



Statement of

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On Behalf of

The Society of Gynecologic Oncologists

Before

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Mr. Chairman, Ranking Member and members of the subcommittee, thank you for inviting me to testify at today's hearing. My name is Dr. John C. Elkas, and I am Vice-Chairman of the Bylaws Committee and a former member of the Government Relations Committee of the Society of Gynecologic Oncologists (SGO). I practice medicine in the DC-metropolitan area, where I am an associate clinical professor in the department of obstetrics and gynecology at the George Washington University Medical Center and in private practice in Annandale, Virginia. I am also a Commander in the US Naval Reserve and an adjunct associate professor of obstetrics and gynecology for the Uniformed Services University of the Health Sciences in Bethesda, Maryland.

I am honored to be here and pleased that this subcommittee is focusing attention on the Department of Defense (DoD) Congressionally Directed Medical Research Program in Ovarian Cancer (OCRP). Since its inception now 13 years ago, this DoD program has delivered benefits to ovarian cancer research that far exceed the annual level of Federal funding.

This morning, I will try to outline some of the important contributions this DoD program has made to ovarian cancer research and the well-being of our patients. In fact, it is quite easy to demonstrate that this investment by the Federal government has resulted in substantial benefits and value to medicine, to science and most importantly improved patient care.

As this subcommittee may know, ovarian cancer usually arises from the cells on the surface of the ovary and can be extremely difficult to detect. According to the American Cancer Society, in 2009, more than 21,500 women were diagnosed with ovarian cancer and approximately 15,000 lost their lives to this terrible disease. Ovarian cancer causes more deaths than all the other cancers of the female reproductive tract combined, and is the fourth highest cause of cancer deaths among American women. One of our biggest challenges lies in the fact that only 19% of all ovarian cancers are detected at a localized stage, when the 5-year relative survival rate approaches 93%. Unfortunately, most ovarian cancer is diagnosed at late or advanced stage, when the 5-year survival rate is only 31%.

Nationally, biomedical research funding has grown over the last decade through increased funding to the National Institutes of Health, in no small part to the amazing efforts of members of this Subcommittee. Yet funding for gynecologic cancer research, especially for the deadliest cancer that we treat, ovarian cancer, has been relatively flat. Since FY 2003, the funding levels for gynecologic cancer research and training programs at the NIH, NCI, and CDC have not kept pace with inflation, with the funding for ovarian cancer programs and research training for gynecologic oncologists actually suffering specific cuts in funding due to the loss of an ovarian cancer Specialized Project of Research Excellence (SPORE) in 2007 that had been awarded to a partnership of DUKE and the University of Alabama-Birmingham. Were it not for the DoD OCRP, many researchers might have abandoned their hopes of a career in basic and translation research in ovarian cancer and our patients and the women of America would be waiting even longer for reliable screening tests and more effective therapeutic approaches.

As a leader in the Society of Gynecologic Oncologists (SGO) and as a gynecologic oncologist who has provided care to women affiliated with the United States Navy, I believe that I bring a comprehensive perspective to our request for increased support. The SGO is a national medical specialty organization of physicians who are trained in the comprehensive management of women with malignancies of the reproductive tract. Our purpose is to improve the care of women with gynecologic cancer by encouraging research, disseminating knowledge which will raise the standards of practice in the prevention and treatment of gynecologic malignancies and cooperating with other organizations interested in women's health care, oncology and related fields. The Society's membership, totaling more than 1,300, is comprised of gynecologic oncologists, as well as other related women's cancer healthcare specialists including medical oncologists, radiation oncologists, nurses, social workers and pathologists. SGO members provide multidisciplinary cancer treatment including surgery, chemotherapy, radiation therapy, and supportive care. More information on the SGO can be found at www.sgo.org.

We, the members of the SGO, along with our patients who are battling ovarian cancer every day, depend on the DoD OCRP research funding. It is through this type of research funding that a screening and early detection method for ovarian cancer can be identified which will allow us to save many of the 15,000 lives that are lost to this disease each year. Therefore,

the SGO respectfully recommends that this Subcommittee provide the DoD OCRP with a minimum of \$30 million in Federal funding for FY 2011.

Department of Defense Ovarian Cancer Research Program: Building an Army of Ovarian Cancer Researchers

- **New Investigators Join the Fight**

Since its inception in FY 1997, the DoD OCRP has funded 209 grants totaling more than \$140 million in funding. The common goal of these research grants has been to promote innovative, integrated, and multidisciplinary research that will lead to prevention, early detection, and ultimately control of ovarian cancer. Much has been accomplished in the last decade to move us forward in achieving this goal.

