IMPACT OF FETAL EXPOSURE TO TESTOSTERONE ON FETAL INSULIN SENSITIVITY TISSUES: A MORPHOLOGICAL AND MOLECULAR APPROACH GP 145

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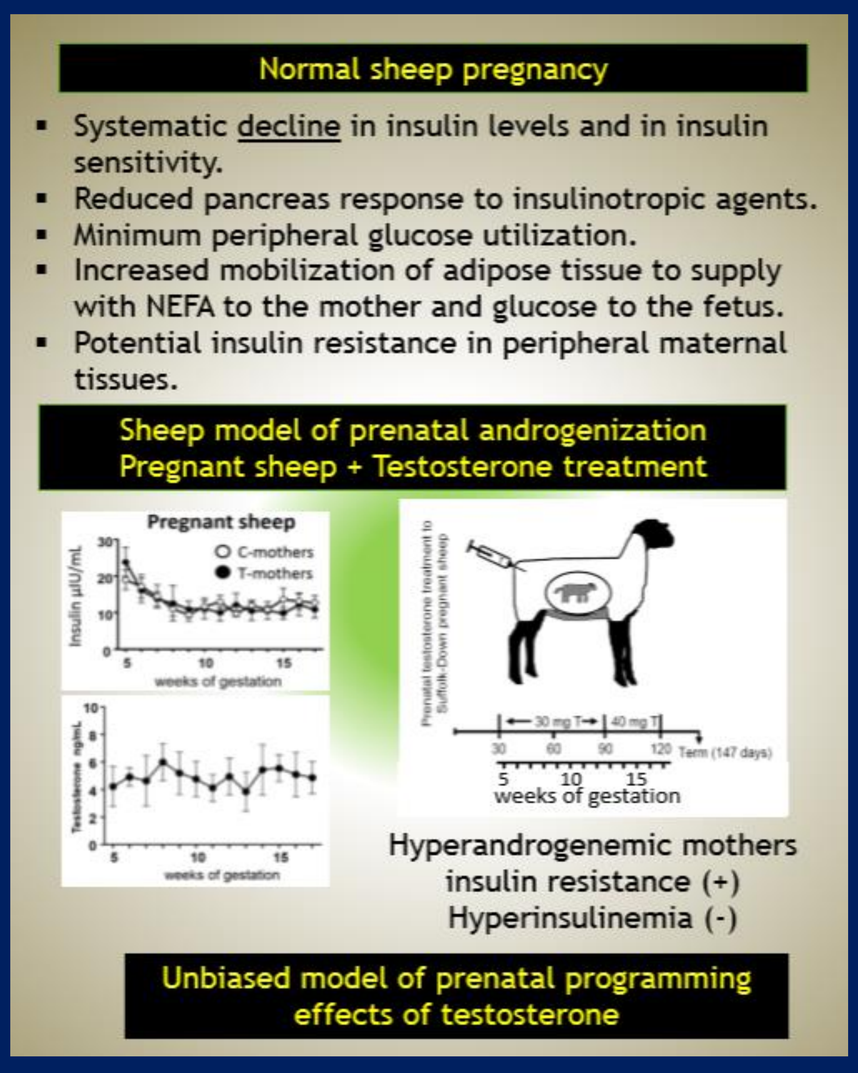
INTRODUCTION

The hyperandrogenemic environment during fetal life has been postulated to be a reprogramming factor to develop PCOS in postnatal life. Women with PCOS show not only reproductive impairments but also metabolic dysfunction that could be initiated during fetal life due to the hyperandrogenemic prenatal environment, or could be triggered postnataly. Hyperandrogenemia, hyperinsulinemia and insulin resistance are features of the PCOS, placing affected women at high risk in case of pregnancy, of perpetuating this syndrome to their daughters.

