primordial follicles of both control and ischemic ovaries, with expansion of staining to the medullar and stromal cells in ischemia. BrDU was detected in growing follicles in all ovaries, with little change due to ischemia and reoxygenation.

CONCLUSIONS: The oxygen concentration of the juvenile rhesus ovary is approximately 5% O2, equivalent to many other tissues. However, the robust pimonidazole and CA-IX staining of the oocyte and granulosa cells suggest that the local environment of the primordial follicle experiences physiological hypoxia (<1.5% O2). Similar levels of BrDU uptake in CTRL and I/R ovaries suggest short-term follicle growth (in secondary and antral follicles) was not affected by O2 fluctuation. The maintenance of physiological hypoxia could be an important consideration for maintaining follicle quiescence and oocyte quality during fertility preservation procedures.

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O-178 2:35 PM Monday, October 19, 2020
SURVIVIN-SODIUM IOIDE SYMPORTER AS A NON-INVASIVE DIAGNOSTIC MARKER TO DIFFERENTIATE BETWEEN UTERINE LEIOMYSARCOMA VERSUS LEIOMYOMA
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OBJECTIVE: The aim of this study is to evaluate the use of Survivin-Sodium iodide symporter (Ad-SUR-NIS) as a reporter gene to differentiate between uterine leiomyoma (LM) and uterine leiomyosarcoma (LMS) by positron emission tomography (PET) imaging.

DESIGN: Laboratory research studies using LMS and LM animal models. MATERIALS AND METHODS: 28 Adult female mM/mu Nude mice, 6-8 weeks of age, weighing between 20-25 g, were used. A total of 2x10^7 cells of LMS or LM cells were inoculated subcutaneously into the right flank. One week after inoculation with visible and palpable tumors, the mice were transacted via retro-orbital with Ad-SUR-NIS (1x10^6 PFU/mouse) or PBS (control). 24 hours after Ad-SUR-NIS injection, 14 animals were submitted to PET/CT scanning using NaBF418 as a radiotracer to assess the expression of NIS reporter gene. For safety evaluation, 14 animals were euthanized after 24 hours of the Ad-SUR-NIS transfection. Tumors and organs (brain, liver, kidney, spleen, lung, ovary, uterus and heart) were collected and histopathologic analysis was performed by a pathologist.

RESULTS: 5 minutes after the NaBF418 administration, the PET/CT scan images showed an increased radiotracer uptake attributable to Ad-SUR-NIS on the LMS tumors when compared to LM. Presumably, due to the overexpression of NIS in LMS in contrast to LM. The nature of the tumor masses (LMS vs LM) were confirmed histologically. 24 hours after the Ad-SUR-NIS or PBS transfection LM and LMS tumors along with the organs, were collected. Hematoxylin and Eosin-stained sections were examined histologically and compared to the PBS group. No pathological changes were found in any of these tissues after Ad-SUR-NIS transfection.

CONCLUSIONS: Ad-SUR-NIS PET reporter is a promising imaging biomarker which differentiates uterine LMS from LM using NaBF418 as a radiotracer. This new diagnostic method can provide a much-needed tool in differentiating between uterine leiomyoma (LM) and uterine leiomyosarcoma (LMS) along with organs, were euthanized after 24 hours of Ad-SUR-NIS transfection. No pathological changes were found in any of these tissues after Ad-SUR-NIS transfection.

SUPPORT: University of Illinois at Chicago

O-197 2:50 PM Monday, October 19, 2020
OVARIAN AGING AND REPRODUCTIVE SENESCENCE IN MOUSE MODEL OF MITOCHONDRIAL DYSFUNCTION.
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OBJECTIVE: To evaluate the mechanisms of female reproductive aging and senescence induced by mitochondrial dysfunction in mice.

DESIGN: Prospective cohort design study, 13 female mice with mitochondrial dysfunction (mtDNA-deleter) and 13 wild-type (WT) female mice were studied at three time points in their reproductive life cycle: 4-6, 8-10, and 11-12 months of age.

