Fertility Preservation Options for Cancer Patients

Options for female and male cancer patients under 40 years old prior to chemotherapy, radiation therapy, and bone marrow treatments

Part 1

What is Oncofertility?

Oncofertility is a new term that describes the effort to preserve fertility for young people with cancer.

This new field includes basic reproductive biology, clinical science, ethics, law, economics, pediatric surgery, and education sciences.

the Oncofertility™ Consortium

Cancer Survival Rate

1 in 49 human females in the USA between the ages of birth and 40 are diagnosed annually with cancer.

5 year survival rate

All Cancers	64%
Breast Cancer	90%
Childhood Cancers	80%

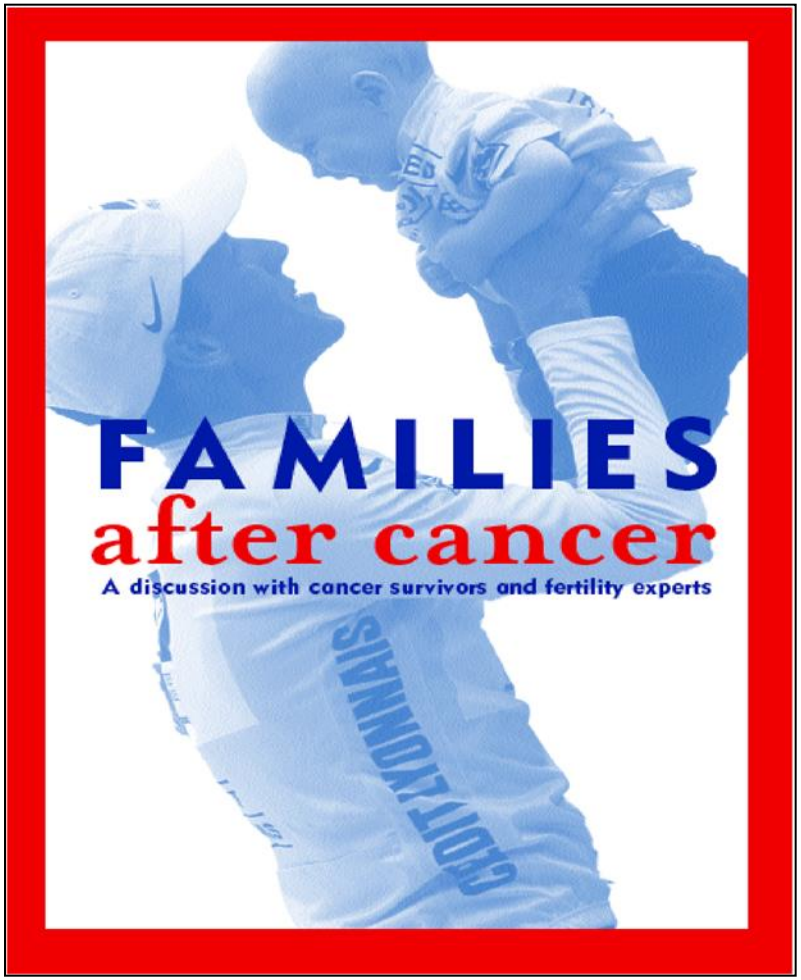
2015 – 1 person in 285 children in the USA will be a diagnosed with cancer before age 20.

Incidence of Cancer

70,000 cancer patients are exposed to chemotherapy and radiation therapy and half are breast cancer patients.