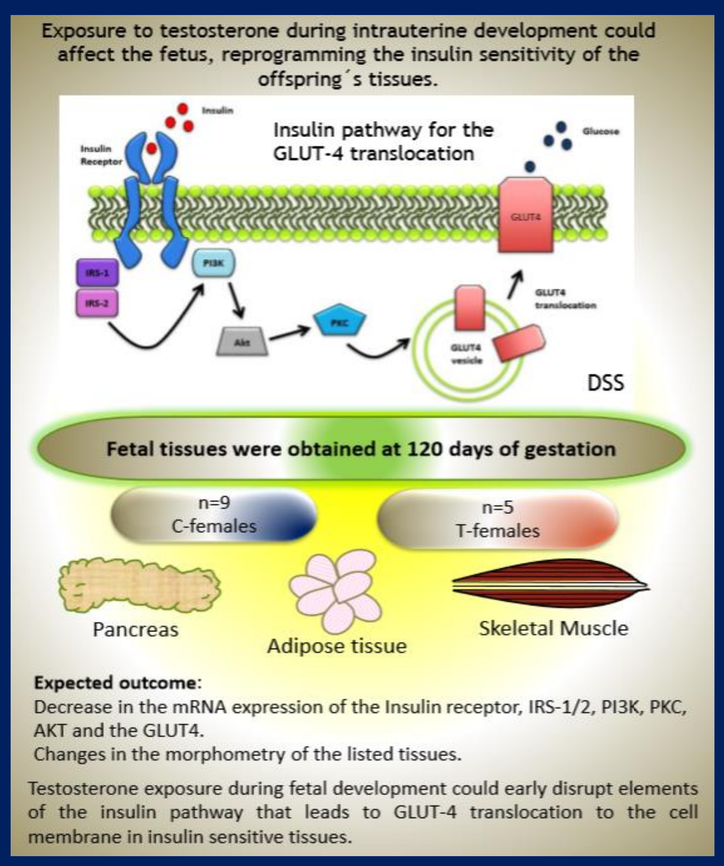
One of the focus in the etiology of the metabolic traits of PCOS are the changes observed in insulin sensitives tissues. There is agreement in a possible defective signaling at the insulin receptor level, leading to the insulin resistance.

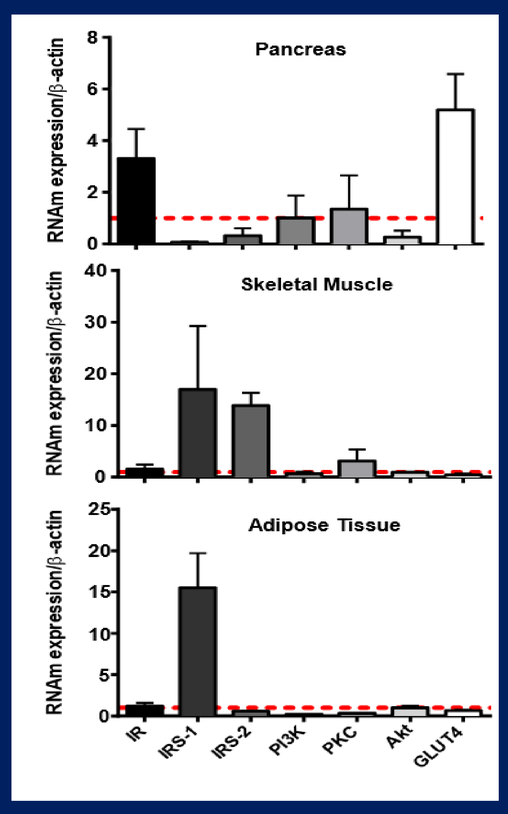
Is the Insulin resistance programmed prenatally in these women? Does the abnormally high levels of testosterone during fetal development have a role in modifying prenatally the insulin pathway in insulin sensitive tissues? This questions could be answered in animal models of PCOS.

Our sheep model of prenatal testosterone exposure has been extensively used to study the programming of PCOS. It has the advantage that occurs without an impact on maternal insulin, glucose or lipids that could add another source of hormonal disarrangement to the fetus.