In Senator Mikulski's home state of Maryland, where many of my patients also live, the DOD OCRP has funded research on important questions such as:

- *Defining biomarkers of serous carcinoma, using molecular biologic and immunologic approaches, which are critical as probes for the etiology/pathogenesis of ovarian cancer. Identifying biomarkers is fundamental to the development of a blood test for diagnosis of early stage disease and also ovarian cancer-specific vaccines;*
- *Developing and evaluating a targeted alpha-particle based approach for treating disseminated ovarian cancer. Alpha-particles are short-range, very potent emissions that kill cells by incurring damage that can not be repaired; one to three alpha-particles tracking through a cell nucleus can be enough to kill a cell. The tumor killing potential of alpha-particles is not subject to the kind of resistance that is seen in chemotherapy; and*
- *Understanding of the molecular genetic pathways involved in ovarian cancer development leading to the identification of the cancer-causing genes ("oncogenes") for ovarian cancer.*

In Senator Murray's home state of Washington, the DoD OCRP has funded five grants in the last five years to either the University of Washington or to the Fred Hutchinson Cancer Center to study research questions regarding:

- *The usefulness of two candidate blood-based microRNA markers for ovarian cancer detection, and the identification of microRNAs produced by ovarian cancer at the earliest stages, which may also be the basis for future blood tests for ovarian cancer detection;*
- *The first application of complete human genome sequencing to the identification of genes for inherited ovarian cancer. The identification of new ovarian cancer genes will allow prevention strategies to be extended to hundreds of families for which causal ovarian cancer genes are currently unknown; and*
- *Proposed novel technology, stored serum samples, and ongoing clinical studies, with the intend of developing a pipeline that can identify biomarkers that have the greatest utility for women; biomarkers that identify cancer early and work well for the women in most need of early detection, that can immediately be evaluated clinically.*

One of the first, and very successful, grant recipients from the DoD OCRP hails from the Fred Hutchinson Cancer Research Center in Seattle, WA, Dr. Nicole Urban. Dr. Urban has worked extensively in the field of ovarian cancer early detection biomarker discovery and validation. Her current program in translational ovarian cancer research was built on work funded in FY 1997 by the OCRP, "Use of Novel Technologies to Identify and Investigate Molecular Markers for Ovarian Cancer Screening and Prevention." Working with Beth Karlan, M.D. at Cedars-Sinai and Leroy Hood, Ph.D., M.D. at the University of Washington, she identified novel ovarian cancer biomarkers including HE4, Mesothelin (MSLN), and SLPI using comparative hybridization methods. This discovery lead to funding in 1999 from the National Cancer Institute (NCI) for the Pacific Ovarian Cancer Research Consortium (POCRC) Specialized Program of Research Excellence (SPORE) in ovarian cancer.

The DOD and NCI funding allowed her to develop resources for translational ovarian cancer research including collection, management, and allocation of tissue and blood samples from women with ovarian cancer, women with benign ovarian conditions, and women with healthy ovaries. The DOD grant provided the foundation for what is now a mature specimen repository that has accelerated the progress of scientists at many academic institutions and industry.

In Senator Feinstein's home state of California, 24 grants have been funded by the DoD OCRP since the program was created in 1997 to study research questions such as:

- *Strategies for targeting and inhibiting a protein called focal adhesion kinase (FAK) that promotes tumor growth-metastasis. With very few viable treatment options for metastatic ovarian cancer, this research could lead to drug development targeting these types of proteins;*
- *Developing a tumor-targeting drug delivery system using Nexil nanoparticles that selectively adhere to and are ingested by ovarian carcinoma cells following injection into the peritoneal cavity. The hypothesis for this research is that the selectivity of Nexil can be substantially further improved by attaching peptides that cause the particle to bind to the cancer cells and that this will further increase the effectiveness of intraperitoneal therapy; and*
- *Using several avenues of investigation, based on our understanding of the biology of stem cells, to identify and isolate cancer stem cells from epithelial ovarian cancer. This has significant implications for our basic scientific understanding of ovarian cancer and may drastically alter treatment strategies in the near future. Therapies targeted at the cancer stem cells offer the potential for long-term cures that have eluded most patients with ovarian cancer.*

In Senator Hutchinson's home state of Texas, 19 grants have been funded since the inception of the DoD OCRP in 1997, to study research questions regarding:

- *Understanding the pre-treatment genomic profile of ovarian cancer to then isolate the predictive response of the cancer to anti-vasculature treatment, possibly leading to the identification of targets for novel anti-vasculature therapies;*
- *Ovarian cancer development directly in the specific patient and her own tumor. While this process has lagged behind in ovarian cancer and improving patient outcomes, it has shown great promise in other solid, tumor cancers; and*
- *Identifying the earliest molecular changes associated with BRCA1- and BRCA2-related and sporadic ovarian cancers, leading to biomarker identification for early detection.*

As you can see from these few examples, the 209 grants have served as a catalyst for attracting outstanding scientists to the field of ovarian cancer research. In the four year period of FY1998 – FY 2001 the OCRP enabled the recruitment of 29 new investigators into the area of ovarian cancer research.

- **Federally Funding is Leveraged Through Partnerships and Collaborations**

In addition to an increase in the number of investigators, the dollars appropriated over the last 13 years have been leveraged through partnerships and collaborations to yield even greater returns, both here and abroad. Past-President of the SGO, Dr. Andrew Berchuck of Duke University Medical Center leveraged his OCRP DoD grants to form an international Ovarian Cancer Association Consortium (OCAC) that is now comprised of over 20 groups from all across the globe. The consortium meets biannually and is working together to identify and validate single nucleotide polymorphisms (SNPs) that affect disease risk through both candidate gene approaches and genome-wide association studies (GWAS). OCAC reported last year in *Nature Genetics* the results of the first ovarian cancer GWAS, which identified a SNP in the region of the BNC2 gene on chromosome 9 (*Nature Genetics* 2009, 41:996-1000.)

