DIFFERENTIAL CONCEPTUS-INDUCED TRANSCRIPTOMIC RESPONSE OF BOVINE ENDOMETRIUM IPSILATERAL AND CONTRALATERAL TO THE CORPUS LUTEUM

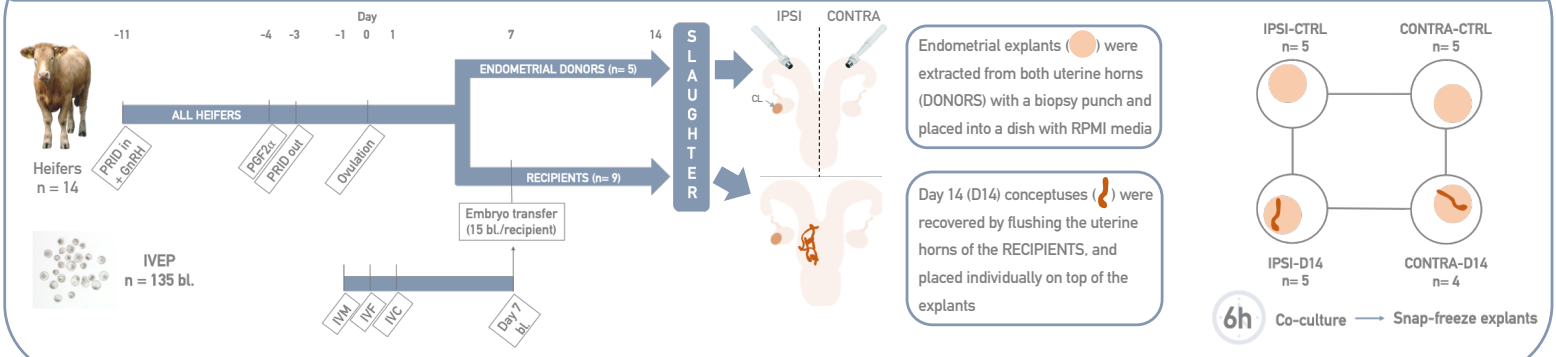
S. Bagés-Arnal[1], J.M. Sánchez[1], B. Fernandez-Fuertes[2], M. McDonald[1], S.K. Behura[3], T.E. Spencer[3], T. Fair[1], P. Lonergan[1]

[1] School of Agriculture and Food Science, University College Dublin, Belfield, Dublin 4, Ireland
[2] Biotechnology of Animal and Human Reproduction (TechnoSperm), Department of Biology, Institute of Food and Agricultural Technology, University of Girona, Spain
[3] Division of Animal Sciences, University of Missouri, Columbia, Missouri, 65211, USA

INTRODUCTION

In cattle, embryo transfer into the uterine horn contralateral (CONTRA) to the corpus luteum (CL) results in a higher incidence of pregnancy loss compared to transfer into the ipsilateral (IPSI) horn (1,2). Those pregnancy losses have been associated with a different progesterone tissue concentration (3) and endometrial transcriptome (4) between the uterine horns, which suggest a different environment. The objective of this study was to compare the local response of the endometrium IPSI and CONTRA to the CL to a day 14 conceptus. Our hypothesis was that the endometrium from the IPSI and CONTRA uterine horns would respond differently to a conceptus, which might explain the differences in embryo loss.

MATERIAL AND METHODS



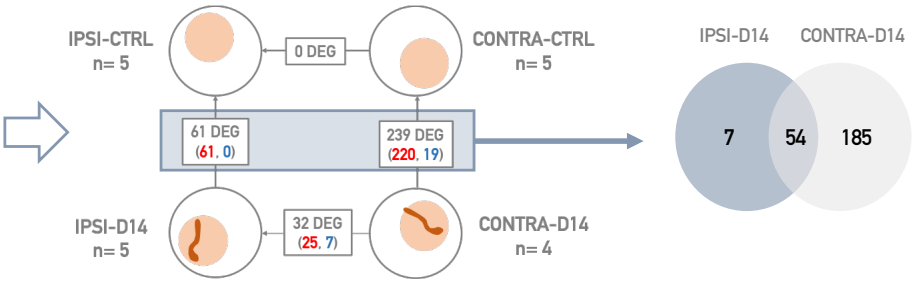
PRID: progesterone-releasing intravaginal device; PGF2α GnRH: gonadotropin-releasing hormone; prostaglandin F2α; IVEP: in vitro embryo production; IVM: in vitro maturation; IVF: in vitro fertilization; IVC: in vitro culture; bl.: blastocysts; CTRL: control

