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SUPPORTIVE CARE MAKES EXCELLENT CANCER CARE POSSIBLE

Oncofertility: from now to next

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MASCC/ISOO
Annual Meeting on Suppportive Care in Cancer
www.mascc.org/meeting

Follow us on Twitter: @CancerCareMASCC

MASCC Multinational Association of Supportive Care in Cancer
ISOO International Society of Oral Oncology

#MASCC19

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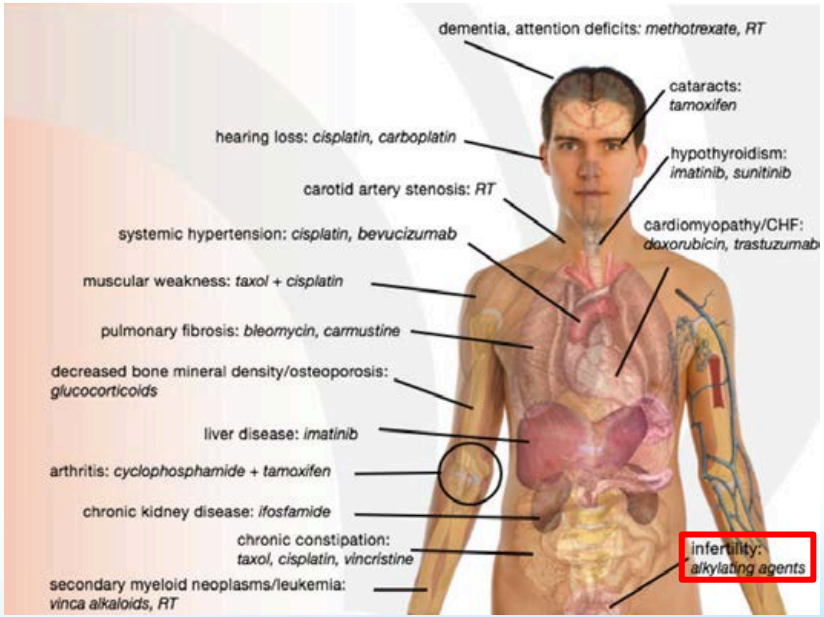
I have nothing to disclose

Cancer treatments, while life preserving, can have off-target effects

Age-related effects of cancer treatments



Cupit-Link CT et al, ESMO Open, 2017

Childhood Cancer Survivor Study – survivors first diagnosed at age 21 and followed up for a median of 24.5 years after diagnosis along with their siblings

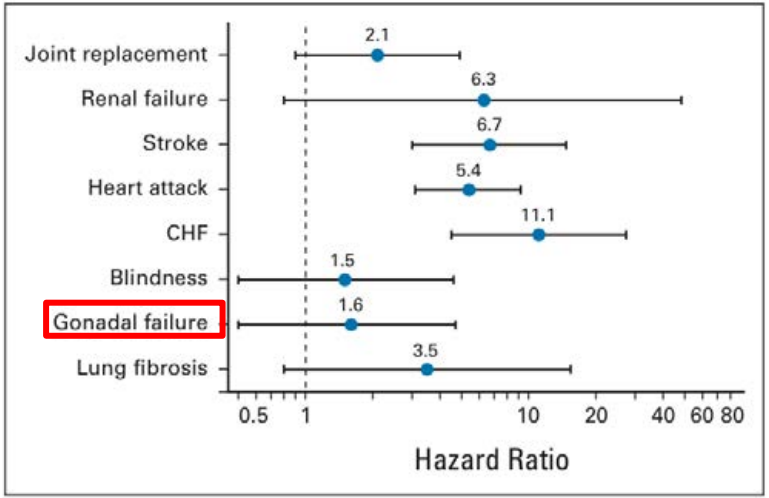


Fig 3. Hazard ratios and 95% CIs of survivors versus siblings for specific chronic conditions that first occurred at or after age 35 years, adjusted for age, race, and sex. CHF, congestive heart failure.

Armstrong GT et al, JCO, 2014

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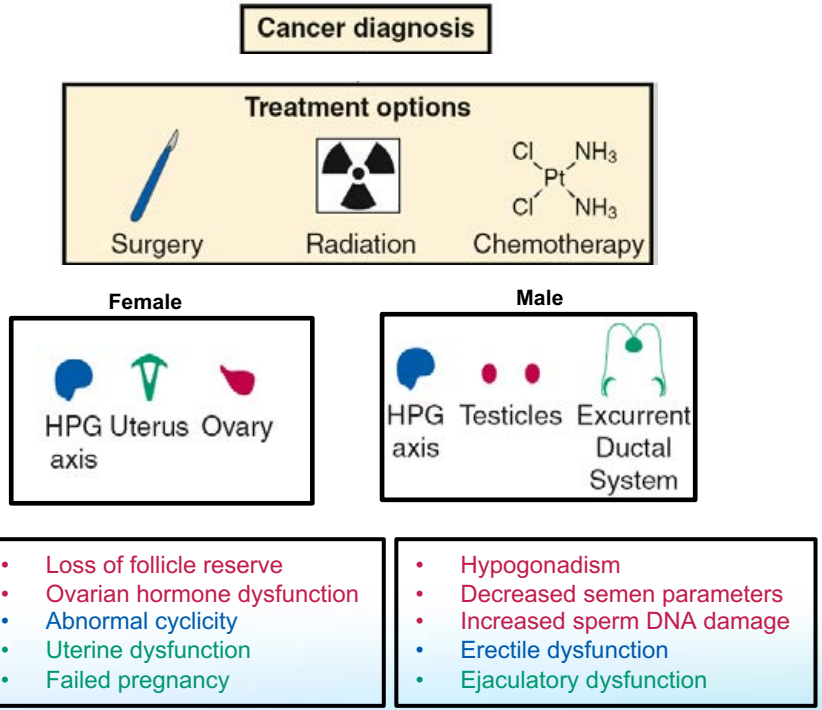
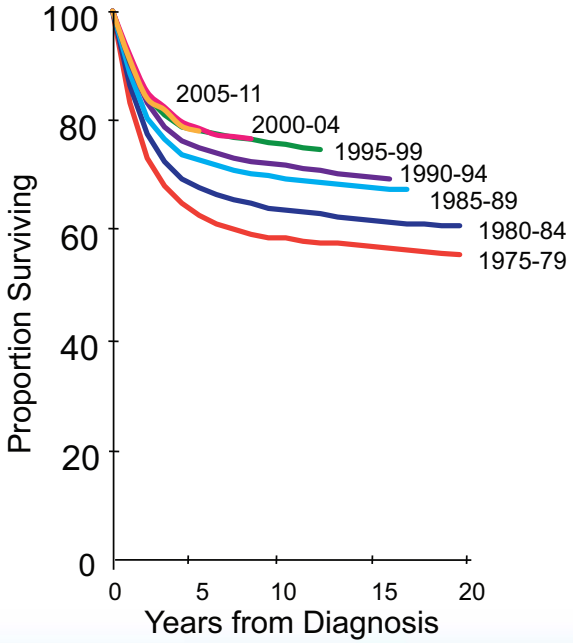
Cancer treatments can affect all aspects of the reproductive axis



