Trophectoderm-specific RNA interference of chorionic somatomammotropin alters glucose metabolism in sheep fetal liver

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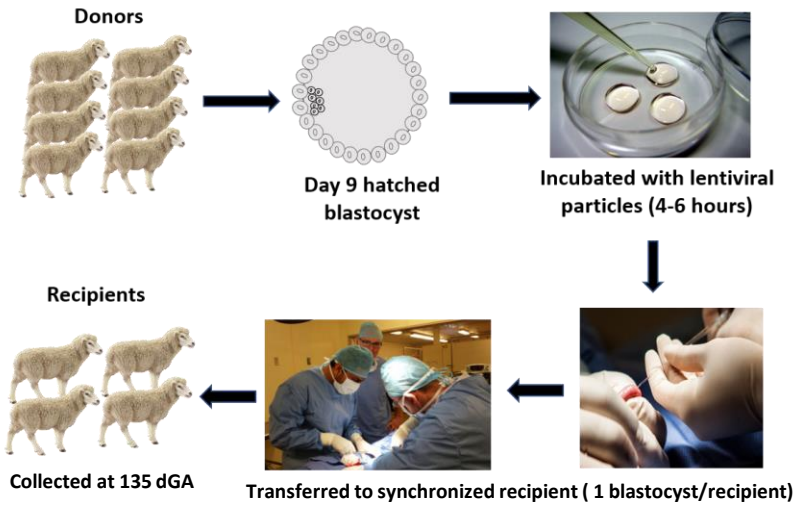
INTRODUCTION

- Chorionic somatomammotropin (CSH) is produced by placental binucleate cells in sheep and secreted in both fetal and maternal circulation.
- CSH deficiency is linked to IUGR in humans and sheep.
- In sheep, trophectoderm-specific CSH RNA interference (RNAi) generates two phenotypes at 135 dGA:
  - Pregnancies with IUGR (RNAi-IUGR)
  - Pregnancies with normal fetal weight (RNAi-NW)
- CSH is also thought to modulate maternal and fetal metabolism.
- We hypothesize that CSH deficiency alters glucose metabolism in sheep fetal liver, with or without IUGR.
- n=8/treatment, *p<0.05.

MATERIALS AND METHODS



RESULTS

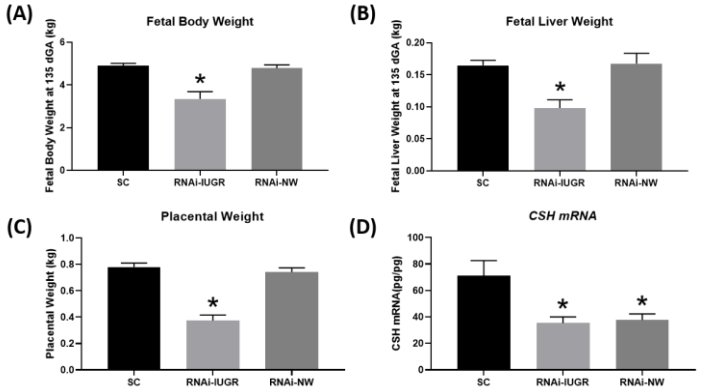


Figure 1. (A-C) Fetal body weight, liver weight and placental weight at 135 dGA in SC, RNAi-IUGR and RNAi-NW pregnancies. (n=8/treatment). (D) *CSH* mRNA concentration in placental cotyledons from SC, RNAi-IUGR and RNAi-NW pregnancies.

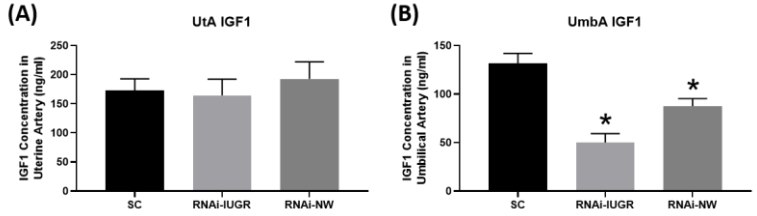


Figure 2. IGF-1 concentration in uterine artery (UtA) and umbilical artery (UmbA) blood.

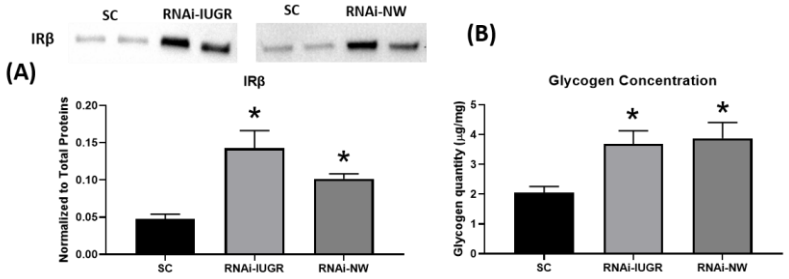


Figure 3. (A) Representative immunoblots and densitometric analysis for IRβ protein in fetal liver from SC, RNAi-IUGR and RNAi-NW pregnancies. (B) Glycogen concentration in fetal liver form from SC, RNAi-IUGR and RNAi-NW pregnancies.

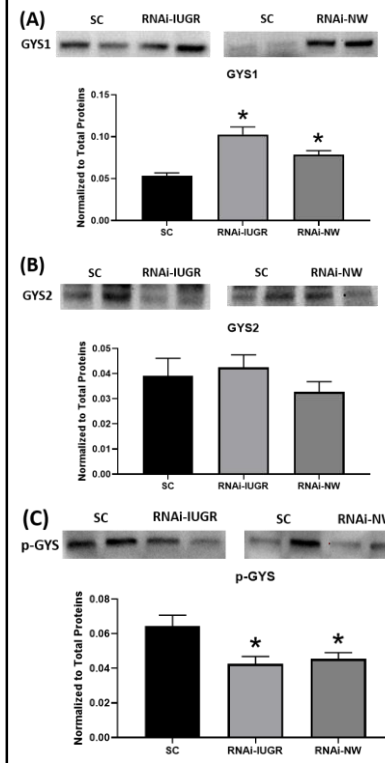


Figure 4. Representative immunoblots for GYS1 and GYS2 in fetal liver from SC, RNAi-IUGR and RNAi-NW pregnancies.

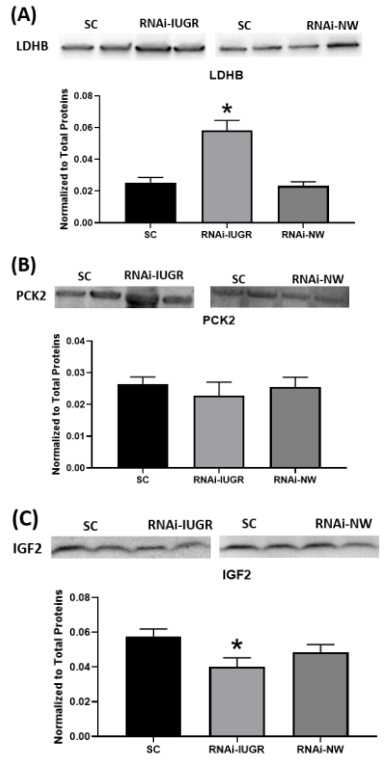


Figure 5. Representative immunoblots for LDHB, PCK2 and IGF2 in fetal liver from SC, RNAi-IUGR and RNAi-NW pregnancies.

CONCLUSIONS

- Fetal liver glucose metabolism is impacted by CSH RNAi, independent of IUGR.
- Altered glucose metabolism is likely tied to enhanced insulin sensitivity in both CSH RNAi phenotypes.

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