

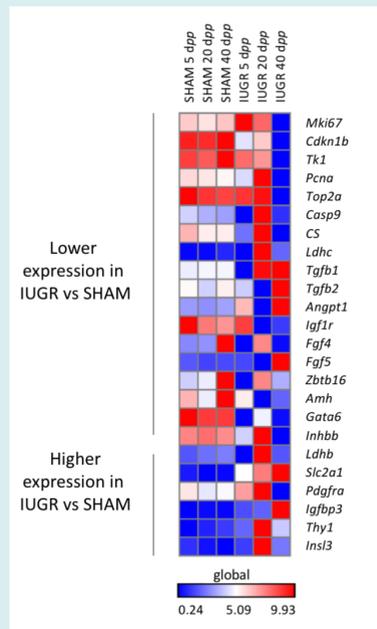
# Effect of IntraUterine Growth Restriction on ovarian follicle pool in rats

V Pampanini<sup>1</sup>, D Germani<sup>2</sup>, A Puglianiello<sup>2</sup>, K Jahnukainen<sup>1</sup>, L Sahlin<sup>1</sup>, S Cianfarani<sup>1,3</sup> and O Söder<sup>1</sup>.

<sup>1</sup> Department of Women's and Children's Health, Karolinska Institutet and University Hospital, Stockholm, Sweden.

<sup>2</sup> Department of Systems Medicine, Tor Vergata University, Rome, Italy.

<sup>3</sup> Dipartimento Pediatrico Universitario Ospedaliero "Bambino Gesù" Children's Hospital – Tor Vergata University, Rome, Italy.



## Conclusions

This study investigated the effects of placental insufficiency on the postnatal female gonad. The ovarian follicle pool was affected in the IUGR rats up to the pre-pubertal age, but this effect did not persist in older ages.

Different genes involved in fundamental cellular processes were affected by fetal hypoxia at all ages, suggesting that long term alterations may occur as a consequence of IUGR.

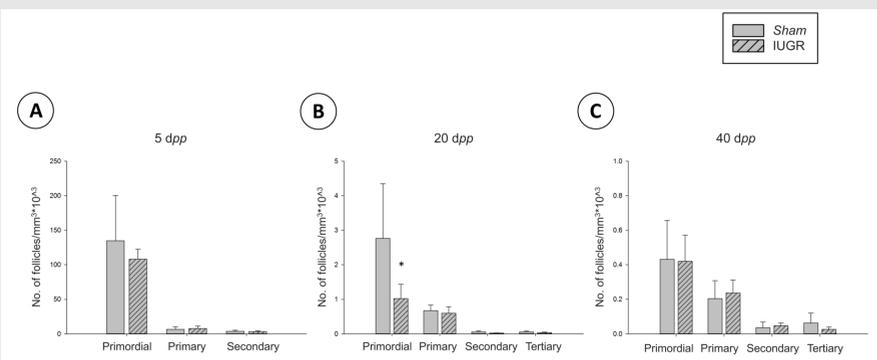
Further analyses are needed to elucidate later effects of IUGR on ovarian function and fertility lifespan.

## Introduction

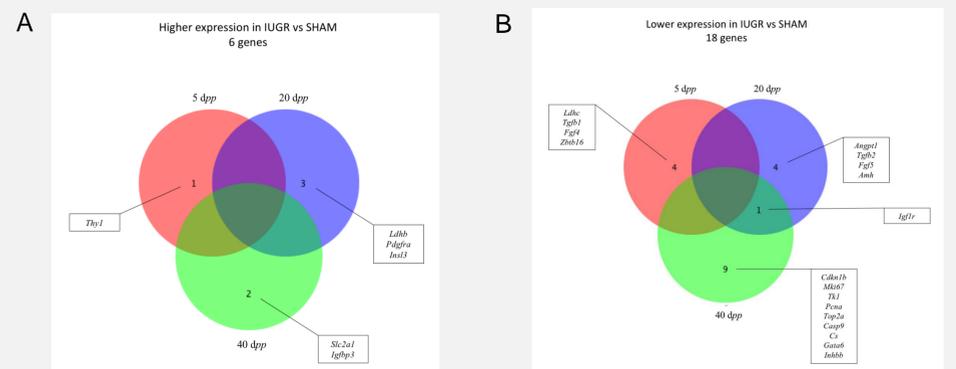
A low oxygen and/or nutrient supply to the fetus, resulting in intrauterine growth restriction (IUGR), can affect gonadal development of the offspring and have a potential impact on fertility. Epidemiological studies on subjects born small for gestational age, as a surrogate measure of IUGR, have reported contradictory results. Data derived from animal models of placental insufficiency are limited.

## Aim

To investigate the effects of placental insufficiency induced by uterine artery ligation (UAL) on the postnatal rat ovary.



**Figure 1.** Densities of follicles in different developmental stages (primordial, primary, secondary and tertiary) in intrauterine growth restricted (IUGR) and sham rats at A) 5, B) 20 and C) 40 days post-partum (dpp). Student's T-test, \* P < 0.05.



**Figure 2 –** TaqMan Low-Density Array analysis of gene expression in IUGR and sham animals at 5, 20 and 40 dpp. (A) Specific differences in gene expression between animal groups, with higher expression in IUGR vs sham animals, and (B) lower expression in IUGR vs sham animals.

## Results

A lower number of total and primordial follicles was detected in 5 and 20 dpp old IUGR animals compared to controls. The number of follicles was no longer different at 40 dpp, suggesting a compensatory reduction in the rate of the physiological follicular attrition occurring during pre-pubertal period (Fig 1). Furthermore, IUGR modified the expression of 24 genes involved in different cellular functions, e.g. proliferation, metabolism and angiogenesis (Fig 2). AMH serum levels were not significantly different in the experimental animals compared to controls, although reduced levels were noted at all ages.

## Methods

Sprague-Dawley rats underwent UAL at day 19 of gestation. Offspring were sacrificed at 5, 20 and 40 days post-partum (dpp), representative of infancy, childhood and peri-pubertal period. One gonad per animal was formalin-fixed and used for histological evaluation. Follicles were counted and classified in three sections per ovary after H&E staining. The second gonad was processed for RNA extraction. Gene expression of 90 genes was analyzed by TaqMan® Low Density Array. Serum AMH was measured by ELISA.

The authors have no conflict of interest to disclose



Karolinska Institutet and University Hospital

Valentina Pampanini, M.D., PhD student

Dept. of Women's and Children's Health, Pediatric Endocrinology Unit, NORDFERTIL

Research group, SE-17164 Stockholm, Sweden

E-mail: valentina.pampanini@ki.se



Karolinska Institutet