Duncan *et al*, Reproductive Endocrinology, 7th Edition

Who is at risk?

- More than **1.4 million** people are diagnosed with cancer in the US annually and **10 million** globally
- **10%** of these individuals are in their reproductive years
- **1 in 750** in the US is a childhood cancer survivor
- Survivors are significantly more likely to be **infertile** or have **difficulty getting pregnant** than their siblings
- **Fertility and sexual functioning** are key health related quality of life concerns in young adult survivors of childhood cancer



Jeruss and Woodruff, *NEJM*, 2009
Howlader N, SEER Cancer Statistics Review 1975-2012
Phillips et al, *CEBP*, 2015 NCI Office of Cancer Survivorship
Robison L. & Hudson MM, *Nature Reviews Cancer* 2014
Nightingale et al, JAYAO, 2011

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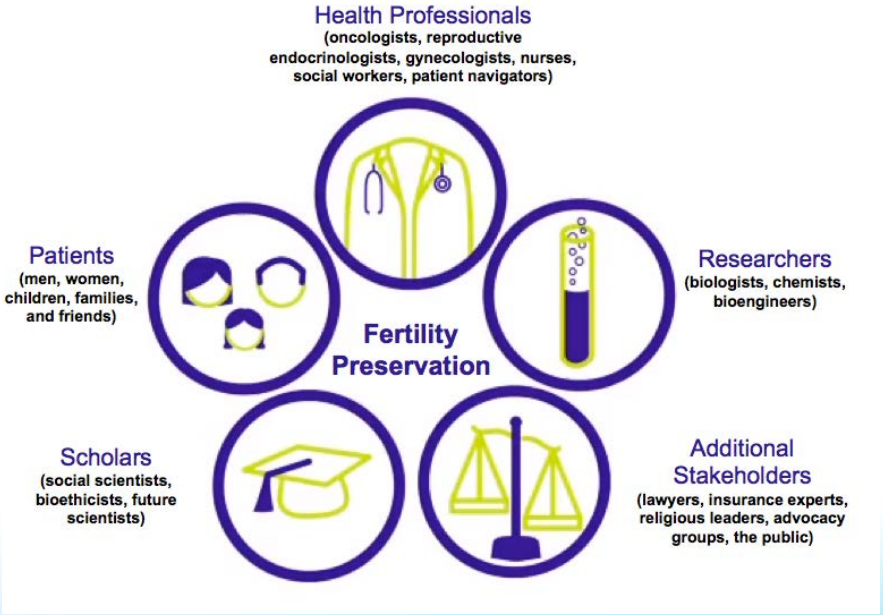
The Oncofertility Consortium - a New Paradigm

A global 10+ year NIH-funded interdisciplinary initiative to explore and expand the reproductive future of cancer survivors



Duncan *et al*, Reproductive Endocrinology, 8th Edition

Fertility Preservation Options for Men

CLINICAL FERTILITY PRESERVATION OPTIONS

For men, standard methods include:

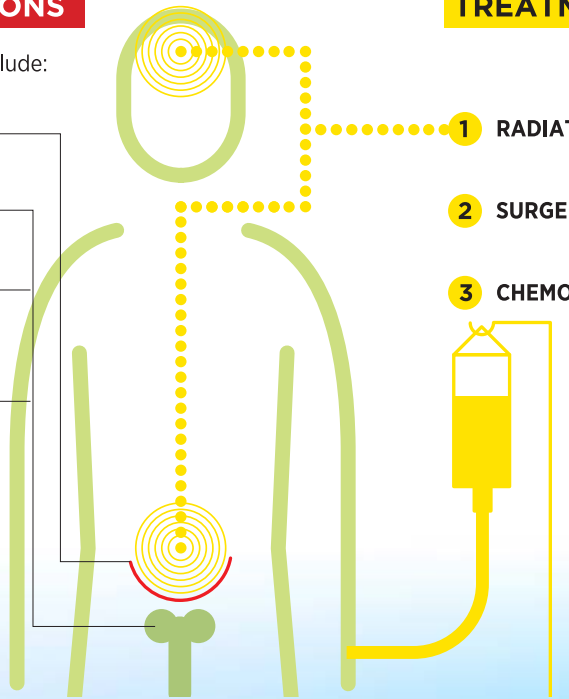
1. TESTIS SHIELDING
2. SPERM BANKING
3. SPERM EXTRACTION

Experimental method:

