Oncofertility Saturday Academy Poster Abstract Form

NAME: Anita Washburn

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Abstract Categories

Check one only:
X Reproductive Biology ☐ **In Vitro Fertilization** ☐ **Cancer Biology** ☐**Oncofertility**

ABSTRACT TITLE: Use of G-CSF in Improving Pregnancy Rates in Women with Unexplained Infertility

AUTHOR: Anita Washburn

LEARNER OBJECTIVE: Please state the educational objective in a measurable, testable question. Then state what the participant's poster will be able to demonstrate to the viewer(s)/audience.

Question: How can G-CSF improve fertility rates in women with unexplained primary RM and repeated IVF failure?

The participant will be able to demonstrate the effect of G-CSF on embryo implantation, ovarian function and endometrial lining and its influence on pregnancy rates.

CONTENT (TOPICS): this topic will include a new potential for G-CSF to improve pregnancy and birth rates in women with unexplained primary RM and repeated IVF failure, along with explaining its potential success with IVF and endometrium related pathologies.

ABSTRACT:

G-CSF is a colony stimulating factor that targets leukocytes and produces stem cells required for establishing and maintaining a pregnancy.[5] Through research development, it is becoming a promising new tool for women with unexplained primary recurrent miscarriages (RM) and biomechanical pregnancies due to implantation failure.[7] Unexplained infertility continues to vex reproductive researchers and clinicians. However, there is hope that G-CSF will increase pregnancy rates through improving the quality and thickness of the endometrium and stopping the immune response that disables an embryo's ability to implant.[4] A trial was conducted with 68 women with unexplained primary RM where researchers randomly administered G-CSF (1 microg/kg/day) starting on the sixth day after ovulation until the occurrence of menstruation or to the end of the ninth week of gestation. The placebo group (33 women) was treated daily with the same dosage of saline solution for the same duration as those treated with G-CSF. The G-CSF was administered in hopes of allowing women with RM or repeated IVF failure to develop the response of the ovary to the pharmacologic stimulatory treatment. In the group treated with G-CSF, 29 out of 35 (82.8%) women experienced little to no pregnancy complications and delivered a healthy baby. Whereas in the placebo group, just 16 out of 33 (48.5%) had a healthy pregnancy and a live birth.[6] With further knowledge and application of G-CSF, researchers can not only improve embryo implantation and ovarian function but also stimulate endometrial thickening and pathologies relating to the endometrium.[3] This will help solve the mystery of unexplained infertility.

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Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

Check one only:
▫ **Reproductive Biology** ☐ **In Vitro Fertilization** ☐ **Cancer Biology** ☐ **Oncofertility**

ABSTRACT TITLE:
Evaluating the Potential Efficacy of Peptide-Lipid Conjugates as a Method of Genetic-Based Therapy for Endometriosis

AUTHOR: Ayesha Aslam-Mir

LEARNER OBJECTIVE:

Question: Do genetic therapies executed through conjugative particles offer a less invasive method to decrease the proliferation of ectopic lesions in endometriosis?

The participant will be able to demonstrate: Recently refined methods of RNA interference (RNAi) and microRNA inhibition, administered through lipid-based nanoparticles, ligand-peptides, and conjugate polymers show potential in targeting endometriotic lesions to prevent their proliferation.

CONTENT (TOPICS): Recent studies observing the similarity between endometriotic and cancerous cell proliferation have led to observation of different regulation of genes that cause cell growth and proliferation. With increasing efficiency of siRNA delivery, a method of RNA interference, there is an outlet for silencing genes that induce the growth and vascularization of lesions through lipid-based and conjugate particles.

ABSTRACT:
Endometriosis, a disease in which endometrial tissue grows outside of the uterus, affects 10% of women in the United States, causing damage to pelvic organs, intense menstrual pain, and infertility. Current treatments include hormonal supplements to induce anovulation and surgical removal of lesions and growths.[1] Recent developments in delivering genetic therapy show promise as a method of less invasive and less obstructive treatment; liposomal and lipid-peptide conjugates have shown efficiency both in transport of genetic therapies and targeting of endometrial lesions respectively. A polymer micelle system using nanoparticle complexes formed from lipid grafted chitosan micelles (CSO-SA) and a pigment epithelium derived factor (PEDF) plasmid were combined as a method of genetic inhibition for angiogenesis. Intravenous injection led to not only 48.79% decrease in lesion volume but also a significantly increased apoptosis index of 11.00 ± 6.83 as compared to the control index of 5.25 ± 1.91.[4] Use of ligand-peptides as vehicles for siRNA's acted against VEGFA genes associated with proliferation of ectopic tissue, revealing 59.67% reduction in lesion growth in rat models for which nanoparticles were injected subcutaneously.[3] Similarly, transcription growth factor-beta (TGF-β), like VEGFA, microRNA-451a, and other genes that influence cytokine pathways causing cell multiplication, was found to be overexpressed in ectopic endometrial tissues; TGF-β is a migratory factor causing invasion and migration of approximately 100 more endometrial stromal cells than cells of control groups.TGF-β activates extracellular signal-regulated kinase (ERK) and mitogen-activated protein kinase (MAPK) signaling pathways.[2,3,5] With the efficiency of delivery methods for genetic material and the targeting of ectopic cells, genetic therapies show potential for stopping the vascularization and migration of endometriotic tissue by inhibiting expression of the culprit genes, transcription factors, and miRNAs.