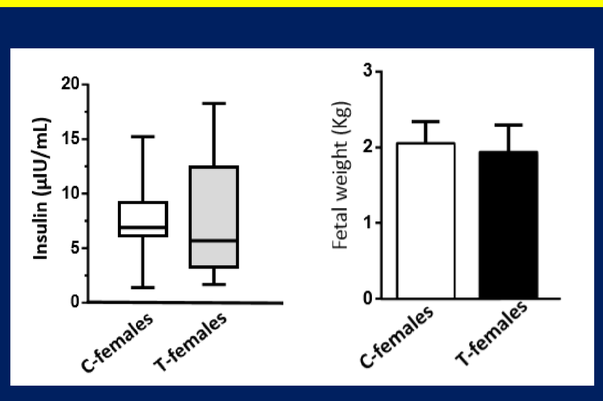


HYPOTHESIS





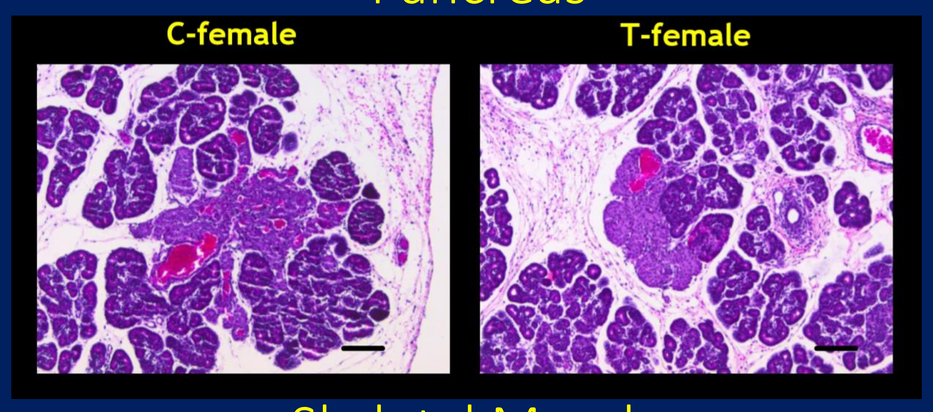
Transcriptional activation of the insulin signaling pathway in T-exposed fetuses compared to control fetuses. The red line indicates the level of expression of the signaling factors in the control female fetuses. Transcriptional activation is higher in T-females in some factors in a tissue-specific manner.



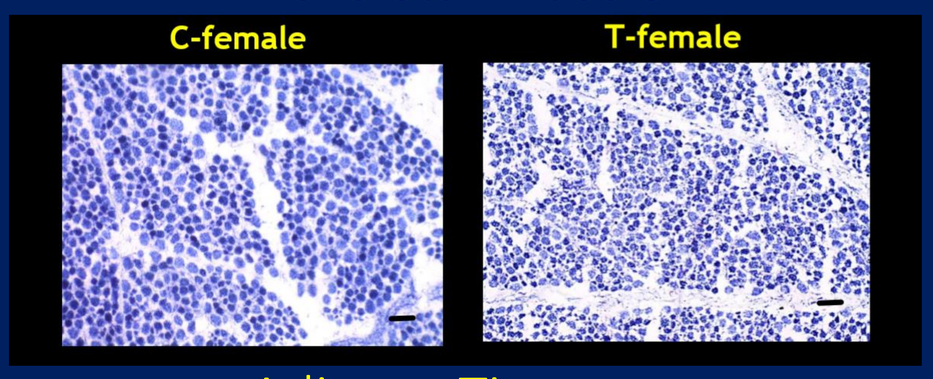
Fetal insulin plasma levels were similar between groups. No difference was observed in fetal weight at 120 days gestation between groups.