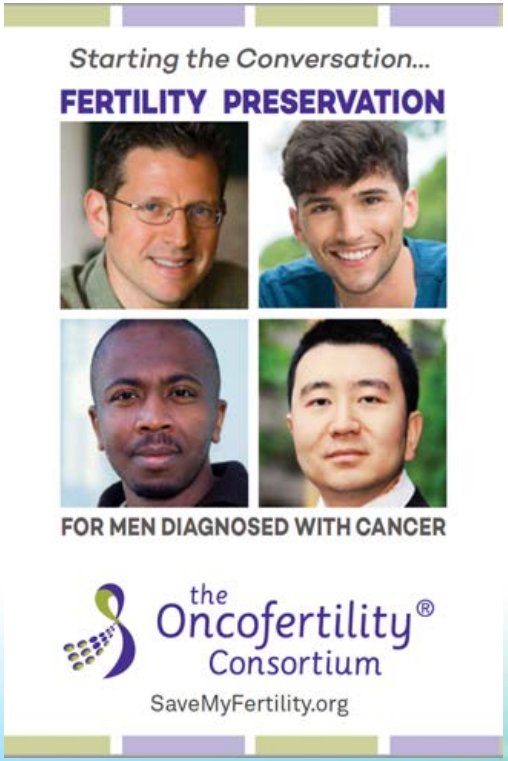
4. TESTICULAR TISSUE CRYOPRESERVATION

CANCER TREATMENT

1. RADIATION
2. SURGERY
3. CHEMOTHERAPY



Duncan *et al*, Reproductive Endocrinology, 8th Edition



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Fertility Preservation Options for Women

CLINICAL FERTILITY PRESERVATION OPTIONS

For women, standard methods include:

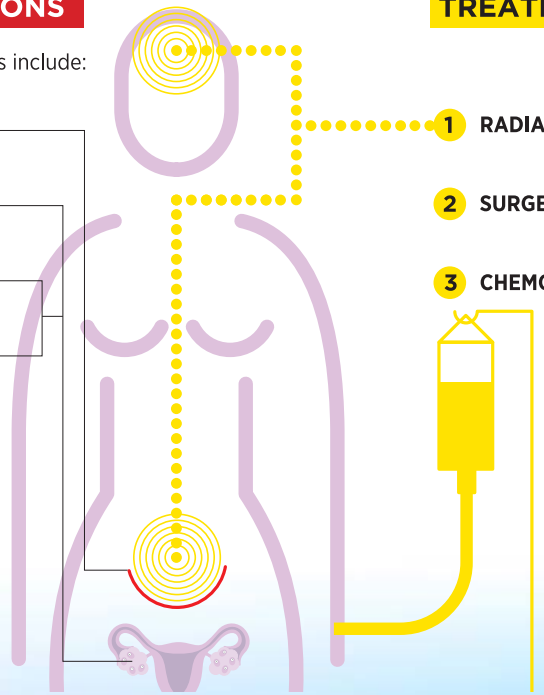
1. PELVIC SHIELDING
2. OVARIAN TRANSPOSITION
3. EMBRYO BANKING
4. EGG BANKING

Experimental methods include:

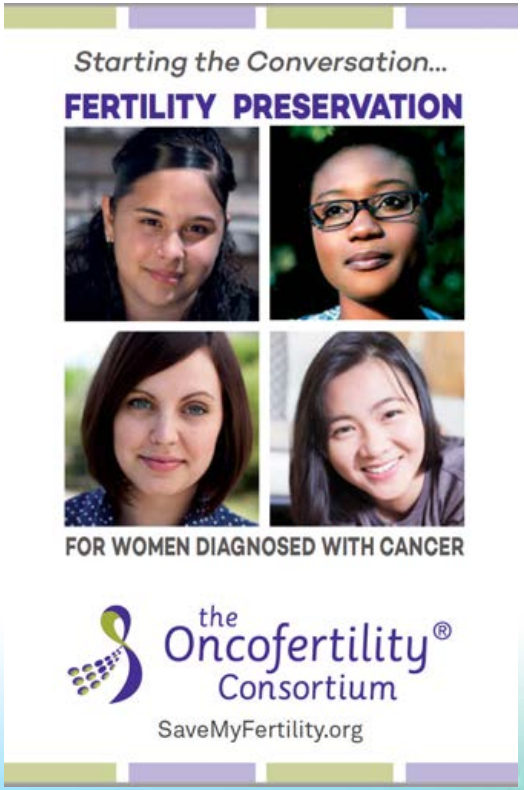
5. GONADAL SUPRESSION
6. OVARIAN TISSUE CRYOPRESERVATION AND TRANSPLANTATION
7. IN VITRO MATURATION

CANCER TREATMENT

1. RADIATION
2. SURGERY
3. CHEMOTHERAPY



Duncan *et al*, Reproductive Endocrinology, 8th Edition



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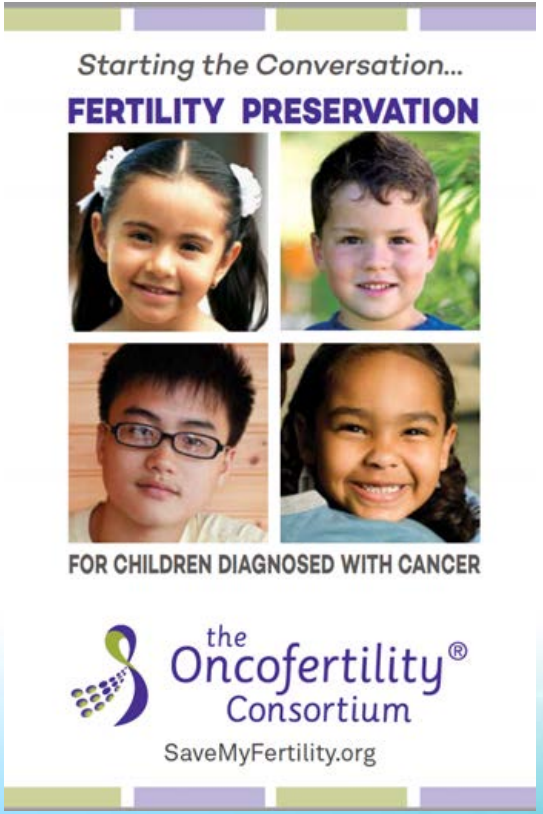
Fertility Preservation Options for Children