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5) **Young, Vicky J., S. F. Ahmad, W. Colin Duncan, and Andrew W. Horne. "The Role of TGF-β in the Pathophysiology of Peritoneal Endometriosis." Human Reproduction Update 23, no. 5 (01 2017): 548-59. https://doi.org/10.1093/humupd/dmx016.**

Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

Check one only:

☒ **Reproductive Biology** ☐ **In Vitro Fertilization** ☐ **Cancer Biology** ☐ **Oncofertility**

ABSTRACT TITLE: Exploring the Effectiveness of Sodium Lauryl Ester Sulfate as a Decellularizing Solution for the Ovaries of Female, Prepubescent Leukemia Patients

AUTHOR: Camila Esparza

LEARNER OBJECTIVE: Please state the educational objective in a measurable, testable question. Then state what the participant's poster will be able to demonstrate to the viewer(s)/audience.

Question: How effective is a 1% SLES solution for decellularization of ovaries?

The participant will be able to demonstrate the potential for bioengineered ovaries, using SLES as a decellularization technique, in prepubescent female leukemia patients.

CONTENT (TOPICS): Please provide a brief statement or outline of the content/topic(s) to be presented: The ability for a decellularization technique utilizing Sodium Lauryl Ester Sulfate (SLES) to support cell and follicle growth on an ovarian scaffold, and ultimately produce a healthy, viable ovary.

ABSTRACT:

As survival rates of childhood cancers, like leukemia, increase due to more new, aggressive treatments, more children are left with an increased risk of infertility. Options for female cancer patients include oocyte or embryo cryopreservation and ovarian tissue preservation,[2] however the inactivity of the hypothalamic-pituitary-ovarian axis prevents cryopreservation in prepubertal leukemia patients.[5] The risk of reintroducing malignant cells upon retransplantation of ovarian tissue in leukemia patients is too high, however one promising experimental method relies on the use of Sodium Lauryl Ester Sulfate as a detergent for ovarian tissue, eventually producing a bioengineered ovary. [4] The use of bioengineered ovaries would allow normal function of the ovaries without the risk of reintroducing malignancy.[3] In a study testing the effects of SLES as a decellularizing detergent, ovarian tissue samples were harvested from 18-35 year old patients. The ovarian samples were then bisected and cut into strips of about 2.0mm. The samples were then decellularized with 1% SLES for 48 hours at 18-20°C. They were rinsed several times with a phosphate-buffered saline (PBS) to remove remaining chemicals and cells. Hematoxylin and Eosin (H&E) and Hoeschst were used to stain the samples to ensure effective decellularization. The ECM was also examined using Heidenhain's AZAN stain. The cytotoxicity of the SLES was analyzed using cultured human Wharton's jelly mesenchymal stem cells, to confirm human compatibility. To test the in vivo success of the scaffolds, primary ovarian cells were harvested from 8 week female rats and cultured on the scaffold. After one day, stroma cells, primordial and primary follicles, and oocyte complexes were found. With the confirmation of the effectiveness of the SLES detergent with the decellularization of ovarian samples, there are future possibilities of utilizing bioengineered ovaries to restore fertility in female, pre-pubescent, leukemia patients.[1]

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Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

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蜉☐**Reproductive Biology**☐ **In Vitro Fertilization** 蜉☐**Cancer Biology** 蜉☐ **Oncofertility**

ABSTRACT TITLE: Effect of hMG on Oocyte Development During In VItro Maturation

AUTHOR:

LEARNER OBJECTIVE: Please state the educational objective in a measurable, testable question. Then state what the participant's poster will be able to demonstrate to the viewer(s)/audience.

To measure the success rate of IVM in patients who have continuously failed IVF, in order to see if it is more successful.

Question: How successful is hMG at stimulating more and better quality oocytes?

The participant will be able to demonstrate: a comparison of quality and quantity of oocytes retrieved with and without hMG.

CONTENT (TOPICS): Please provide a brief statement or outline of the content/topic(s) to be presented:
This will look into the effect that hMG has on the success of IVM.