Breast Cancer	30,000
Lymphoid Malignancies	30,000
Childhood Cancers	6,500
Solid Tumors (Cervical, Osteosarcoma)	5,000

Options for Men



- Sperm Bank
- Donor Sperm
- Adoption

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Male Fertility Preservation

Adult Males

Store sperm → Cryopreserve → Unthaw sperm → Insert into oocyte by Intra-Cytoplasmic Sperm Injection (ICSI) then *In Vitro* Fertilization (IVF)

Adult Males with Partner

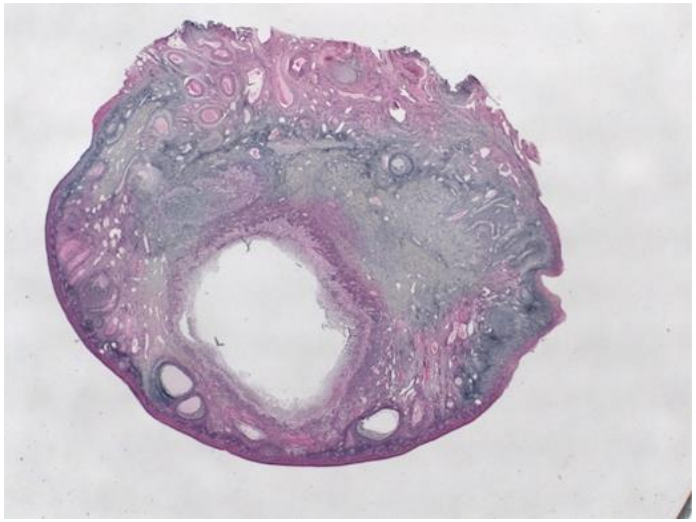
Combine sperm & oocyte to form embryo → Cryopreserve → Unthaw embryo → IVF

Prepubescent Males

Testis tissue biopsy → Cryopreserve → Unthaw tissue → Autograft → ICSI → IVF

Cancer Therapy Often Damages the Ovary and Leads to Infertility

Normal Functional Ovary

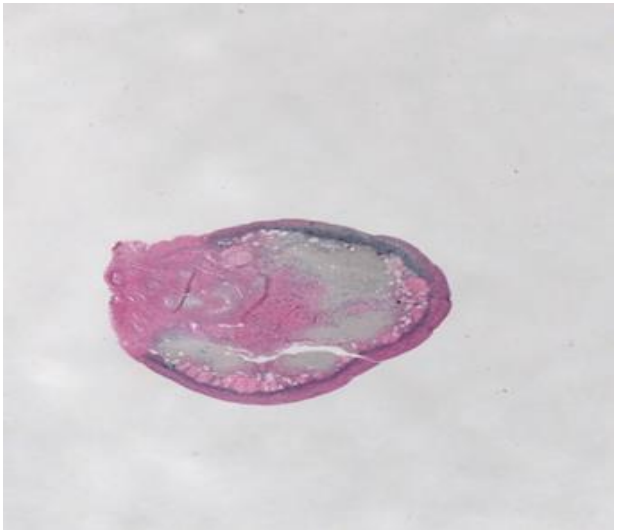


Chemotherapy or Radiation Therapy

→

Apoptosis (cell death)

Premature Ovarian Failure Infertility



Can Fertility Be Preserved in Female Cancer Patients?

Photos: Mary Zelinski, PhD, ONPRC

Options for Women

Options for women are fewer because:

- the number of oocytes is finite.
- mature oocytes are difficult to freeze.
- mature oocytes are only available on certain days of a woman's cycle.
- immature eggs can be frozen but are difficult to mature *in vitro*.

Goals for Fertility Preservation in Women

The goals of Oncofertility are to:

- understand the fundamentals of follicle development.
- develop methods to mature follicles in vitro
- provide germline preservation as an option to:

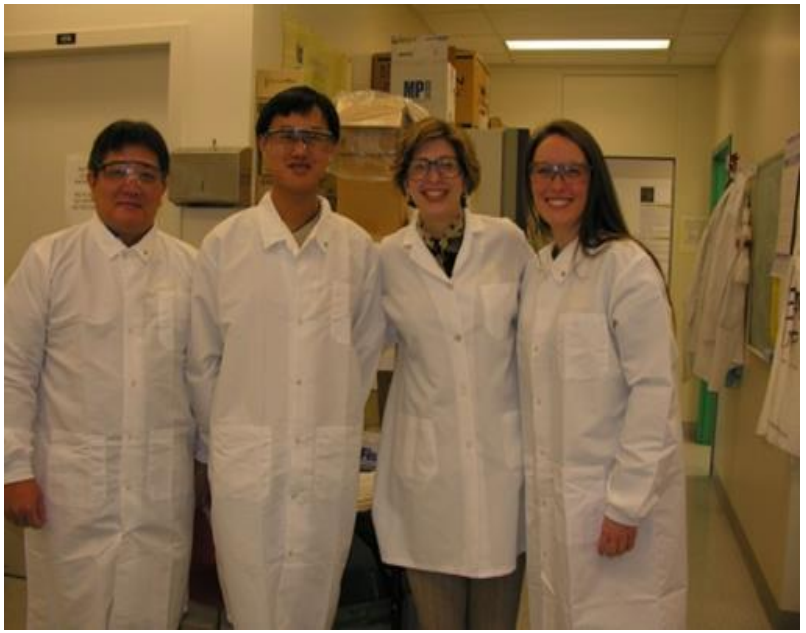
  - female cancer patients
  - NASA deep space astronauts
  - endangered and threatened species

Novel Strategies for Fertility Preservation in Women

- Ovarian protection
- Follicle culture
- Ovarian auto-grafts
- Cryopreservation – See Cryobiology section, Chapter 8.

Bioengineering Primate Follicles: From Immature Eggs to Live Births

ONPRC/OHSU



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Improving Health Advancing Science

OHSU

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Ovarian Protection

Female Rhesus Macaque
Macaca mulatta

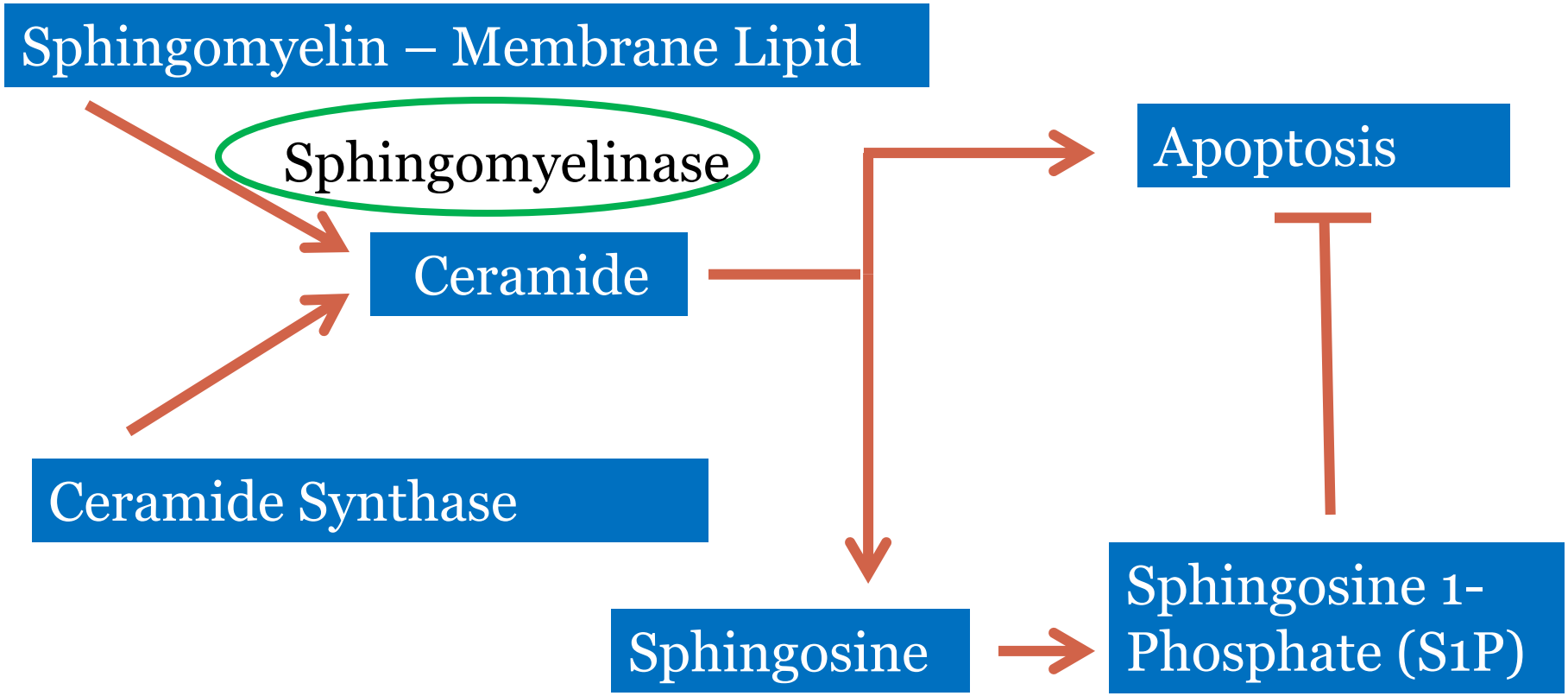
Strategies to Preserve Fertility in Females (Theoretically Possible)