- Radiation shielding
- Ovarian transposition
- Ovarian/testicular tissue cryopreservation*

*Investigational



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The Fertility Preservation Decision Making Process is Complex

Challenges of making the decision

- Existential crisis about self, survival, and future
- Decision peripheral to primary diagnosis
- Time constraints
- Overwhelming array of options
- Access to care
- Financial constraints

Challenges of navigating the decision

- Sex
- Age
- Diagnosis
- Treatment type
- Stage of treatment
- Baseline fertility

Duncan *et al*, Reproductive Endocrinology, 8th Edition

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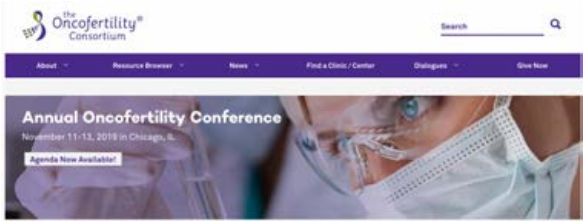
Oncofertility resources for diverse stakeholders

Websites, materials, branding



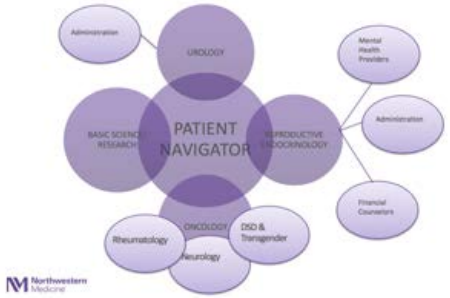
the Oncofertility® Consortium

AT [YOUR INSTITUTION HERE]

Oncofertility.northwestern.edu
Savemyfertility.org
Preservefertility.northwestern.edu

Conferences, virtual grand rounds, training programs

Patient navigation



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Scholarship

Professional networks

A clinical and field-wide infrastructure to support fertility preservation

The National Physicians Cooperative (**NPC**)
and
Oncofertility Professional Engagement Network (**OPEN**)

- 117 US Sites
- 231 Sites Globally in 42 Countries
- 19 Pediatric Sites
- Subset perform OTC under IRB-approved protocols

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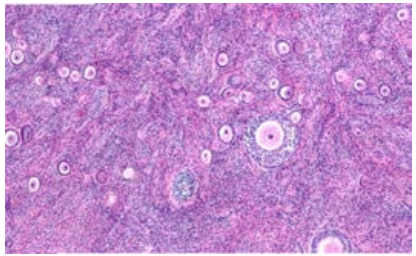
A focus on female fertility preservation – ovarian tissue cryopreservation

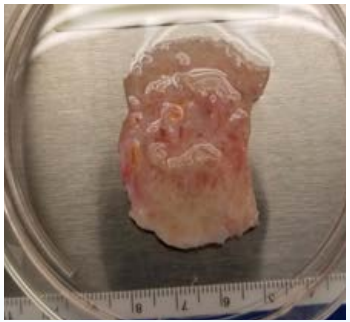
Standard ART protocols (i.e. egg and embryo banking) may not apply to those who:

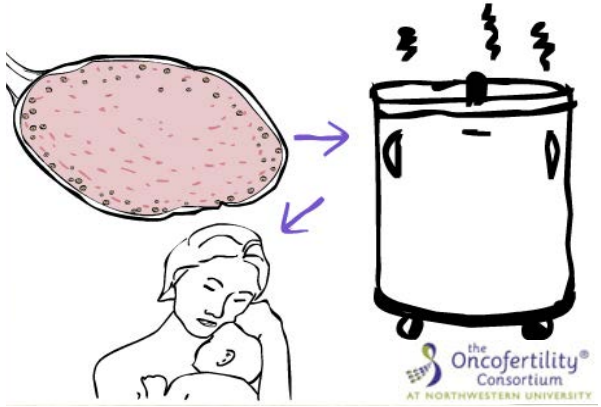
- Are pre-pubertal
- Can not delay cancer treatment
- Can not tolerate hormonal stimulation

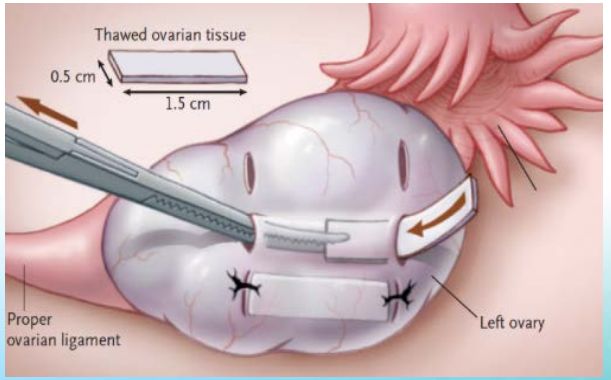
Ovarian tissue removal and **cryopreservation** with future use for **transplantation** or additional **emerging technologies**