ABSTRACT:

In Vitro Maturation (IVM) is a fertilization procedure in which the prospective mother has her immature oocytes harvested so that they can be fully developed and artificially fertilized in a laboratory. IVM is helpful for women with resistant ovary syndrome because it allows oocyte development even when the patient's hormones aren't balanced. Although IVM does improve her ability to have children greatly, having the patient produce enough quality oocytes is a great setback. One approach to this is to stimulate the ovaries by using human menopausal gonadotropin (hMG) since it encourages many follicles to develop, but isn't one of the hormones that aren't processed properly by the patients. This study compares the quality, measured in fertilization and live birth rates, as well as the quantity, measured in the number of oocytes retrieved, of immature oocytes produced by women with and without hMG. This study resulted in an average of 2.14 cumulus-oocyte complexes (COC) being retrieved without any stimulation compared with 6.43 COC being retrieved using hMG stimulation. This resulted in 54.1% of unstimulated COC being fertilized, and 14.3% used resulting in a live birth, while 54.6% of stimulated COC were fertilized and 16.7% used resulted in a live birth. These results show that although hMG does greatly increase the number of COC retrieved, it has no substantial effect on the quality of oocytes produced. A future step to take would be to investigate which hormones or oocyte media result in the best quality oocytes to maximize the potential of the eggs.

Keywords: In Vitro Maturation·infertility·hMG·resistant ovary syndrome

References:

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Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

Check one only:
☐ **Reproductive Biology** ☐ **In Vitro Fertilization** ☒ **Cancer Biology** ☐ **Oncofertility**

ABSTRACT TITLE: Capturing Excess Doxorubicin with 3D Printed Absorbers

AUTHOR: Claire Wang

LEARNER OBJECTIVE: Please state the educational objective in a measurable, testable question. Then state what the participant's poster will be able to demonstrate to the viewer(s)/audience.

Question: Can 3D printed absorbers effectively capture excess doxorubicin to minimize systemic circulation levels?

The participant will be able to demonstrate: The participant will demonstrate the viability of implanting 3D printed absorbers in order to capture chemotherapy drugs from the bloodstream after they have had their effects on the tumors, but before they can cause hazardous side effects in the body. It will focus on a recent study demonstrating the effectiveness of the introduction of these absorbers into the blood of swine models.

CONTENT (TOPICS): Please provide a brief statement or outline of the content/topic(s) to be presented:
In a recent study, 3D printed tiny, cylindrical "sponges" were tested in pigs. The researchers observed its efficacy in absorbing excess drugs before it spreads to the entire body, thus lessening chemotherapy's harmful side effects. The most recent design has shown that the absorber can capture nearly 2/3 of the common chemotherapy drug doxorubicin.

ABSTRACT:

Cancer is a major health problem worldwide and is the second leading cause of death in the United States.[1] However, doctors are forced to limit the doses of drugs in chemotherapy, particularly doxorubicin, due to its toxic side effects such as skin eruptions, dilated cardiomyopathy, and heart failure.[2] During intra-arterial chemotherapy infusion to a target organ, excess drugs that do not remain in the target organ pass through and circulate to the rest of the body.[3] Typically, over 50-80% of injected drugs pass by the tumor and enter general circulation. One approach to mitigating this off-target damage is to insert a 3D printed absorber into the draining veins of the organ that contains the chemotherapy-targeted tumor though a microsurgery.[4] The absorber absorbs excess drugs before it enters the systemic circulation. The device contains a hole through the length of the cylinder that allows the insertion of the device with minimally invasive image-guided endovascular surgical procedures. The porous cylinder structure was printed by the cross-linking of PEGDA. Inside the structure is a square lattice structure that is coated in polystyrene sulfonate, which binds to doxorubicin and thus significantly reduces side effects. [5] The introduction of the absorbers into the blood of swine models undergoing infusion in the common iliac vein of 50 mg of doxorubicin over 10 minutes enabled the capture of 64 ± 6% of the doxorubicin without any immediate any noticeable effects. Doxorubicin concentrations in blood samples were determined using fluorescence spectroscopy. Moving forward, further decreasing lattice size and changing the chemical composition and thickness of the coating layer may enhance drug capture. In future human trials, absorbers can be customized to fit optimally in the veins of the patient by doing a pre-procedure MRI.

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Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

Check one only:

☐ **Reproductive Biology** ✔ **In Vitro Fertilization** ☐ **Cancer Biology** ☐ **Oncofertility**

ABSTRACT TITLE: Basic Fibroblast Growth Factor (bFGF) to Improve *In Vitro* Oocyte Maturation in a Tissue-Engineered 3D Culture System

AUTHOR: Dhruti Pandya

LEARNER OBJECTIVE:

Question: How does basic fibroblast growth factor influence *in vitro* oocyte maturation in 3D culture systems?

The participant will be able to demonstrate: The effects of basic fibroblast growth factor (bFGF) on *in vitro* follicular growth in tissue-engineered 3D alginate culture systems for *in vitro* maturation as an alternative to ovarian tissue transplantation in cancer patients.