Dr. Berchuck and his colleagues in the association envision a future in which reduction of ovarian cancer incidence and mortality will be accomplished by implementation of screening and prevention interventions in women at moderately increased risk. Such a focused approach may be more feasible than population-based approaches, given the relative rarity of ovarian cancer.

The DoD OCRP program also serves the purpose of strengthening US relationships with our allies, such as Australia, the United Kingdom, and Canada. Dr. Peter Bowtell, from the Peter MacCallum Cancer Centre in Melbourne, Australia, was awarded a Fiscal Year 2000 Ovarian Cancer Research Program (OCRP) Program Project Award to study the molecular epidemiology of ovarian cancer. With funds from this award, he and his colleagues formed the Australian Ovarian Cancer Study (AOCS), a population-based cohort of over 2000 women with ovarian cancer, including over 1800 with invasive or borderline cancer. With a bank of over 1100 fresh-frozen tumors, hundreds of formalin-fixed, paraffin-embedded (FFPE) blocks, and very detailed clinical follow-up, AOCS has enabled over 60 projects since its inception, including international collaborative studies in the United States, United Kingdom, and Canada. AOCS has facilitated approximately 40 publications, most of which have been released in the past two years.

One last important example of the value of the DoD OCRP's contribution to science is the program's focus on inviting proposals from the Historically Black Colleges and Universities and Minority-Serving Institutions. This important effort to reach beyond established clinical research partnerships expands the core research infrastructure for these institutions which helps

them to attract new investigators, leveraging complementary initiatives, and supporting collaborative ventures.

Over the decade that the OCRP has been in existence, the 209 grantees have used their DoD funding to establish an ovarian cancer research enterprise that is much greater in value than the annually appropriated Federal funding.

- **Opportunities are Lost Because of Current Level of Federal Funding**

These examples of achievement are obscured to a great degree by opportunities that have been missed. At this current level of funding, this is only a very small portion of what the DoD OCRP program could do as we envision a day where through prevention, early detection, and better treatments, ovarian cancer is a manageable and frequently curable disease. Consistently, the OCRP receives over 500 letters of intent for the annual funding cycle. Of this group, about 50 percent are invited to submit full proposals. Prior to FY 2009, the OCRP was only able to fund approximately 16 grants per year, a pay line of less than 7 percent. With an increase in funding to \$20 million in FY 2009, the OCRP was able to fund 22 awards. However, for FY 2010 the program was cut by \$1.25 million and so the possibility of the OCRP being able to fund even 20 grantees is in jeopardy. To provide sufficient and effective funding to enable us to do our jobs and create an environment where our scientific research can succeed, we need a minimum investment of \$30 million in FY 2011.

Department of Defense Ovarian Cancer Research Program: Exemplary Execution with Real World Results

- **Integration Panel Leads to Continuous Evaluation and Greater Focus**

By using the mechanism of an Integration Panel to provide the two-tier review process, the OCRP is able to reset the areas of research focus on an annual basis, thereby actively managing and evaluating the OCRP current grant portfolio. Gaps in ongoing research can be filled to complement initiatives sponsored by other agencies, and most importantly to fund high risk/high reward studies that take advantage of the newest scientific breakthroughs that can then be attributed to prevention, early detection and better treatments for ovarian cancer. An example

of this happened in Senator Mikulski's and my home state of Maryland regarding the development of the OVA1 test, a blood test that can help physicians determine if a woman's pelvic mass is at risk for being malignant. The investigator, Zhen Zhang, Ph.D. at Johns Hopkins School of Medicine, received funding from an Idea Development Award in FY2003. Dr. Zhang discovered and validated five serum biomarkers for the early detection of ovarian cancer. This bench research was then translated and moved through clinical trials. The OVA test was approved by the FDA and is now available to clinicians for use in patient care.

- **More Than a Decade of Scientific Success**

The program's successes have been documented in numerous ways, including 469 publications in professional medical journals and books; 576 abstracts and presentations given at professional meetings; and 24 patents, applications and licenses granted to awardees of the program. Investigators funded by the OCRP have succeeded with several crucial breakthroughs in bringing us closer to an algorithm for use in prevention and early detection of ovarian cancer.

The Society of Gynecologic Oncologists joins with the Ovarian Cancer National Alliance and the American Congress of Obstetricians and Gynecologists to urge this Subcommittee to increase Federal funding at a minimum to \$30 million in FY 2011 for the OCRP. This will allow for the discoveries and research breakthroughs in the first decade of this program to be further developed and expanded upon, hopefully bringing us by the end of the second decade of this program to our ultimate goal of prevention, early detection and finally elimination of ovarian cancer. I thank you for your leadership and the leadership of the Subcommittee on this issue.