

OECD

Co-operative Research Program Biological Resource Management for Sustainable Agricultural Systems

FELLOWSHIP SUMMARY REPORT

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Embryo-maternal communication in the bovine oviduct: crucial for successful embryo development

Theme III. Transformational Technologies and Innovation

Host Institution: School of Agriculture and Food Science,
University College Dublin (UCD), Ireland
Host Collaborator: Prof. Pat Lonergan
Fellowship Dates: 6th March to 24th July 2017

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What were the objectives of the research project? Why is the research project important?

The aim of this project was to study early embryo-maternal interaction, when the embryo is still in the oviduct, in order to enhance embryo survival, improve assisted reproductive technologies and reproductive efficiency and profitability in modern cattle industry.

We **hypothesised** that the presence of the embryo induces specific changes in the transcriptome of the oviduct at the precise site at which it is located, which plays a key role in optimizing subsequent embryo developmental competence and quality.

The Specific Objective was to study the “local” embryo effect on the transcriptional response of the epithelial cells of the oviduct *in vivo*.

Importance of the project: Fertility is a key driver of cattle dairy farm productivity through effects on calving pattern and capacity for expansion. Improving reproductive performance at farm level requires a combination of strategies to immediately increase submission and conception rates and to reduce embryo mortality and longer term strategies to boost the inherent fertility of dairy cattle. This proposal addressed the issue of embryo mortality by improving our understanding of the interaction between the maternal environment and the developing. More specific we determined the physiological functions of genes expressed in the isthmic part of the oviduct (*in vivo*) and how their expression is modified in response to the presence of an embryo. This knowledge will be used to develop *in vitro* culture systems that mimic as much as possible the cell morphology and physiology found *in vivo* with a view to improving assisted reproductive techniques. Preliminary data showed that co-culture system of bovine oviductal epithelia cells is a promising *in vitro* model to study signals of embryo-maternal communication.

1. Were the objectives of the fellowship achieved?

According to *in vivo* studies in cattle, the presence of a single 8-cell embryo does not alter the transcriptome of the cells of the oviductal isthmus, although a local effect at the precise position of the embryo cannot be ruled out. This study aimed to examine the local embryo effect on the transcriptomic response of the epithelial cells of the bovine oviduct *in vivo*.

All objectives have been achieved successfully. The fact that several transcripts were different between the segment where the embryo was collected and other locations (before and after) in the same oviduct suggests the presence of embryo site-specific signal. On the other hand, the comparison between the ipsilateral embryo site with the contralateral site revealed only one transcript different, which needs further analysis. Moreover, the similarities found in the ipsilateral oviduct between embryo and proximal site may be due to the passage of the embryo (Rodríguez-Alonso *et al.*, 2018).

Furthermore, **an additional experiment** using an *in vitro* model for studying embryo-maternal communication was performed. Thus, bovine oviduct epithelial cells (BOEC) were co-cultured directly with embryos (2- and 8-cell) or indirectly with embryo-conditioned media (CM). The relative abundance of candidate genes previously shown to be affected by the presence of embryo *in vivo* or *in vitro* was assessed by RT-qPCR. The results showed that the stage of early embryo differentially affects the transcriptome of BOEC *in vitro*, although, these changes may be related either with direct embryo contact or embryo secretions released into the media (Hamdi *et al.*, 2018)

The findings, as **2 short communications**, have been accepted for presentation at the “44th Annual Conference of the International Embryo Technology Association, 14-17 of January 2018 in Bangkok, Thailand, and they will be published in the “*Reproduction Fertility and Development*” scientific journal, January 2018 issue (see below).

I. Rodríguez-Alonso B, Hamdi M, Sánchez Gomez JM, Gutierrez-Adán A, Lonergan P, Rizos D. *In vivo* transcriptomic response of bovine oviduct epithelial cells to the early embryo. *Reproduction Fertility and Development* - January 2018 issue.