RESULTS

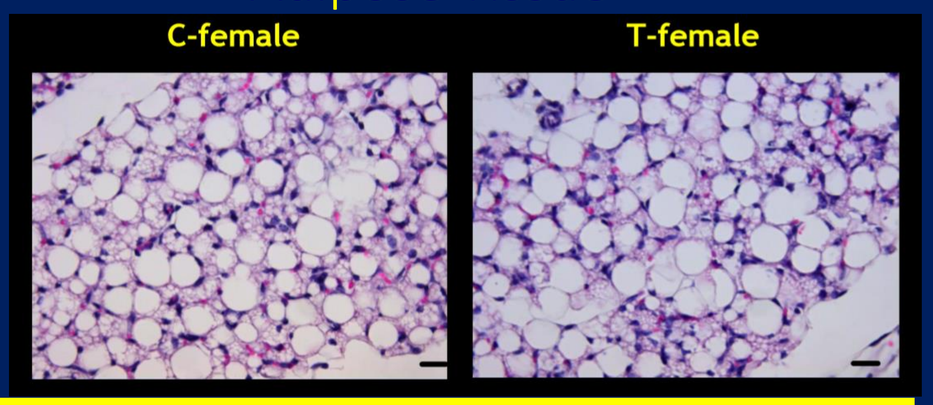
Pancreas



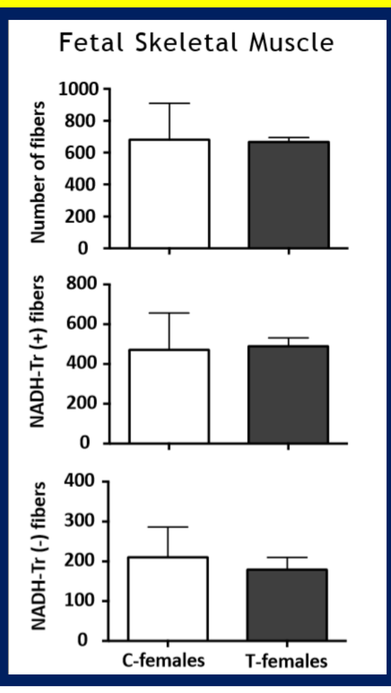
Skeletal Muscle

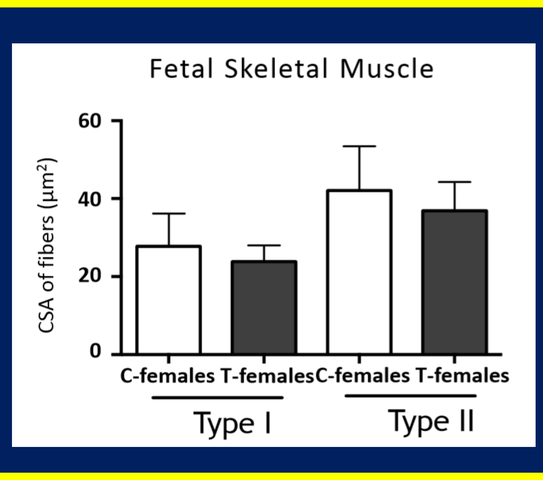


Adipose Tissue

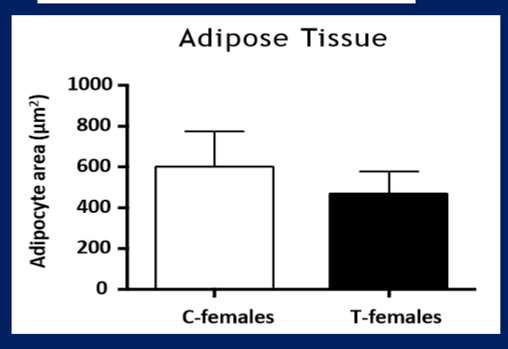


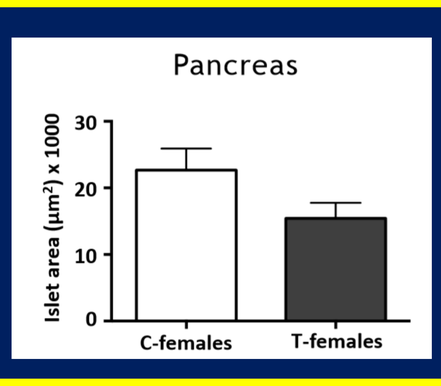
Representative photomicrographies showing no significant differences in the morphological characteristics of the insulin sensitive fetal tissue. Bar= 100 µm in pancreas and skeletal muscle and 25 µm adipose tissue.





The composition of the skeletal muscle was similar between both groups of fetuses regarding the total amount of fibers and its phenotype.





The area of the adipocytes and of the pancreatic islets were similar between groups.

CONCLUSIONS

These results provide evidence that testosterone exposure during fetal sheep development induces differential transcriptional activation of the insulin signaling, without significant effects on morphological organogenesis.

Funding: Research grant FONDECYT # 1140433