OTC and tissue transplantation to restore endocrine function and fertility









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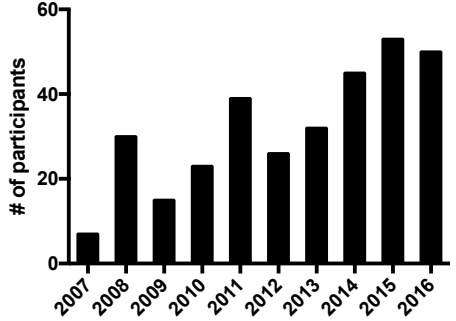
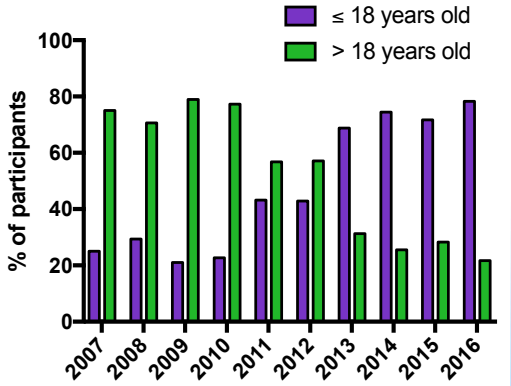
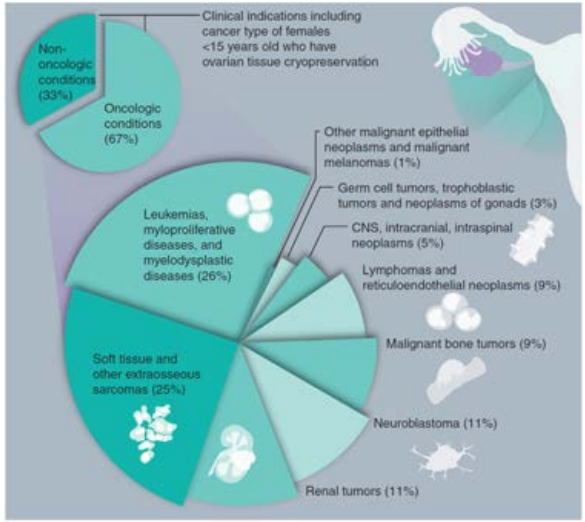
OTC and tissue transplantation has been successful

Annual Enrollment
>450 total participants



Age Distribution Trends





- **>130 live births worldwide**
  - 26% live birth success rate
- **Hormone production up to 12 years**
  - Average 5 years

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Jeruss and Woodruff NEJM, Donnez NEJM 2017
Pacheco Reprod Sci 2017
Kim et al J Gynecol Oncol 2016
Armstrong et al, Future Oncology, 2018
Smith et al, Future Oncology, 2018

How do we continue to reduce the reproductive health burdens for cancer survivors?

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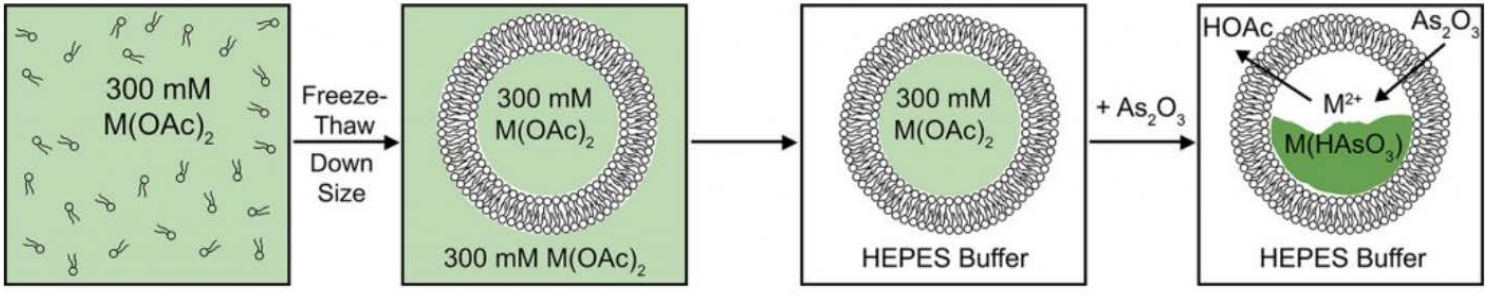
- Make safer (“smart”) cancer treatments
- Determine the fertotoxicity of cancer treatments
- Develop fertoprotective adjuvant therapies
- Engineer new fertility preservation methods

Making safer or “smart” cancer treatments

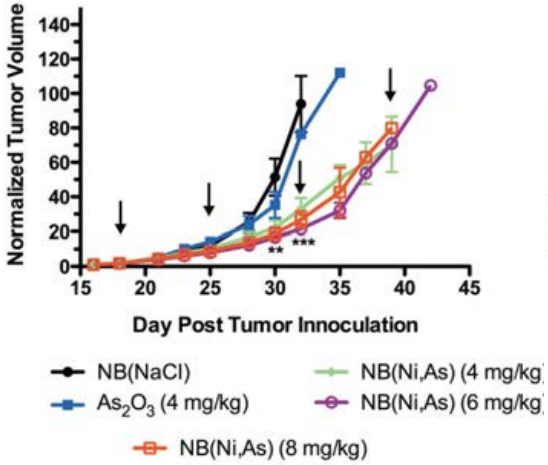
- Arsenic trioxide has serious systemic toxicities but is a front line treatment for acute promyelocytic leukemia and has shown promise in adult T-cell leukemia/lymphoma

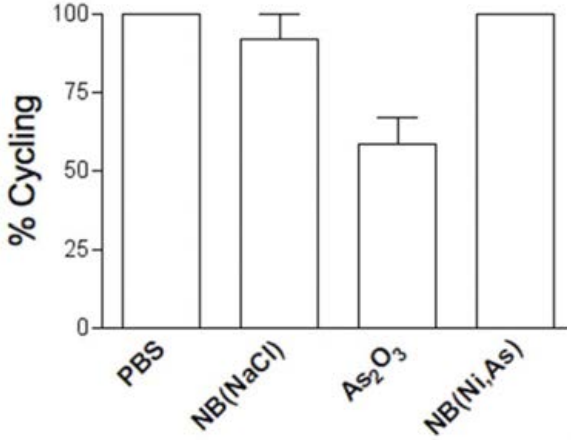
- This therapeutic hurdle can be lowered by encapsulating drugs into liposome particles (or nanobins)

