Vascular Health (GRIVAS-Health), Chile; [5] *Vascular Physiology Laboratory, Department of Sciences, Universidad del Bío-Bío, Chillán, Chile;* [6] *Department of Physiology, Faculty of Pharmacy, Universidad de Sevilla, Seville, Spain;* [7] *University of Queensland Centre for Clinical Research (UQCCR), Faculty of Medicine and Biomedical Sciences, University of Queensland, Herston, Queensland, Australia*

Gestational diabetes mellitus (GDM) characterizes by abnormal maternal D-glucose metabolism, and associates with reduced maternal circulating free tyroxine (fT4) and increased nitric oxide (NO) generation in the placenta vasculature. Deiodinase 3 (DIO3) is a thyroid hormones inactivator enzyme that catalyses deiodination of thyroxine (T4) into reverse triiodothyronine (rT3) and triiodothyronine (T3) into 3,3'-diiodothyronine (T2). DIO3 is increased in syncytiotrophoblast and endothelial cells from GDM pregnancies, but the role of NO in this phenomenon is unknown.

Objective: To evaluate whether D-glucose and NO increase *Dio3* mRNA level in human umbilical vein endothelial cells (HUVECs).
Methods: HUVECs from normal pregnancies were exposed (24 hours) to D-glucose (5-20 mM) in the absence or presence of N^G-nitro-L-arginine methyl ester (L-NAME, 100 μM). Total mRNA was extracted with Trizol reagent and used for real time PCR to estimate the relative abundance of *Dio3* and *28S* mRNA using the $2^{-\Delta\Delta Ct}$ method.
Results: *Dio3* mRNA level was higher (1.8 ± 0.2 fold) in HUVECs exposed to D-glucose from 15 to 20 mM (effective half-maximal concentration (EC_{50}) 12 ± 1 mM). L-NAME blocked D-glucose increase in *Dio3* mRNA level.
Conclusions: D-Glucose increases *Dio3* mRNA level via a mechanism that involves NO in HUVECs. GDM-increased NO generation could result in modulation of DIO3 expression in HUVECs.
Funding: Dirección de Investigación, Universidad San Sebastián (DIUSS), Chile. Apoyo a la realización de Tesis, Comité Productivo Regional (2016-67535), Chile. FONDECYT 1150377/1150344 (Chile).

http://dx.doi.org/10.1016/j.placenta.2017.01.077

THE ROLE OF ENDOGENOUS ANNEXIN A1 (ANXA1) IN PREGNANCY

J.B. Moreli [1], C.B. Hebeda [2], I.D. Machado [2], I. Reif-Silva [2], S.M. Oliani [1,5], M. Perretti [3], E. Bevilacqua [4], S.H.P. Farsky [2].

[1] *Post-Graduation in Structural and Functional Biology, Federal University of São Paulo, UNIFESP, São Paulo, Brazil;* [2] *Department of Clinical and Toxicological Analyses, School of Pharmaceutical Sciences, University of Sao Paulo, USP, São Paulo, Brazil;* [3] *The William Harvey Research Institute, Barts and The London School of Medicine, Queen Mary University of London, London, United Kingdom;* [4] *Department of Cell and Developmental Biology, Institute of Biomedical Sciences, University of São Paulo, USP, São Paulo, Brazil;* [5] *Department of Biology, Instituto de Biociências, Letras e Ciências Exatas, São Paulo State University, UNESP, São José do Rio Preto, Brazil*

Annexin A1 (AnxA1) is a glucocorticoid-induced anti-inflammatory protein secreted by phagocytes in the innate response. AnxA1 also controls the secretion of steroids hormones and is found in the testis, ovaries, placenta, and seminal fluid.

Objective: This work was performed to investigate the role of AnxA1 on pregnancy.
Methods: In this study, male and female BALB/c mice wild type (WT, n = 10) and AnxA1 knockout (KO, n = 10) were used. In females during or at term of pregnancy parameters related to gestation success were evaluated. In male, spermatozoids characteristics and Y and X chromosome proportion were evaluated.
Results: The coupled AnxA1 KO mice delivered higher number (5.0 in WT and 8.0 in KO) of puppies from a little, with upper percentage of female (female/male = 55/45 in WT and 28.3/71.7 in KO). This profile seems to be not dependent on male characteristics, as sperm of KO mice did not present functional alterations and equal proportions of Y and X chromosomes than WT mice. Furthermore, mismatched male WT mice with female KO had higher female puppies from a litter, which was not observed on male KO mice mated with female WT. Indeed, female of KO mice presented, arrested of oestrous cycle at proestrous phase, increased sites of implantation, reduced pre and post implantation losses, exacerbated inflammatory reaction in the uterine fluid during implantation phase, and enhanced plasma progesterone in the beginning of pregnancy.
Conclusions: Together, the results highlight, for the first time, that AnxA1 pathway may be a target to be controlled during the early phase of the pregnancy.
Funding: CNPq (308144/2014-7).

http://dx.doi.org/10.1016/j.placenta.2017.01.078

DIABETES AND FETAL PROGRAMMING: EFFECTS ON NEPHROGENESIS AND BASEMENT MEMBRANES OF RENAL CORPUSCLES OF MOUSE FETUS

M.R.P.T. Morais [1], F.A.C. Barrence [1], V.M. Mazucato [2], C.P. Dias [1], C.S.B. Silva [1], R.R. Favaro [1], S. San-Martin [3], T.M.T. Zorn [1].

[1] *Department of Cell and Developmental Biology, Institute of Biomedical Sciences, University of São Paulo, São Paulo, Brazil;* [2] *Department of Morphology, Faculty of Medicine, University of São Paulo, Ribeirão Preto, Brazil;* [3] *Centre for Research in Reproductive Biology, School of Medicine, Universidad de Valparaiso, Valparaiso, Chile*

Maternal hyperglycaemia can disturb embryonic differentiation and organogenesis, predisposing the offspring to urinary and cardiovascular dysfunctions in adulthood. This phenomenon is known as fetal programming.

Objective: Using a mouse model of pregnancy complicated by alloxan-induced type 1 diabetes, we are investigating the effects of maternal diabetes on nephrogenesis, particularly on the structure and molecular composition of renal basement membranes.
Methods: For this, the number and volume of renal corpuscles of 19 days-foetuses from diabetic (FDM) and nondiabetic (FNDM) females were stereologically estimated and compared. Renal basement membranes were evaluated by PAS staining and immunohistochemistry for collagen type IV, laminin and perlecan.
Results: We found a number of differentiated and undifferentiated renal corpuscles in FDM significantly lower ($P<0.001$, n = 8) than that in FNDM. Moreover, FDM had a corpuscular hypertrophy. The levels of mRNA of collagen type IV (*Col4a1* and *Col4a3*), laminin (*Lama5*) and perlecan did not change in FDM kidneys, except *Lama1*, which transcript level was elevated (1.3 ± 0.04 fold). However, Western blot result indicated decreased LAMA1 level (34 ± 7%) in FDM kidneys. Furthermore, we found both glomerular and tubular basement membranes thickened, and an increased deposition of collagen type IV, laminin and perlecan.
Conclusions: These results indicate that maternal type 1 diabetes promotes renal dysmorphogenesis by (*i*) reducing the number of differentiating renal corpuscles leading to a compensatory corpuscular hypertrophy; (*ii*) thickening of glomerular and tubular basement membranes due to an increased local deposition of extracellular matrix glycoproteins and proteoglycans.
Funding: FAPESP, process number 2015/03525-2.

http://dx.doi.org/10.1016/j.placenta.2017.01.079