Project number: 6003
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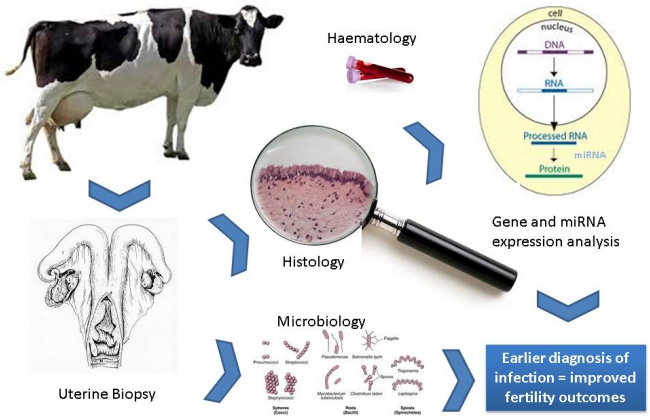
Understanding immunity in the post-partum cow



Key external stakeholders:

DAFM, Teagasc commercial partners, dairy industry

Practical implications for stakeholders:

- Prolonged inflammation in the uterus of some cows after calving leads to the development of endometritis and subfertilty.
- Certain markers may predict cows at risk of developing uterine disease much earlier than current diagnostics.
- Early identification of cows at risk would enable targeted intervention which would reduce the negative effects of this disease on subsequent fertility.

Main results:

- Until now, analysis of the post-partum immune response was performed in a piecemeal manner. This project was the first to apply high throughput sequencing technology to dissect the interdependent relationship between inflammation and fertility in the post-partum cow.
- This project integrates cellular, molecular and clinical data from the same cows at multiple levels to define the factors affecting fertility in the post-partum cow.
- Our results have identified the differences in immunity between cows which develop endometritis and healthy controls which could ultimately be used as early predictors to identify cows at risk of developing disease.

Opportunity / Benefit:

This project led to a much larger collaborative project, funded by DAFM, to investigate these results in more detail, and in additional cows across multiple farms.

Collaborating Institutions:

TCD
UCD

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Teagasc project team: Dr. Kieran Meade (PI)
External collaborators: Prof. Cliona O' Farrelly, Trinity College Dublin

1. Project background:

Postpartum uterine infections are a leading cause of compromised fertility, which is the single biggest threat to the Irish cattle sector. The consequences of infertility, together with production losses and treatment costs associated with uterine disease, costs farmers an estimated €292/cow/year.
While all cows experience an influx of bacteria into the uterus after calving, it is not known why some cows on the same farm, under identical management conditions develop uterine disease while others do not. The aim of this project was to integrate information from multiple levels to build a comprehensive picture of the various factors that may impact on fertility in the post-partum dairy cow.

2. Questions addressed by the project:

1. Could recent developments in technology be used to identify changes in gene expression in the post-partum uterus?
2. Could differences in post-partum immunity be identified between cows that develop disease, and healthy cows?
3. Would these differences be reflected systemically – i.e. in blood for ease of detection?
4. Could these differences be detected earlier than when current clinical diagnosis occurs?

3. The experimental studies:

Comprehensive sampling was undertaken in a cohort of post-partum beef, and then dairy cows at two critical time-points after calving. At Day 7 and Day 21 post-partum, blood samples, uterine swabs and uterine biopsies were collected from 16 cows. Histopathological assessment diagnosed six animals with sub-clinical (or cytological) endometritis, while nine cows were healthy. High-quality RNA was extracted from biopsies and used to generate libraries for next-generation sequencing of both genes (mRNA) and non-coding RNAs (miRNA). Culture independent techniques were used to assess the microbial population in the uterus of these cows from the uterine swabs collected. Haematology analysis was performed from blood samples and serum was used to profile metabolites and immune proteins.

4. Main results:

Our results reflect the first comprehensive integration of multiple important layers of data on the same post-partum cows, recognised by leaders in the field as key to understanding the complexity of factors that may subsequently impact on cow reproductive performance. We have identified that cows which develop endometritis fail to regulate the inflammation that occurs in response to the influx of bacteria after calving. Our results suggest that the development of disease is not mediated by negative energy balance, as metabolites were not differentially expressed systemically, and is more likely a result of immune dysregulation. We have also identified, using culture independent techniques, that the bacterial populations in the uterus of cows which develop disease are different to those in cows with a healthy uterus. We have shown that some of the local changes in the uterus are reflected in serum. We have also identified a number of molecules that will be validated for potential use as early prognostic or diagnostic markers of uterine disease.

5. Opportunity/Benefit:

This project developed a strong foundation for our research in uterine immunity and led to a much larger collaborative project, funded by DAFM, to investigate these results in more detail, and in more cows across multiple farms.

6. Dissemination:

Main publications:

1. Foley, C., C. O. Farrelly, and K. G. Meade. 2011. Technical note : Comparative analyses of the quality and yield of genomic DNA from invasive and noninvasive, automated and manual extraction methods. Journal of Dairy Science 94: 3159-3165.
2. Chapwanya, A., Meade, K. G., Foley, C., Narciandi, F., Evans, A. C., Doherty, M. L., Callanan, J. J., O'Farrelly, C. 2012. The postpartum endometrial inflammatory response: a normal physiological event with potential implications for bovine fertility. Reproduction Fertility and development

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24(8):1028-39.
3. Foley, C., Chapwanya, A., Creevey, C., Narciandi, F., O'Farrelly, C., Kenny, E., Cormican, P., Meade, K.G. 2012. Global endometrial transcriptomic profiling: transient immune activation precedes tissue proliferation and repair in healthy beef cows. BMC Genomics Sep 18;13:489.
4. Foley, C., Chapwanya, A., Lynn, D., Callanan, J. J., Narciandi, F., O'Farrelly, C., Meade, K.G. 2014. Arrested Endometrial Inflammatory Transition Associated with the Development of Cytological Endometritis. For submission in Dec 2014 (Cell, Host and Microbe).

Presentations:

Research was presented at multiple national and international conferences including:

1. Oral presentation at the Irish Grassland and Animal Production Association (IGAPA) forum. Tullamore Court Hotel, Tullamore, Co. Offaly, Ireland, 10th & 11th March 2014.
2. Oral presentation Walsh Fellowship Seminar. Royal Dublin Society, Ballsbridge, Dublin 4, Ireland, 28th November 2013.
3. Oral presentation at the Irish Grassland and Animal Production Association (IGAPA) forum. Tullamore Court Hotel, Tullamore, Co. Offaly, Ireland, 11th & 12th March.
4. Poster presentation at the 4th European Veterinary Immunology Workshop (EVIW). Royal College of Physicians of Edinburgh, Scotland, UK, 2nd – 3rd September.
5. Poster presentation at the 16th Annual Meeting of the European Society for Domestic Animal Reproduction (ESDAR). University College Dublin, Ireland, 29th – 31st August.
6. Poster presentation at the 4th International Symposium on Animal Functional Genomics (ISAFG). The Burlington Hotel, Dublin, Ireland, 10th – 12th October.
7. Poster presentation at the 44th Scientific Session of the Association of Veterinary Teachers and Research Workers. Newry, Co. Down, Northern Ireland, 1st October.
8. Poster presentation at the 2nd International Symposium on Animal Genomics and Animal Health. Maison de la Chimie, Paris , 31st May – 2nd June.

Popular publications:

Teagasc TResearch Volume 8: Number 1. Spring 2013 ISSN 1649-8917 pages 42 – 43
Dublin talks – presentation by Professor Cliona O' Farrelly;
https://www.youtube.com/watch?v=8UoZwhS1E1M&sns=tw

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