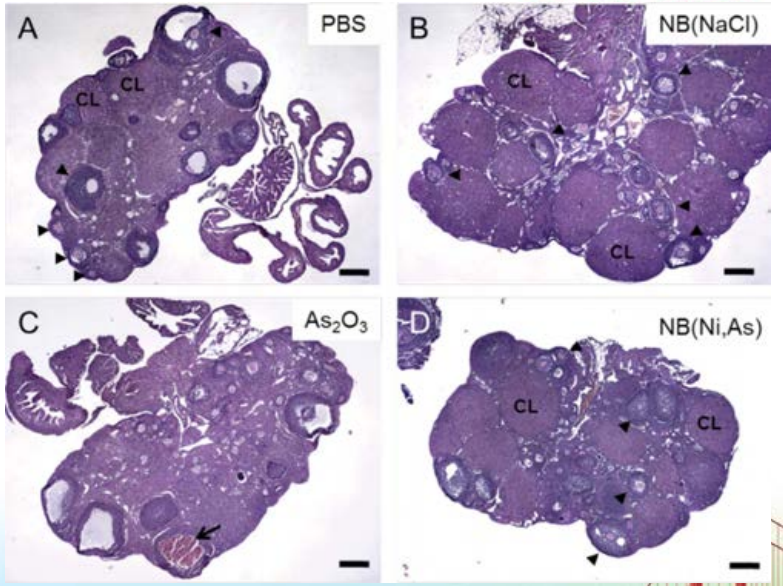


Ahn et al, PLOS One, 2013

Nano-encapsulation of arsenic trioxide enhances efficacy against lymphoma in a murine model while minimizing reproductive toxicity

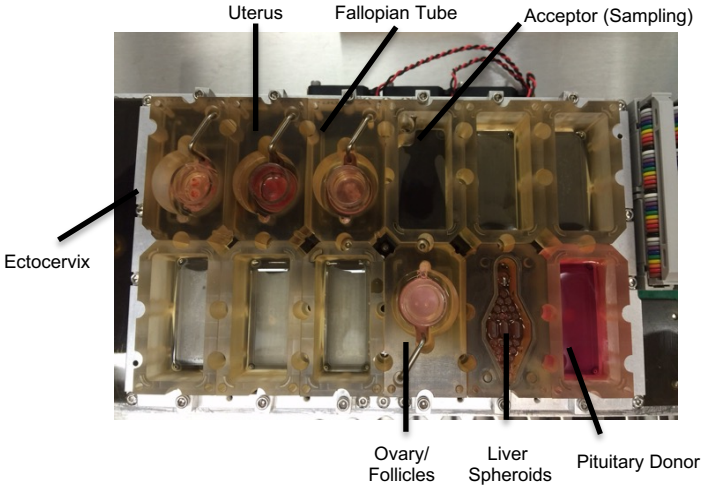


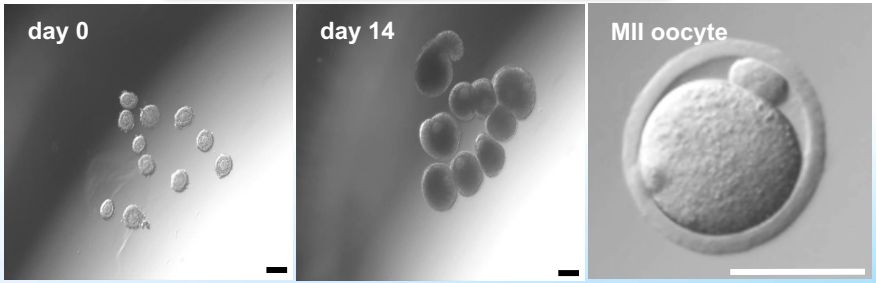


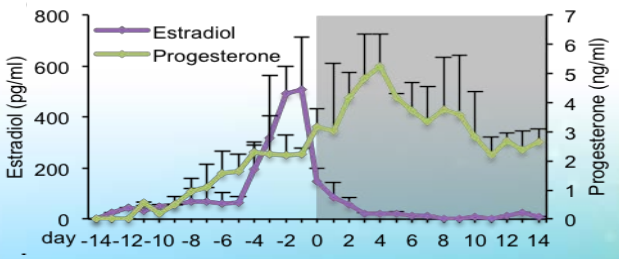


Ahn et al, PLOS One, 2013

Using microphysiologic platforms to screen for the fertoxicity of cancer treatments







Xiao et al, Nature Communications, 2017

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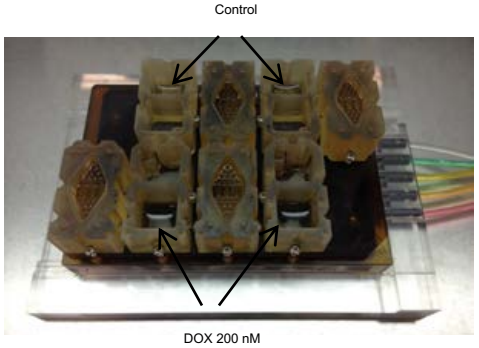
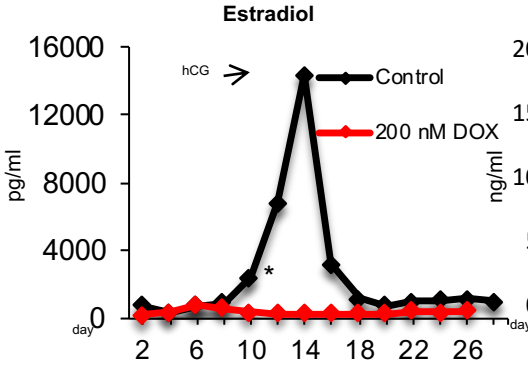
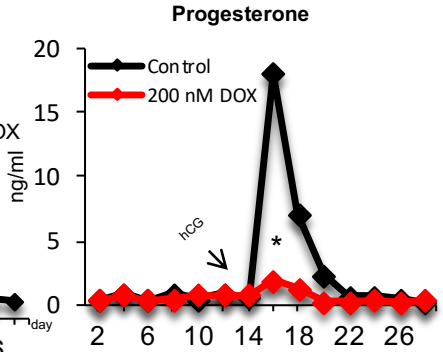
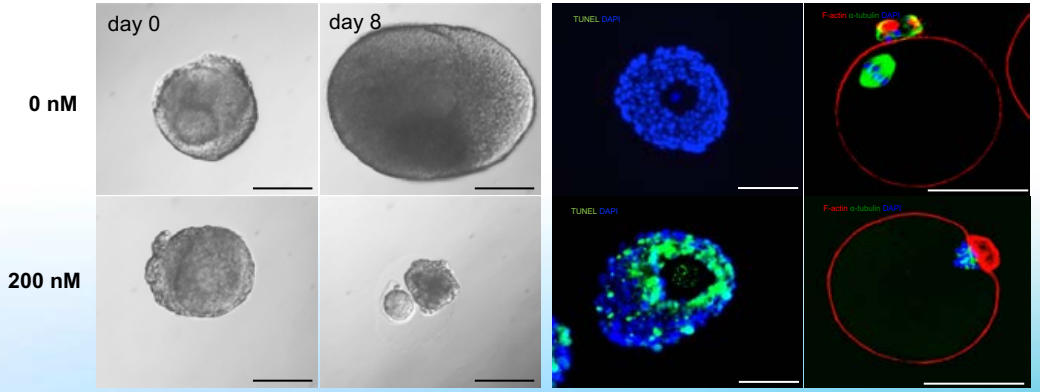
Identifying the reproductive toxicity of chemotherapeutics