RESULTS: Twenty-six female mice were studied from 4 to 12 months of age. The estrous cycles in 4-6-month mtDNA-deleter mice were prolonged, 9.4 days (n = 7), versus 5.3 days in WT (n = 9), p-value of 0.021. By 11-12 months, both groups had prolonged estrous cycles consistent with physiology aging. AMH levels in 4-6-month mtDNA-deleter mice were decreased, 84 (n = 4), versus 114 ng/mL in WT mice (n = 5), p-value of 0.013. AMH was reduced in older mice at 8-10 and 11-12 months, but there were no significant differences between groups. Looking at the data collectively for all three time points, there were fewer tertiary (early antral, antral, or pre-ovulatory) follicles in mtDNA-deleter mice than in WT, 3.5 versus 4.9 per cut section, respectively (p-value of 0.039). There were fewer corpora lutea in mtDNA-deleter mice than in WT, 0.90 versus 1.7 per cut section, respectively (p-value of 0.027). Collectively, average uterine weight in mtDNA-deleter mice was lower, 62.2, versus 92.3 mg in WT mice, p-value of 0.0028. Vaginal epithelium in 4-6-month mtDNA-deleter mice was thinner, 98 μm (n = 4), versus 200 μm in WT mice (n = 4), p-value of 0.015. In breeding experiments, mtDNA-deleter mice at age 3 and 5 months did not produce litters. Estrogen receptor levels were reduced in mtDNA-deleter mouse ovary relative to WT, evident from both immunofluorescence and semi-quantitative PCR analysis.

CONCLUSIONS: Mitochondrial dysfunction in mice is associated with premature reproductive aging and senescence, as evidenced by early onset of prolonged estrous cycles, diminished ovarian reserve, uterine and vaginal atrophy, and infertility. Mitochondrial dysfunction is also associated with premature estrogen receptor down-regulation in the mouse ovary.


SUPPORT: UAB Department of Obstetrics and Gynecology

O-180 3:05 PM Monday, October 19, 2020
INVESTIGATION OF APOPTOSIS AND FOLLICLE ACTIVATION BY PROTEOMICS IN AN EXPERIMENTAL MODEL OF CYCLOPHOSPHAMIDE-INDUCED FOLLICLE DEPLETION IN OVARIAN TISSUES.
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OBJECTIVE: The mechanisms of primordial follicle depletion (PrFD) and infertility following cyclophosphamide (CPA) treatment remain unclear. This study investigated mechanisms of CPA-induced PrFD focusing on apoptosis and follicle over-activation and associated protein profile changes.

DESIGN: Experimental controlled study using a mouse ovarian culture model.

MATERIALS AND METHODS: Ovaries (n=24) from B6CBA/F1 postnatal day-4 mice were cultured according to O’Brien et al [1]. The ovaries were randomly assigned to CPA-treated group (5 μM 4-hydroperoxyCPA) or control. Ovaries were analyzed 24, 48 or 72 hr after treatment. Follicle density on histology (counted number of follicles/area) was estimated for primordial follicle density (PFD) and growing follicle density (GFD). Apoptosis was assessed by a qualitative analysis of TUNEL assay at 24 hr. Mass spectrometry-based proteomics analysis was performed at 24 h (4 ovaries/group), followed by gene ontology analysis on PANTHER for protein class, molecular function, biological process and pathways.

RESULTS: In CPA-treated ovaries, PFD showed a marked progressive reduction and a lower PFD was found at all timepoints compared to controls. At 72 hr, PFD decreased by 82.4% from 401.4±266.7 follicles/mm2 at 24 h in the CPA-treated group, whereas it decreased by 25.2% from 673.2±231.9 follicles/mm2 at 24 h in control. On the contrary, GFD was higher in CPA-treated ovaries than in controls at all timepoints. At 24 h, 109±63.8 follicles/mm2 were counted in CPA-treated group vs 61.8±1.6 follicles/mm2 in