the oestrous cycle are highly variable amongst animals but very highly repeatable within individuals. Also, cows that consistently have relatively high numbers of follicles during waves have higher serum inhibin-A concentrations, but lower serum FSH and similar oestradiol concentrations during the first follicular wave compared with cows with low numbers of follicles during waves. While the link between follicle numbers and fertility had not been studied, we had recently found differences in superovulatory response (quality and number of embryos) and also noted that progesterone concentrations were greater in animals with high numbers of follicles.

The focus of the research reported here was to further our understanding of the links between the environment in which cattle embryos/foetuses develop, the numbers of ovarian follicles, and reproduction and fertility in cattle. We proposed to test an overarching hypothesis that a major factor contributing to fertility in cattle is the numbers of follicles in the ovaries and that this is regulated by the conditions present during foetal development.

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### 2. Questions addressed by the project:

- Is the number of follicles per wave linked to ovarian size, number of oocytes (eggs), and circulating concentrations of reproductive hormones?
- Is ovarian development in offspring affected by maternal nutritional status in early gestation?
- Is the number of follicles present on the ovary linked to reproductive performance?

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### 3. The experimental studies:

The research used complex statistical analyses of large data sets (national database containing several million records), animal models to examine foetal development, oocyte quality and follicle development, and cellular and molecular techniques to understand the development of tissues in the ovaries. This wide range of methods was chosen as they each probed the issues being studied in a slightly different way to increase our knowledge of the relationship between foetal development, the numbers of ovarian follicles and fertility in cattle.

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#### 4. Main results:

Analysis of the national data set on Irish Holstein-Friesian dairy cows indicated that, after accounting for genetic merit of the cow, greater milk yield prior to conception and during gestation was associated with reduced survival and milk yield and greater SCC in the progeny. This suggests that offspring survival and performance is affected by conditions that they experience in utero — as an oocyte, embryo or foetus — mediated through factors related to milk production of the dam.

Restricting maternal nutrition (to simulate the metabolic stress of high milk production) during the first 100 days of gestation (period encompassing ovarian organogenesis and oogenesis) resulted in the birth of calves with altered numbers of ovarian follicles. This finding supports our initial hypothesis that maternal nutritional status during in utero development impacts postnatal ovarian function.

We showed for the first time in a single-ovulating species that the inherently high variation in follicle numbers during follicular waves is also associated with significant alterations in intra-follicular oestradiol production, which is the hallmark of follicular function. Expression of key genes important for differentiation, function and survival of follicular cells were also different in animals with high versus low numbers of ovarian follicles. Hence, there are functional differences between follicles from animals with high versus low numbers of ovarian follicles.

Finally, we tested the hypothesis that the numbers of follicles in the ovaries is associated with fertility in dairy cattle. The results suggest a positive association between the numbers of follicles in the ovaries and fertility in post partum dairy cows. Additional analysis of the data indicated that the number of ovarian follicles and the fertility of the adult offspring may be affected by dam parity, and that follicle numbers are moderately heritable. These effects warrant further investigation.

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#### 5. Opportunity/Benefit:

This research has improved our understanding of the links between maternal status at the time of conception and subsequent ovarian function and fertility performance. Further work is necessary to determine if direct or indirect measures of ovarian follicle numbers could be incorporated into the national breeding objective.

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#### 6. Dissemination:

##### Main publications:

- Berry, D. P., Lonergan, P., Butler, S.T., Cromie, A.R., Fair, T., Mossa, F. and Evans, A.C. (2008) 'Negative influence of high maternal milk production before and after conception on offspring survival and milk production in dairy cattle.' *Journal of Dairy Science* 91:329-337.
- Evans, A. C., Mossa, F., Fair, T., Lonergan, P., Butler, S.T., Zielak-Steciwo, A.E., Smith, G.W., Jimenez-Krassel, F., Folger, J.K., Ireland, J.L. and Ireland, J.J. (2010) 'Causes and consequences of the variation in the number of ovarian follicles in cattle.' *Society of Reproduction and Fertility supplement* 67:421-429.
- Mossa, F., Jimenez-Krassel, F., Walsh, S., Berry, D.P., Butler, S.T., Folger, J., Smith, G.W., Ireland, J.L.H., Lonergan, P., Ireland, J.J. and Evans, A.C.O. (2010) 'Inherent capacity of the pituitary gland to produce gonadotropins is not influenced by the number of ovarian follicles  $\geq 3$  mm in diameter in cattle.' *Reproduction, Fertility and Development* 22:550-557.
- Mossa, F., Walsh, S.W., Butler, S.T., Berry, D.P., Carter, F., Lonergan, P., Smith, G.W., Ireland, J.J. and Evans, A.C.O. (2012). 'Low numbers of ovarian follicles  $\geq 3$  mm in diameter are associated with low fertility in dairy cows.' *Journal of Dairy Science* 95:2355-2361.

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#### 7. Compiled by: Dr. Stephen Butler

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