II. Hamdi M, Rodríguez-Alonso B, Almansa-Ordonez A, Gutierrez-Adán A, Lonergan P, Rizos D. *In vitro* transcriptomic response of bovine oviduct epithelial cells to direct or indirect embryo contact. *Reproduction Fertility & Development* - January 2018 issue

2. What were the major achievements of the fellowship? (up to three)

- Identification of embryo site-specific signal in the bovine oviduct - genes expression abundance in the isthmic part of the oviduct related to the presence of an embryo.
- Standardized *in vitro* experimental models seem to be suitable to study temporal and local effects.
- The direct contact-depending signalling of the embryos has an effect on the BOEC transcriptome, and so it has the embryo secretions.

3. Will there be any follow-up work?

- *Is a publication envisaged? Will this be in a journal or a publication? When will it appear?*

We have sent two short communications, which are accepted, to present at the “44th Annual Conference of the International Embryo Technology Association”, 14-17 of January 2018 in Bangkok, Thailand. Both will be published in the “Reproductive Fertility and Development” scientific journal, January 2018 issue.

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When all data are analysed a paper will be published in a high impact scientific journal in the area of reproduction (e.g.: *Biology of Reproduction* or *Reproduction*)

- *Is your fellowship likely to be the start of collaboration between your home institution and your host?*

This fellowship has helped to consolidate our existing collaboration and certainly continue in the future, involving student exchange and joint grant applications.

- *Is your research likely to result in protected intellectual property, novel products or processes?*

No

4. How might the results of your research project be important for helping develop regional, national or international agro-food, fisheries or forestry policies and, or practices, or be beneficial for society?

Please express this in terms of environmental/food security/food safety/economic/health (human and livestock and plant) benefits, etc.

Fertility is a key driver of cattle dairy farm productivity on these days through effects on calving pattern and capacity for expansion. Improving the fertility of dairy cattle will significantly increase the efficiency of dairy production. This is necessary to ensure food security with reduced impact on the environment and increased impact on sectors economy. This project addressed the issue of embryo mortality by improving our understanding of the interaction between the maternal environment and the developing embryo. We aimed to identify networks of genes related with fertility which may help improving the current strategies of early embryo loses in cattle. Our findings

increased our understanding of the basic regulatory networks underpinning embryo development in relation to the maternal environment. Thus, the economic impact contribution in dairy cattle sector national and international will be increased. Improving embryo survival through increased understanding of the factors affecting early embryo development will impact many of the parameters affecting profitability at farm level. Furthermore, this knowledge may improve the current Assisted Reproductive Technologies in mammals, such as produce higher quality embryos in vitro.

5. How was this research relevant to:

- The objects of the CRP? The CRP research theme?

This proposal is directly relevant to CRP for Theme III: Transformational technologies and innovation. This theme focus on the development and application of biotechnological methods in reproduction which offer significant opportunities for enhanced livestock breeding and maximize fertility, directly address agricultural productivity constraints, and issues related to food security, human nutrition and health. A high proportion of embryonic losses occur between Day 8 and 17 of pregnancy in cattle sometime after the embryo has entered the uterus. However, the oviduct represents the first environment to which the early embryo is exposed (until to 4) and it is considered the starting point to search for any signal between the embryo and the mother. The aim of this project was to develop new knowledge on the molecular mechanisms regulating mammalian embryo development, leading to a greater understanding of the factors regulating female fertility, particularly in dairy cattle and to further development of new in vivo and in vitro interventions.

6. Satisfaction

- Did your fellowship conform to your expectations?

Yes, in all scientific and personal aspects.

- Will the OECD Co-operative Research Programme fellowship increase directly or indirectly your career opportunities? Please specify.

Yes, directly on my Career development, Promotions, Research funds, International reputation etc.

- Did you encounter any practical problems?

None, the professionalism and administrative efficiency of OECD staff was outstanding.

- Please suggest any improvements in the Fellowship Programme.

None

7. Advertising the Co-operative Research Programme

- How did you learn about the Co-operative Research Programme?

I was a host researcher/institute in 2008; from OECD emails; and other colleagues

- What would you suggest to make it more “visible”?

None

- Are there any issues you would like to record?

None