CONTENT (TOPICS): Basic FGF is a heparin-binding growth factor that serves as a signaling molecule for various developmental, physiological, and pathological functions in cells. The studies explore the effect of bFGF in a 3D culture system for individually isolated follicles from the ovarian cortex and the potential use of bFGF and substances such as Retinoic Acid for a synergistic effect on *in vitro* follicle maturation.

ABSTRACT:

Ovarian tissue transplantation is the main fertility treatment option for prepubescent female cancer patients undergoing cytotoxic treatments, however, it poses the risk of reintroducing malignant cells.[5] The ability to grow primordial follicles *in vitro* is vital because they are abundantly present in females of all ages, thus allowing for *in vitro* maturation of oocytes followed by IVF.[3,4] During primordial follicle growth, a signalling molecule called basic fibroblast growth factor (bFGF) assists ovarian granulosa, stromal and theca cell proliferation and cumulus cell apoptosis inhibition.[2,3,5] In a study, ovarian tissue from 14 females aged 6–38 years was cultured in a cell medium supplemented with 0, 50, 100, or 300 ng bFGF/mL.[3] 60% of 107 follicles cultured with 300 ng/mL bFGF had increased E2 secretions and were developing after the fourth week compared to 4% of 181 follicles developing in the thawed control group.[3] In another study, 154 follicles were isolated from ovarian tissue from 11 women and encapsulated into 1% 3D alginate cultures with 0, 100, 200 or 300 ng/ml bFGF. After 8 days, the follicle diameters in the 200 ng/ml bFGF group were 133.3 ± 35.1 µm compared to 90.2 ± 29.8 µm in the 0 ng/ml bFGF group.[5] The survival rate of follicles in the group of 0 ng/ml bFGF was only 36.8% while the survival rate of follicles in the group of 100, 200 and 300 ng/ml bFGF increased to 73.8, 76.9 and 65.7%, thus indicating the advantageous effect of bFGF on *in vitro* oocyte maturation.[1,5] Further research is required on utilizing multiple growth factors for synergistic effects on follicle growth and developing sequential culture media to mature healthy human oocytes.[1]

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Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

Check one only:
Reproductive Biology **In Vitro Fertilization** **Cancer Biology** **Oncofertility**

ABSTRACT TITLE: Puberty Induced by Transplanted Xenografted Ovarian Tissue

AUTHOR: Elaine Yoon

LEARNER OBJECTIVE: Please state the educational objective in a measurable, testable question. Then state what the participant's poster will be able to demonstrate to the viewer(s)/audience.

Question: Can transplanted cryopreserved ovarian tissue offer more hope in inducing puberty and restoring ovarian function for a chance at a natural and live birth?

The participant will be able to demonstrate: Inducing puberty is possible for young girls who want to preserve their fertility in the same ways older women can.

CONTENT (TOPICS): Please provide a brief statement or outline of the content/topic(s) to be presented:
Studies have shown that prepubertal female cancer patients can use transplanted/cryopreserved ovarian tissue to induce puberty.

ABSTRACT:

There is a group that faces the greatest challenge in protecting their fertility, and that is the pediatric and prepubertal female cancer patients. Girls who have not reached puberty yet are not ovulating, therefore there are no eggs to freeze or preserve. As of now, their only option is to cryopreserve their ovarian tissue. However, there have been recent cases of puberty being induced by the transplantation of cryopreserved ovarian tissue.[5] A case of ovarian tissue auto-transplantation with fertility restoration resulted in a live birth as the tissue was collected at an age of 13 years and 11 months, before puberty.[1] With a way to induce puberty, young girls would be able to have their first period and ovulate as a result. In a case report by Ernst E., a 9 year old had a transplantation of cryopreserved ovarian tissue, and she regained ovarian function while secreting estradiol in a sufficient amount to induce puberty.[2] In another case recorded in 2003, a 10-year old girl had a transplantation of an autograft of cryopreserved ovarian tissue that was also used to induce puberty.[3] The similarities within each of these cases is the effect transplantation has on a woman's reproductive hormones. With more research, we can see how effective this process can be in a broad age range of prepubertal young girls. The transplantation of grafted or frozen ovarian tissue can induce puberty while also preserving fertility options later in the future. Finding ways to induce puberty should be the step taken prior to searching for fertility preservation options.

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Oncofertility Saturday Academy Poster Abstract Form

NAME: Elena Medina
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Abstract Categories

Check one only:
☐ Reproductive Biology ☐ In Vitro Fertilization ☒ Cancer Biology ☐ Oncofertility

ABSTRACT TITLE: Using endometrial and ovarian cancer DNA shed during pap smears as a form of early detection

AUTHOR: Elena Medina

LEARNER OBJECTIVE: Please state the educational objective in a measurable, testable question. Then state what the participant's poster will be able to demonstrate to the viewer(s)/audience.