Doxorubicin





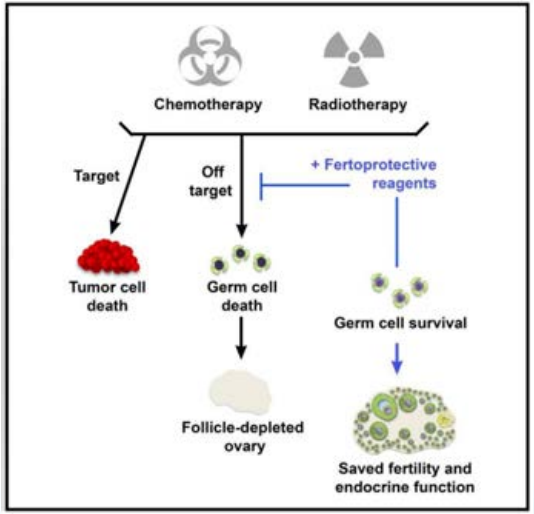


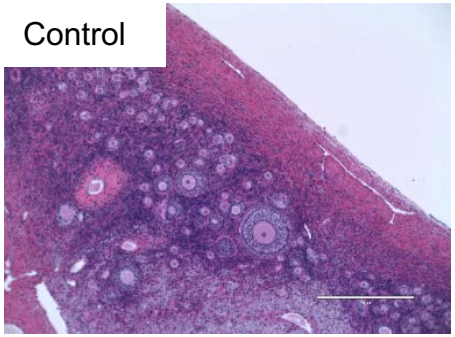


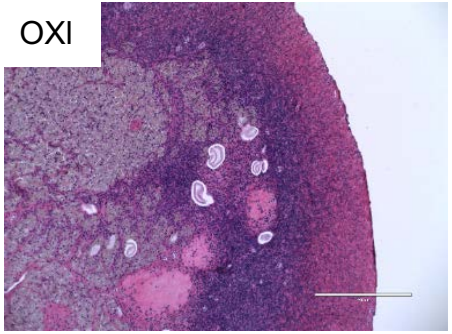
Xiao et al, Toxicol Sci, 2017

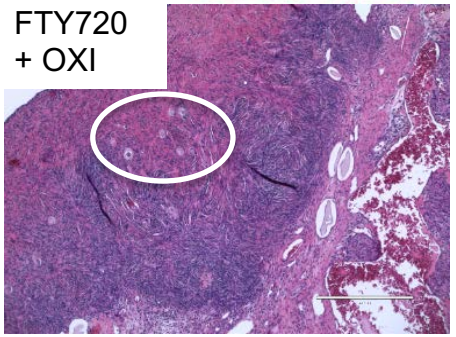
Development of fertoprotective adjuvant therapies

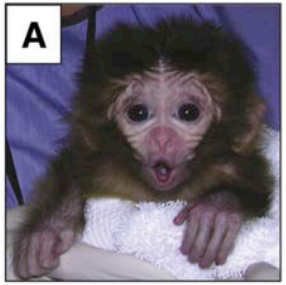
Ovarian pre-treatment with anti-apoptotic agents protects against radiation damage and preserves follicles and fertility

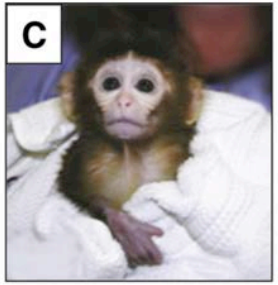


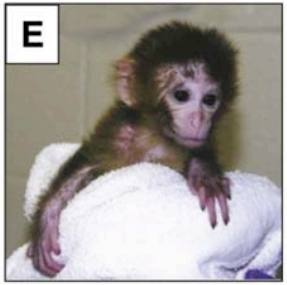










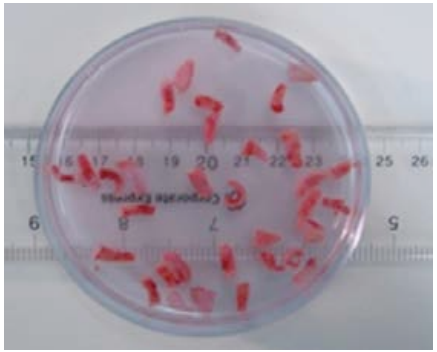


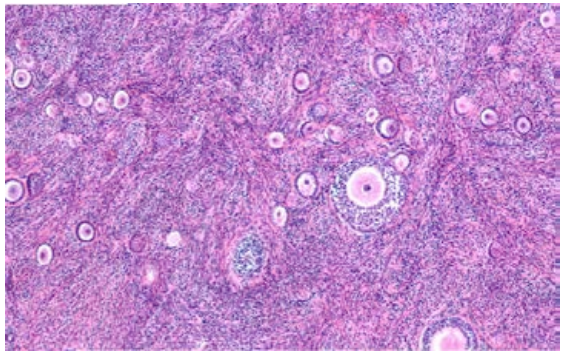
Zelinski *et al*, Fertility Sterility, 2011