Reduce or eliminate the gametotoxic effects of cancer therapy on the ovary *in vivo* by applying intraovarian Sphingosine-1-phosphate (S1P) before X-irradiation.

Hypothesis: S1P-based strategies are feasible for preserving ovarian function and fertility in primates after cancer therapies.

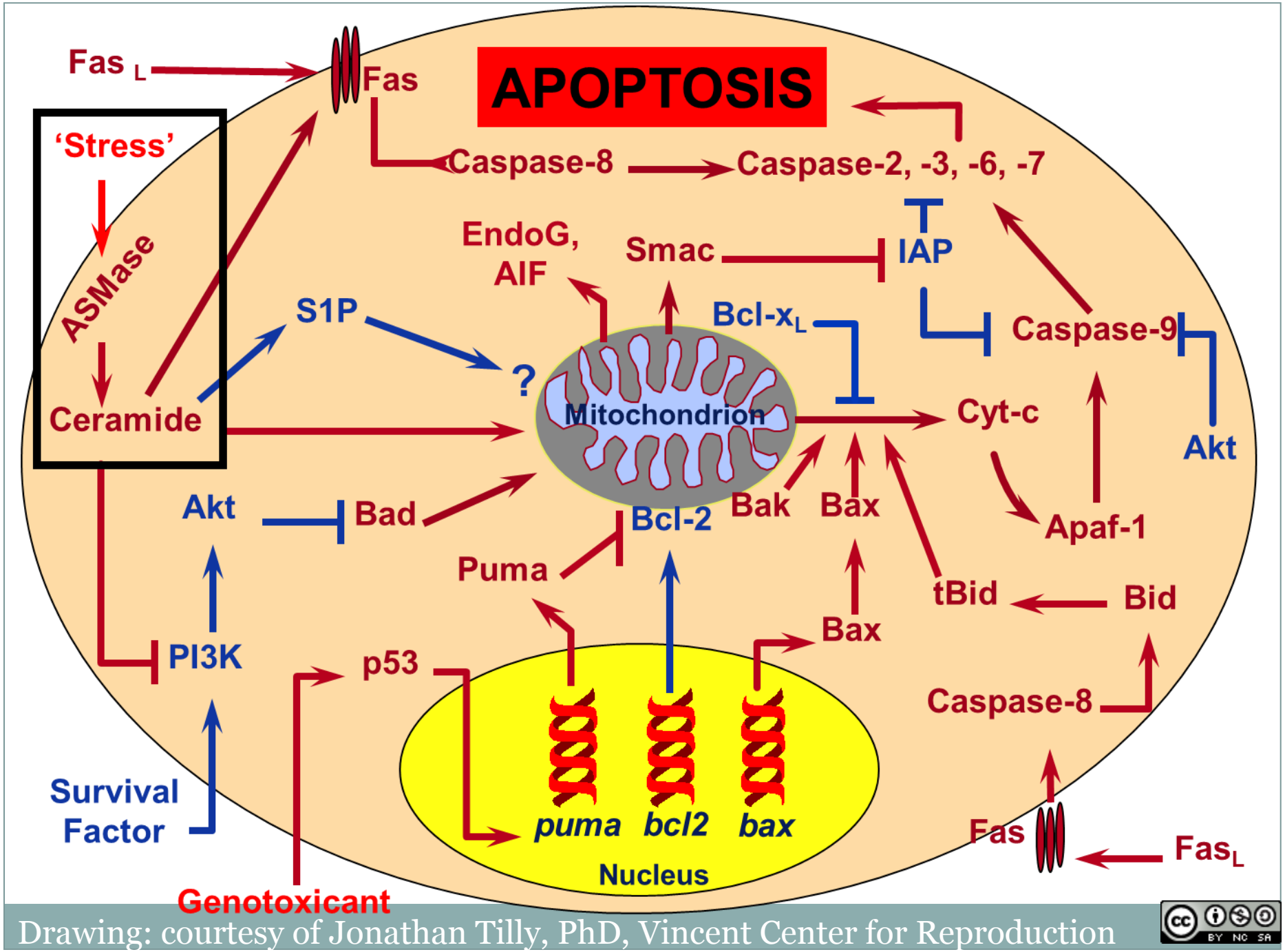
Specific Aim: To determine if S1P delivered directly into rhesus monkey ovaries can protect follicles and oocytes from radiotherapy-induced damage and preserve ovarian function.