Question: How does the PapSEEK technique use DNA to detect cancer in a woman's endometrium or ovaries?

The participant will be able to demonstrate: The participant will be able to demonstrate how the new technique PapSEEK is able to detect mutations in the DNA that is shed from ovarian and endometrial cancers.

CONTENT (TOPICS): Please provide a brief statement or outline of the content/topic(s) to be presented: Both ovarian and endometrial cancers do not have good options to help detect the cancer at an early, treatable stage so many women unfortunately die because their cancer was caught too late. The new PapSEEK technique would combine pap smears, which a woman is supposed to get every three years, with PCR technology that allows scientists to look for mutations in 18 genes.

ABSTRACT:
There are currently no good early screening tests for both endometrial and ovarian cancers, which then causes them to have high mortality rates and be the most common female reproductive cancers. If an early screening method was proved to be accurate enough to be used in a clinical setting many women could catch their cancers before they show symptoms, and before the cancer can metastasize. If a woman were to have either endometrial or ovarian cancer DNA from that tumor will shed and can be found on the cervix[3]. The PapSEEK technique uses the sample that is taken from a pap brush during a pap smear and uses the purified DNA from the preservative that is normally used to test for HPV. The DNA is then put into Safe-SeqS -which is a PCR error reduction technology- and primers allow us to look at 18 specific genes, and look for mutations; also to look for aneuploidy a single primer is applied to LINEs and a PCR method will help detect abnormalities in the chromosomes. Two different brushes were used, the first being the pap brush which was able to detect 81% of endometrial cancer and 29% for ovarian[2]. The other brush used is the Tao brush which is a thin brush that doesn't damage the cervix, making sampling the endometrial cavity easy; and it was able to detect 93% of endometrial cancer and 45% of ovarian cancer. It was also shown that looking for ctDNA in a woman's plasma[5] can increase the specificity of detecting ovarian cancer to 63%. The next step for this technique would be to do another study, but instead of it being a retrospective study change it to a prospective study in order to show how it would work in a clinical setting.

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Oncofertility Saturday Academy Poster Abstract Form

NAME: Emily Kang
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Abstract Categories

Check one only:
☐ Reproductive Biology ☐ In Vitro Fertilization ☐ Cancer Biology ☒ Oncofertility

ABSTRACT TITLE: Potential of RNF212, PUMA, and NOXA as Drug Targets Against DNA Damage-Induced Oocyte Apoptosis

AUTHOR: Emily Kang

LEARNER OBJECTIVE:

Question: How do the RNF212, PUMA, and NOXA genes contribute to the process of oocyte apoptosis due to DNA double-strand breaks (DSBs)?

The participant will be able to identify the key genes, molecular pathways, and mechanisms by which DNA damage leads to oocyte death through apoptosis, as well as potential methods to prevent oocyte apoptosis in female cancer patients.

CONTENT (TOPICS):
Topics include the role of DSB-induced apoptosis in females, the underlying mechanisms of genes and pathways that lead to such apoptosis, ideas to prevent oocyte apoptosis in cancer patients, and possible unintended effects of prevention.

ABSTRACT:
Due to the aggressive nature of cancer therapy, survivors often face struggles regarding their fertility; however, current fertility preservation options can delay crucial treatment and impact cancer prognosis. Chemotherapy and radiation commonly induce DNA damage to oocytes, which can result in apoptosis and diminished ovarian reserve.[1] Thus, there is a need for greater understanding of DSB (double strand break)-induced apoptosis, which may lead to improved options for cancer patients. In one study, RNF212 knockout mice were exposed to 0.35 Gy γ-irradiation; $RNF212^{-/-}$ oocytes averaged 68% survival, while wild-type counterparts yielded 13% survival. After immunostaining for γH2AX, a DNA-damage marker, $RNF212^{-/-}$ oocytes displayed a five-fold reduction in staining compared to the wild-type, suggesting that RNF212 impedes DNA-damage repair.[5] RNF212 also likely enhances DSB-induced oocyte apoptosis regulated by TAp63.[2,3,5] Another study analyzed the mechanism that TAp63-mediated oocyte apoptosis uses by examining PUMA and NOXA, both of which are induced by TAp63.[4] $PUMA^{-/-}$ and $PUMA^{-/-}$ $NOXA^{-/-}$ mice were exposed to 0.45 Gy γ-irradiation; while all primordial follicles were destroyed in wild-type mice, 16% of $PUMA^{-/-}$ oocytes and 52% of $PUMA^{-/-}$ $NOXA^{-/-}$ oocytes survived, with both types of surviving oocytes subsequently giving rise to healthy offspring.[2] These studies illustrate how targeting RNF212, PUMA, and NOXA may develop options that maintain both quantity and genomic integrity of oocytes throughout cancer treatment. In the future, further pharmacodynamics studies must be conducted to ensure specificity and efficacy of the described inhibition.