RESULTS + DISCUSSION

The RNA from the endometrial explants was extracted and processed for RNA sequencing. This figure shows the summary of the differentially expressed genes (DEG) found between groups.

The direction of the arrows indicates how the comparisons were made, i.e. there are 61 genes upregulated in IPSI-D14 relative to IPSI-CTRL. Increased and decreased transcripts are indicated in red and blue, respectively.

GO: Gene ontology; BP: biological processes



1 IPSI-D14 vs. IPSI-CTRL:

61 DEG → 7 unique from the IPSI: *ADIRF, AMY2B, GADD45G, GFRA4* +

- *AMT* → DNA synthesis → Support conceptus growth?
- *IL6* → Immune response → Th17/Treg balance
- *SLC26A10* → ULF ph balance → Favourable environment?

GO analysis of the 61 DEG revealed 39 enriched BP → 2 unique from the IPSI:

- Response to IFN-alpha
- Cytoplasmic pattern recognition receptor (PRRs) signalling

2 CONTRA-D14 vs. CONTRA-CTRL:

239 DEG → 185 unique from the CONTRA uterine horn:

166 upregulated, i.e.:

- *SLFN11*
- *CXCL10*, *CXCL11* → Immune cell recruitment
- *TIMD4* → Th1/Th2 balance
- *IFI47*

19 downregulated i.e.:

- *NLRP12*
- *CDH9*
- *C15H11orf34* → Potential predictor of successful pregnancy establishment
- *AQP3*, *CFTR* → Water transport

GO of the 239 DEG revealed 87 enriched BP → 50 unique from the CONTRA:

- Many related to response to and production of type I IFN (alpha and beta) and type II IFN, IFNG

3 CONTRA-D14 vs. IPSI-D14

32 DEG → 25 upregulated in CONTRA-D14 relative to IPSI-D14:

- 23 of the 25 are interferon stimulated genes (ISG)
- Different response to interferon (IFN)?
  - Type I IFN can lead to immune cell recruitment and activation → Exacerbated response in the CONTRA uterine horn? → Increased risk of tissue rejection and pregnancy loss

GO analysis of the 32 DEG revealed 10 enriched BP:

- 6 associated to response to stimulus → Different capacity to respond to extracellular signals produced by the conceptus?
- 4 related to immune response → Deregulation immune response → Pregnancy losses?

CONCLUSIONS

Despite the lack of differences between the IPSI and CONTRA endometrial transcriptome, the response to an elongating conceptus was remarkably different. The presence of a conceptus on day 14 on the CONTRA uterine horn may provoke an exaggerated response, particularly immune-related, that may cause problems later during the implantation period and lead to a pregnancy loss. Furthermore, differential expression of genes related to homeostasis suggest that the environment in the CONTRA uterine horn may not be favourable for embryo development.

References: (1) Christie et al., (1979). J. Reprod. Fertil. 56, 701–706. (2) Del Campo et al., (1983). Reprod. Nutr. Dev. 23, 303–308. (3) Takahashi et al., (2016). J. Vet. Med. Sci. https://doi.org/10.1292/jvms.15-0366. (4) Sánchez et al., (2018). Biol. Reprod. https://doi.org/10.1093/biolre/ioy185

Correspondence: sandra.bagesarnal@ucdconnect.ie

52nd Annual Meeting of the Society for the Study of Reproduction

This work was supported by European Union, Horizon 2020 Marie Sklodowska-Curie Action, REPBIOTECH (675526)