The Sphingomyelin Pathway and Cell Death



http://www.nature.com/nrm/journal/v2/n11/full/nrm1101-838a.html

Drawing: Mary Zelinski, PhD, ONPRC and Lynda Jones, MS, ONPRC



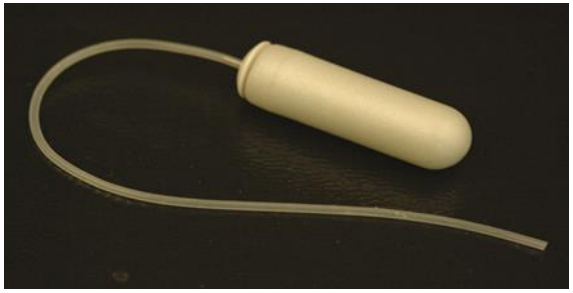
Drawing: courtesy of Jonathan Tilly, PhD, Vincent Center for Reproduction

Experimental Procedure and Results

Rhesus Females

Ages 6 – 9

Normal menstural cycles



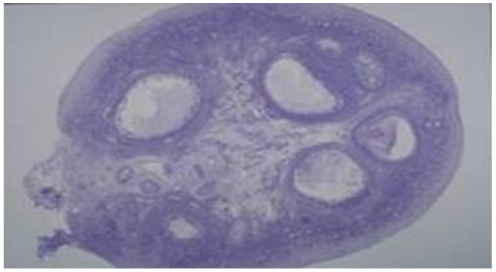
Osmotic Minipump

Method
2 osmotic minipumps sc
1 pump in each ovary
Intra-ovarian catheters

Vehicle (solution without S1P)
S1P
FTY720 (long-acting S1P)

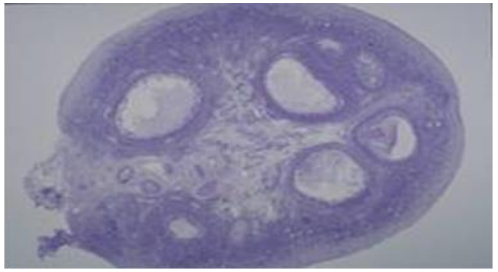
7 days

Pumps removed



One ovary removed, Before X-ray

Both ovaries intact - Females successfully mated with fertile males



One ovary removed, After X-ray 9 – 11 months

Photos: Mary Zelinski, PhD, ONPRC