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Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

☒ **Reproductive Biology** □ **In Vitro Fertilization** □ **Cancer Biology** □ **Oncofertility**

ABSTRACT TITLE: Decreasing Hyperalgesia in Endometriosis: Utilizing miR-146b as a Biomarker of Diseased Macrophages to Inhibit IGF-1 via Linsitnib

AUTHOR: Emily Tianshi

LEARNER OBJECTIVE:

Question: How can decreasing IGF-1 expression in diseased macrophages lead to lower hyperalgesia in endometriosis?

The participant will be able to demonstrate how nerve-stimulating macrophages in endometriosis can be inhibited and possibly identified.

CONTENT (TOPICS): Topics include endometriosis, disease-modified macrophages, lesion nerve growth, global inhibition, microRNAs, and upregulation.

ABSTRACT:

Over 176 million women worldwide suffer from endometriosis, a disease where uterine tissue grows outside of the uterus and causes extreme pelvic pain. The goal of this study is to explore a method of decreasing hyperalgesia.

Macrophages stimulate the growth of endometrial lesions. Forster et al. depleted diseased mice of macrophages through liposomal clodronate injections. These mice exhibited similar grooming behavior to healthy mice and had decreased expression of **Cox-2,** an inflammatory gene, compared to baseline diseased mice, meaning hyperalgesia decreased. Through comparing peritoneal fluid from diseased and non-diseased women, they found diseased macrophages expressed higher levels of the protein IGF-1. Thus, IGF-1 causes extra sensitivity in the nerve cells of lesions during endometriosis. The receptor inhibitor of IGF-1, linsitinib, an experimental drug, reduced pain levels in diseased mice, quantified through mouse movements (grooming, abdominal retraction, paw withdrawal). However, linsitinib by itself would cause global inhibition of IGF-1 and negative side effects on other cell growth. Distinguishing disease-promoting from healthy macrophages is essential for the efficacy of this treatment.[2]

Zhang et al. discovered miR-146b is prevalent in diseased macrophages through genotyping over 90 patient samples and determining cytokine production through subsequent ELISA.[5] Wu et al. found that curcumin, an antioxidant from the **Curcuma longa** herb, upregulates the expression of miR-146b while studying human glioblastoma. Sensitization from curcumin was quantified through rates of cell apoptosis and proliferation.[4]

A recommended area of study is to analyze whether the upregulation of miR-146b also causes the upregulation of IGF-1. This could form a drug that uses curcumin to make diseased macrophages more sensitive to linsitinib than healthy macrophages, thus specifically targeting the needed cells and reducing negative side effects. This treatment may have indications for women where treatment, such as GnRH-antagonist/estrogen depressant pills[3] and laparoscopic incision[1], is ineffective.

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Reproductive and Oncofertility Science Academy Poster Abstract Form

NAME: Joyce Yang

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Abstract Categories

Check one only:

X Reproductive Biology ☐ **In Vitro Fertilization** ☐ **Cancer Biology** ☐ **Oncofertility**

ABSTRACT TITLE: Sulfiredoxin-1 (SRXN1) is Essential for the Reproductive Health of Women with Abnormal Hypothalamic-Pituitary Functions

AUTHOR: Joyce Yang

LEARNER OBJECTIVE:

Question: Is SRXN1 a potential drug target to improve fertility rates in women with abnormal hypothalamic-pituitary functions, such as obese, diabetic, or polycystic ovarian women?

The participant will be able to demonstrate: Sulfiredoxin-1 (SRXN1) is essential for the reproductive health of women with abnormal hypothalamic-pituitary functions and is a potential drug target for infertility in obese, diabetic, and polycystic ovarian women.

CONTENT (TOPICS):

Reactive oxygen species (ROS) is necessary for the hypothalamic-pituitary-gonadal axis, but excessive oxidative stress can distort signals. Sulfiredoxin-1 (SRXN1) manages GnRH induced ROS levels and shows potential as a drug target for obesity, diabetes, and polycystic ovarian syndrome (PCOS) related infertility.

ABSTRACT:

Gonadotropin-releasing hormone (GnRH) is released by the hypothalamus to stimulate anterior pituitary secretion of gonadotropins to regulate fertility. Proper signaling requires activation of NADPH/dual specificity oxidases (NOX/DUOX) and mitogen activated protein kinase (MAPK) 1/3 by reactive oxygen species (ROS), but excessive ROS can distort GnRH signals[2]. Free fatty acids (FFA) have been shown *in vitro* to distort gonadotropin transcription and induce the unfolded protein response by participating in cell signaling pathways and increasing ROS production[3,4], and diet induced obesity has been shown *in vivo* to inhibit ovulation in female mice[4]. Various plasma biomarkers of oxidative stress and serum FFA levels are increased with obesity, diabetes, and polycystic ovarian syndrome (PCOS)[5,6,7,8,]. The sulfiredoxin-1 (SRXN1) reductase shows potential as a future drug target[1]. Normal and lentiviral *Srxn1* knockdown LβT2 cells were cultured with 10 nM GnRH for up to 6 hours or hourly. LβT2 cells were also treated with inhibitors of NOX/DUOX, MAPK 1/3, and ROS inhibitors. RT-PCR, western blotting, wide field fluorescence imaging, and flow cytometry measured gene expression and cell ROS production. The results show that inhibition of NOX/DUOX, MAPK 1/3, and ROS inhibitors significantly reduces *Srxn1* gene expression. Knockdown also significantly reduces baseline gonadotropin subunit mRNA and increases ROS production. These results show that SRXN1 is specifically targeted by GnRH signaling to reduce pituitary ROS and is essential for healthy hypothalamic-pituitary functions, showing potential as a drug target for treating obesity, diabetes, and PCOS related infertility.

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Oncofertility Saturday Academy Poster Abstract Form

NAME: Kaitlin Ordonio
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Abstract Categories

Check one only:

✓ **Reproductive Biology** **In Vitro Fertilization** **Cancer Biology** **Oncofertility**

ABSTRACT TITLE: Using the post-implantation amniotic sac embryoid (PASE) as an in vitro platform to model and study human amniotic sac development

AUTHOR: Kaitlin Ordonio

LEARNER OBJECTIVE:

Question: Can a pluripotent stem cell-based model called the PASE (post-implantation amniotic sac embryoid) be a viable in vitro platform to represent the embryogenic events in the human amniotic sac?

participant will be able to demonstrate: The participant will be able to demonstrate that the PASE is a stem cell model of an amniotic sac that allows investigators to observe post implantation embryogenic events and can be of enormous importance to new infertility solutions if the model can replicate the amniotic sac and its physical components. The participant will also demonstrate that the development of the amniotic sac is the keystone for early human embryogenesis.

CONTENT (TOPICS):Topics include the creation of PASE, characteristics of the PASE that are similar to an actual amniotic sac, pluripotency markers OCT4, NANOG and SOX2 that are similar to markers in monkey embryonic disc, BMP-SMAD pathway seen in the PASE structure that is critical during early embryonic development, future plans for the PASE in further studies and treatment of infertility.

ABSTRACT:

A form of infertility is caused when the implanted embryo fails to develop within the amniotic sac. [2] The PASE was created and tested to see if the model was a viable amniotic sac replica to solve technical and ethical challenges of harvesting and studying early human embryos. One study showed the development of a biomimetic 3D culture system where hPSCs were placed as single cells onto different densities of Geltrex beds.[7] Results showed similar human amniotic ectoderm-epiblast tissue patterning only if cell plating density was in the intermediate range of 30,000-50,000 cells cm^{-2}.[7] Another study used immunofluorescence analysis to characterize cell fates. The results from staining showed that the columnar side of the asymmetric cyst is composed of epiblast-like cells that contain the pluripotency markers OCT4, NANOG and SOX2.[8] These same markers have been seen exclusively in the embryonic disc of post-implantation monkey embryos.[6] Immunofluorescence analysis of OCT4 also revealed that in day 5 PASE, there is EMT which is a phenotype associated with PS-initiation found in Carnegie stage 6 embryos.[8]The results of this study show similar PS-initiation among both human amniotic sacs and PASE. During another study on embryogenesis in mice, BMP-SMAD signaling also played an important role in morphogenesis.[3] Results showed if there is no Bmp2 or Smad5, there are defects in both amniotic and embryonic patterning.[7,8] Therefore, the PASE can approach the critical need for a viable in vitro platform to model and study key steps involved in human amniotic sac development.

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Oncofertility Saturday Academy Poster Abstract Form

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Abstract Categories

Check one only:

☐ **Reproductive Biology** ☐ **In Vitro Fertilization** ☐ **Cancer Biology** ☐ **Oncofertility**

ABSTRACT TITLE: Comparing the Efficacy of Progestin-Primed Ovarian Stimulation as an Alternative to GnRH Analogs through Oocyte Count

AUTHOR: Krista Nguyen

LEARNER OBJECTIVE:

Question: Does the addition of oral progestins in ovarian stimulation efficiently block incidence of LH surge, the result of positive estradiol feedback, at equal or greater rates than conventional GnRH antagonist/agonist protocols?

The participant will be able to demonstrate: the effect of progesterone inhibiting the LH surge on preventing spontaneous ovulation and creating mature oocytes for retrieval based on comparison of completed clinical cycles of IVF, ICSI, or oocyte donation.

CONTENT (TOPICS): The content will discuss the basic science of progesterone's role in the female body and correlate to how both progestin-primed and GnRH antagonist ovarian stimulation actively block ovulation and increase the oocyte count for retrieval.

