A close-up photograph of a woman with short, grey hair and brown eyes, smiling gently. She is holding a black and tan dachshund puppy in her arms. The puppy is looking towards the camera. The background is a soft, out-of-focus green, suggesting an outdoor setting. The text 'V. Ovarian Cancer Research Program' is overlaid in white on the right side of the image.

V. Ovarian  
Cancer  
Research  
Program



“Never in my career have I witnessed a more exciting period in the field of ovarian cancer research. The past several decades have secured a foundation of scientific information that we have only just begun to apply in the clinic. Reflecting this intense period of opportunity, the past year in ovarian cancer research has been characterized by the emergence of individualized prevention programs and treatment regimens, particularly for those women at increased risk of developing ovarian cancer. This rapid translation of science into the clinic has demonstrated potential to profoundly impact the prevention and treatment of ovarian cancer—and we have only just begun. It is vitally important in the year ahead that we continue to work together—patients and their families, physicians, and scientists—to advocate for support for this delicate web that has such great potential to advance the science into the clinic, thereby bringing much-needed improvements in the care and treatment of ovarian cancer patients.”

**Nita Maihle, Ph.D.**  
**Yale University School of Medicine**  
**FY07–FY08 Integration Panel Chair**





# Accelerating Discoveries



# Vision

To eliminate ovarian cancer.

# Mission

To support research to detect, diagnose, prevent, and control ovarian cancer.

# The Disease

- ❖ One in 72 women will develop ovarian cancer in her lifetime.
- ❖ In 2008, approximately 21,650 women will be diagnosed with ovarian cancer.
- ❖ An estimated 15,520 women will die from ovarian cancer in 2008.
- ❖ The 5-year survival rate for all ovarian cancer stages is approximately 45.5 percent. For localized ovarian cancer, the 5-year relative survival rate is 92.7 percent.<sup>1</sup>
- ❖ Almost two out of every three women diagnosed with ovarian cancer die within 5 years.

## Signs and Symptoms

The following symptoms are more likely to occur in women with ovarian cancer than in women in the general population:

- ❖ Bloating
- ❖ Pelvic or abdominal pain
- ❖ Difficulty eating or feeling full quickly
- ❖ Urinary symptoms (urgency or frequency)<sup>2</sup>

Women with ovarian cancer report that symptoms are persistent and represent a change from what is normal for their bodies. The frequency and/or number of such symptoms are key factors in the diagnosis of ovarian cancer. Several studies show that even early-stage ovarian cancer can produce these symptoms. Women who have these symptoms almost daily for more than a few weeks should see their doctor, preferably a gynecologist.

Prompt medical evaluation may lead to detection at the earliest possible stage of the disease. Early-stage diagnosis is associated with an improved prognosis.

While these nonspecific symptoms are not always related to a serious condition, many women with ovarian cancer recall experiencing these symptoms.

Studies show that outcomes appear better for women whose surgery has been performed by a gynecologic oncologist with 5-year survival rates and disease-free intervals far surpassing the 5-year survival rate of patients whose doctor was a non-oncologist, obstetrician/gynecologist.

<sup>1</sup> American Cancer Society, *Cancer Facts & Figures*, 2008.

<sup>2</sup> The Gynecologic Cancer Foundation, the Society of Gynecologic Oncologists, and the American Cancer Society led an effort to develop a landmark consensus statement on ovarian cancer symptoms. This statement was released in June 2007 and was endorsed by more than 15 organizations including the Ovarian Cancer National Alliance.



# Program Background

Ovarian cancer advocates have been highly successful in their grassroots campaign to increase federal funding for ovarian cancer research. Their effort, which began in the 1990s, resulted in increased public awareness for additional research, and in fiscal year 1997 (FY97), Congressional Appropriations Conference Committee Report No. 104-863 provided \$7.5 million (M) for peer-reviewed ovarian cancer research to the Department of Defense (DOD) Ovarian Cancer Research Program (OCRP). Congress continued to appropriate to the OCRP targeted funds totaling \$121.7M from FY97 to FY08 (see Figure V-1, OCRP Funding History). Since its inception, the program has accelerated discoveries in the field of ovarian cancer research through its support for research resources, innovative research, and training of talented investigators. Today, the OCRP is recognized as a key source of extramural ovarian cancer research in the United States. A total of 170 awards were made through FY07 across research, training and recruitment, and research resources.

