

Women & Infants researchers examine role of hormone in patient responses to ovarian cancer treatment

PROVIDENCE – Researchers at Women & Infants Hospital of Rhode Island recently published the results of an investigation into how we might better tailor therapy for ovarian cancer.

The work comes out of the molecular therapeutic laboratory directed by **RICHARD G. MOORE, MD**, of Women & Infants' Program in Women's Oncology. Entitled "HE4 expression is associated with hormonal elements and mediated by importin-dependent nuclear translocation," the research was recently published in the international science journal *Scientific Reports*, a Nature publishing group.

The goal of the study was to investigate the role of the hormone HE4 in modulating an ovarian cancer's response to hormones and hormonal therapies. HE4 is a biomarker that is elevated in ovarian cancer and is known to play a role in resistance to chemotherapy.

"There is little known about the biologic functions of HE4 but we did know that there were hormonal responsive elements within the promoter region of the HE4 gene, which regulates gene expression. For this reason, we hypothesized that steroid hormones could influence expression of HE4 in ovarian cancer," Dr. Moore explains.

The study resulted in multiple findings:

Hormonal therapies like Tamoxifen and Fulvestrant are effective because they bind the estrogen receptor. If cells have less estrogen receptor expression, these drugs can't do

their job. This, the researchers believe, is due to epigenetic modifications which modify the DNA structure but not the DNA sequence itself. Overexpression led to the epigenetic modification known as decreased DNA methylation in cell culture and in human tissue samples.

Treatment of ovarian cancer cells with Tamoxifen and Fulvestrant all cause HE4 to translocate to the nucleus, where it can then effect further gene expression in cancer cells.

Using the drug Ivermectin, the researchers were able to inhibit the protein import in-4, which then inhibited HE4 from translocating to the nucleus. If HE4 can't enter the nucleus, it cannot affect gene expression. The ability to block HE4 from entering the nucleus restored sensitivity to hormonal therapy.

"We are not certain but believe this might mean there could be a subset of women whose tumors are more likely to respond to hormonal therapy. Moreover, we might be able to eventually identify which tumors these are and target treatment," Dr. Moore says.

His lab will continue to investigate the expression of estrogen receptors in both primary and recurrent ovarian cancers and how that relates to HE4 expression. In addition, he and other researchers will investigate how importin inhibitors may play a role in addressing chemoresistance to standard therapeutics, particularly in HE4 overexpressing tumors. ❖

RI is national leader in vaccination rates for children and teens

ATLANTA – Immunization rates for child and teenagers in Rhode Island are among the highest in the country, according to data released by the Centers for Disease Control and Prevention (CDC) in September.

The data was gathered through the National Immunization Survey, an annual study conducted through random telephone calls to parents and guardians and follow-up with health-care providers. Rhode Island highlights include:

- Rhode Island's immunization rate for children from 19 to 35 months of age was first in the nation for the childhood vaccine series that protects against 11 diseases (diphtheria, tetanus, pertussis, polio, measles, mumps, rubella, Haemophilus influenzae type b, hepatitis B, varicella, and pneumococcal disease). 82% of Rhode Island children completed this vaccine series.
- The vaccination rates for children in Rhode Island from 19 to 35 months

of age for varicella and hepatitis B were both greater than 96%, the best in the nation.

- Among adolescents, Rhode Island's immunization rates for the vaccines that protect against chicken pox (varicella), hepatitis B, tetanus, pertussis, diphtheria, measles, mumps, and rubella were all above 92%, well above the national averages.
- 77% of Rhode Island girls and 69% of Rhode Island boys received at least one dose of Human papillomavirus (HPV) vaccine, the highest rates in the country.
- 57% of Rhode Island girls and 43% of Rhode Island boys completed the three-dose HPV series. These rates were also first in the nation, considerably higher than the national averages of 38% for girls and 14% for boys.

"Children in Rhode Island are protected against many dangerous diseases thanks to the dedication of Rhode

Island's pediatricians, family physicians, school personnel, and many other unsung heroes," said Director of Health **MICHAEL FINE, MD**. "But as proud as I am of these numbers, we still have more work to do."

The goals of Healthy People 2020 include immunization rates of 90% for most childhood and adolescent vaccines. Healthy People is undertaken every 10 years by CDC to set national health goals.

In addition to the hard work of healthcare providers, other factors in Rhode Island's immunization success include KIDSNET, a statewide health information system, and Rhode Island's Universal Vaccine Policy. This Universal Vaccine Policy allows healthcare providers to order all vaccines for children from birth through 18 years of age at no cost.

The most recent National Immunization Survey data was gathered during 2013. ❖

Link to full report: <http://www.cdc.gov/vaccines/imz-managers/coverage/imz-coverage.html>