ABSTRACT: Individual patient responsiveness, an incomplete understanding of the ovaries, and varying infertility causes leave conventional ovarian stimulation [COS] challenged by low success rates. In hundreds of conventional GnRH-antagonist cycles, 0.34-38% of patients experienced premature LH surge[4]. This attempt hopes to define the efficacy of progestin-primed ovarian stimulation[PPOS] compared to conventional GnRH antagonist protocol towards blocking spontaneous ovulation, offering women better control of the oocyte production process and thus increasing the probability of completing in vitro fertilization. The studies in question utilized randomized clinical trials with two groups. The study group received a daily oral progesterone pill and the control group received GnRH-antagonist subcutaneous injections on day 8 of stimulation, with both retrievals taking place after 14 days. Both stimulation groups were ultimately tracked for their mature MII oocytes to directly measure the effectiveness of progestins in stopping LH surge incidence and subsequently higher numbers of oocytes for retrieval. The Wang et al. trials found that only 3.0% of their poor responders receiving PPOS had an incidence of premature LH surge versus 8.0% of GnRH antagonist patients[7]. Martinez et al. carried out similar trials using desogestrel, a type of progestin, and found that fewer injections and a total lower cost produced similar oocyte yield and 52.0% vs. 58.6% birth rates[5]. The PPOS and GnRH-antagonist groups were not significantly different in their mature oocyte counts. However, the use of PPOS for oocyte retrieval holds up for women with varying ovarian reserves, from PCOS to normal responder patients, as a strong alternative with potential lower costs, being an overall simpler procedure. PPOS methods have potential avenues in comparing the efficiency of different types of progestins available and analyzing if any type suits specific patient populations.

References:

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Oncofertility Saturday Academy Poster Abstract Form

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ABSTRACT TITLE: Targeting Lactate Metabolism in Hypoxic Tumor Cells Via Inhibition of MCT1 and MCT4 as a Therapeutic Approach to Pancreatic Adenocarcinoma Cancer Recurrence

AUTHOR: Priya Khandelwal

LEARNER OBJECTIVE:

Question: Which inhibitor of MCT1 and MCT4 best targets lactate metabolism in hypoxic pancreatic tumor cells?

The participant will be able to demonstrate: c19, an inhibitor of MCT1 and MCT4, can be used clinically to make hypoxic pancreatic tumor cells more susceptible to radiation and chemotherapy in order to overcome cancer recurrence.

CONTENT (TOPICS):

Topics covered include cancer metabolism, hypoxia in tumor cells, the immunosuppressive effects of lactate, the various substrates of MCTs and how the knowledge of these can be used to make pancreatic cancer significantly more susceptible to radiation and chemotherapy and mitigate the likelihood of recurrence. This poster will also discuss the clinical implications and applications to biotechnology of this research.

ABSTRACT:

Despite recent strides made in oncology, cancer recurrence has consistently eluded oncologists and researchers. No cancer better exemplifies this struggle than pancreatic adenocarcinoma (PDAC), which has a 5% 5-year survival rate and high risk of recurrence.[3,4] Hypoxic tumor cells, including those in PDAC, exhibit enhanced resistance to radiation and chemotherapy due to metabolic reliance on lactate and are thought to be the primary perpetrators of cancer recurrence.[1,4] In absence of lactate, hypoxic tumor cells suffer from glucose deprivation and become susceptible to radiation and chemotherapy.[2] Monocarboxylate transporters (MCTs) 1 and 4 control lactate uptake and transfer in hypoxic tumor cells and are not expressed in healthy pancreas cells.[1,5] Targeting lactate metabolism in hypoxic pancreatic tumor cells via inhibition of MCT1 and MCT4 provides a promising non-toxic approach to PDAC cancer recurrence. In a recent study, 23 aminocarboxycoumarin derivatives were synthesized using palladium-catalyzed Buchwald–Hartwig type coupling reactions.[6] A primary assay was performed to identify compounds that selectively inhibited tumor cell proliferation (experimental cells derived from human cervix carcinoma cell line SiHa).[6] In lactate medium, 10μM of compound 19 (c19), a 7-alkylamino 3-carboxycoumarin, resulted in SiHa cell proliferation of less than 20% cell density, whereas CHC, the reference compound, had 50% cell density.[6] Additionally, IC_{50} (compound concentration to reduce lactate uptake by 50%) and EC_{50} (compound concentration to reduce cell proliferation by 50%) of c19 were 0.059μM and 0.22μM, respectively, compared to 43.5μM and 10.7μM for CHC.[6] Though other substrates of MCT1 and MCT4 were identified, c19 is a promising candidate due to its excellent *in vitro* ADME and *in vivo* PK properties along with no anticoagulant side effects.[6] c19's ability to minimize toxicity without compromising efficacy makes c19 a viable solution to pancreatic cancer recurrence.

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