Kim *et al*, J Gynecol Oncol, 2016

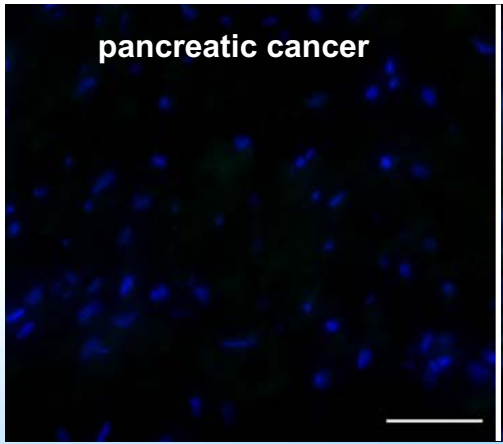
Engineering new fertility preservation methods

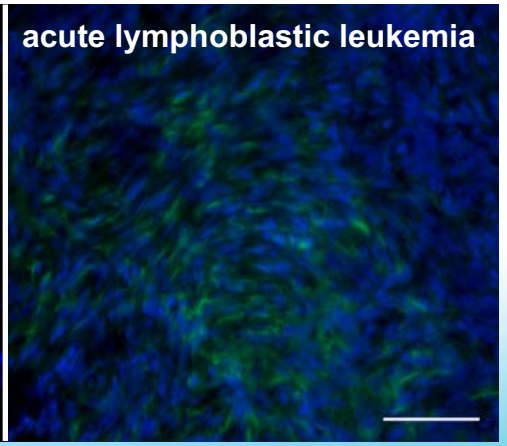
Ovarian tissue transplantation – while successful - may be contraindicated





SALL4 / DAPI





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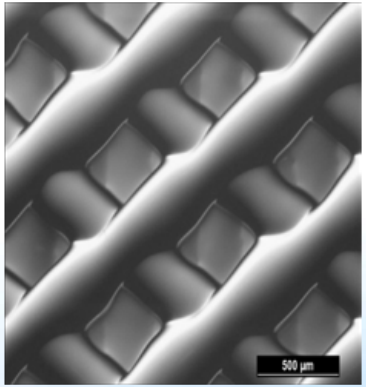
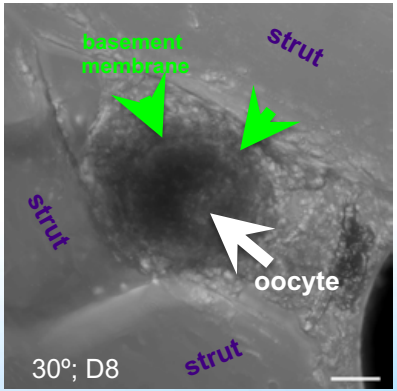
Laronda *et al*, Biomaterials, 2015

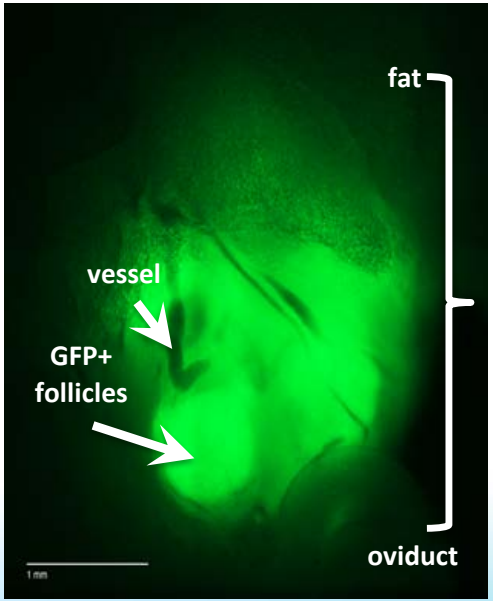
Engineering a 3D printed bioprosthetic ovary

Bioinspired scaffold serves as an ovarian soft tissue transplant

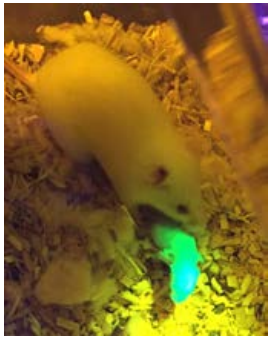




Bioprosthesis, bursa



Multiple generations



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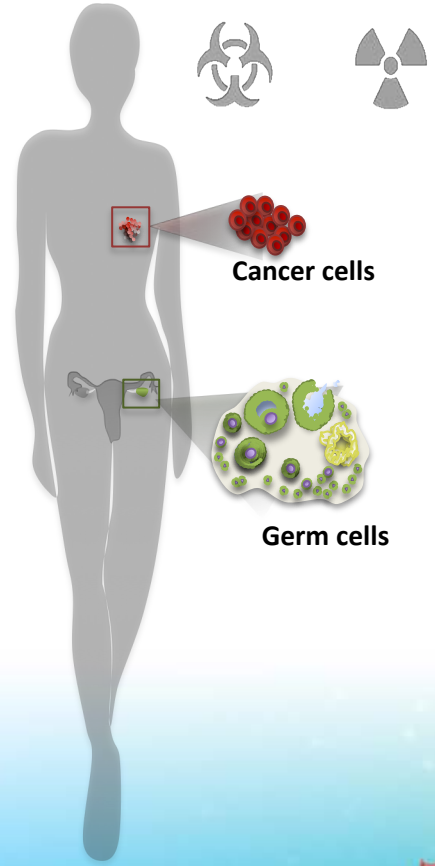
Laronda, et al, Nature Communications, 2017

The Future: where we are going

- **No More Cancer**
  - Treatments are changing in real time
- **Full Fertility**
  - Interventional options to preserve fertility
  - Mitigation strategies
- **Fully Accessible**
  - Low/no resource environments
- **Fully Considered by all Stakeholders**
  - Providers, patients, partners, public
- **Eliminate the field**



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