The remainder of this section highlights some of the efforts and progress the OCRP-supported community has made toward eliminating this disease.

“The fight against ovarian cancer has made great strides since the inception of the CDMRP Ovarian Cancer Research Program in 1997. We are in an exciting time, marked by an explosion of new areas of success in the laboratory that are translated rapidly to patients and observations from patients that have stimulated advances in the laboratory. Our progress has drawn the best and brightest into the field of ovarian cancer research, expanding our critical mass of researchers and the depth and breadth of the work now ongoing. The DOD’s Ovarian Cancer Research Program has been instrumental in identifying and addressing areas of research need, generating a balanced and forward-driving portfolio of prevention, basic biology, biomarker, and translational research. Success of OCRP-funded investigators has been amplified by subsequent funding through other mechanisms. Each funded investigator’s research brings the OCRP one step closer to fulfilling the program’s vision of eliminating ovarian cancer.”

**Elise Kohn, M.D.**  
**National Cancer Institute**  
**FY08 Integration Panel Chair-Elect**



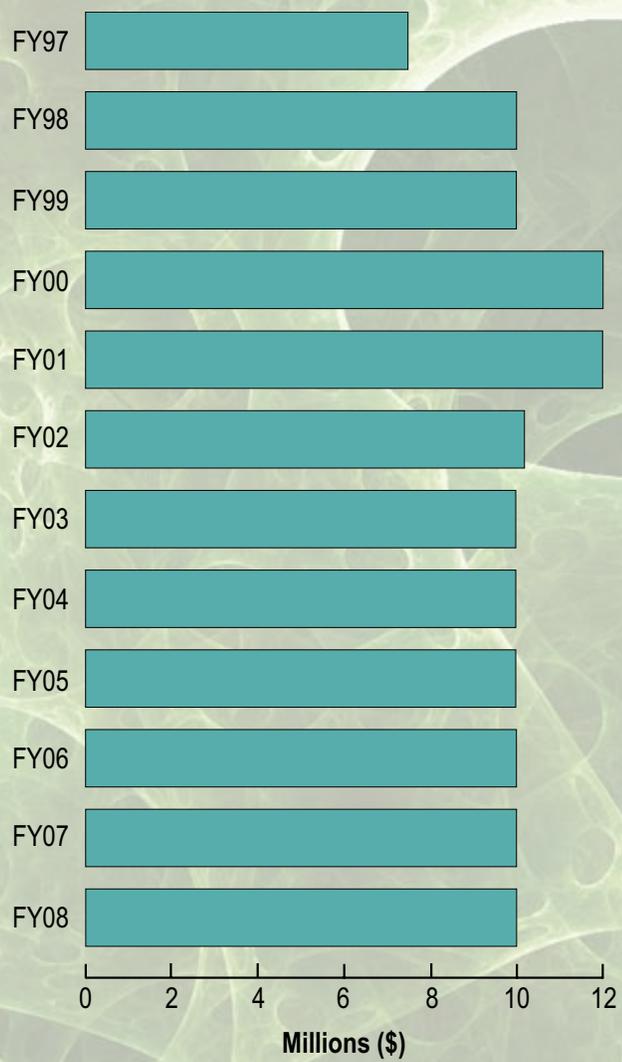


Figure V-1. OCRP Funding History

# Outstanding People

Consumer advocates (ovarian cancer survivors), peer review panel members, Integration Panel (IP) members, and OCRP-supported investigators have helped shape the program and accelerate science in the field of ovarian cancer. The OCRP recognizes the contributions and commitment of the following groups of exceptional individuals.

## Consumer Advocates

The ovarian cancer advocacy community has devoted thousands of hours to the OCRP by advocating for additional research dollars, participating in the DOD OCRP stakeholders meeting, contributing to the peer and programmatic review of proposals, and recommending program priorities. Their efforts have not gone unnoticed. Consumer advocates have contributed to peer and programmatic review since 1997. Consumer advocates' firsthand experiences with ovarian cancer provide a unique perspective that is complementary to the expertise of the scientists and clinicians on the panels. Moreover, this perspective helps

scientists understand the human side of how research will impact the community and allows for funding decisions that reflect the concerns and needs of patients, the clinicians who treat them, and survivors and their families. Equally important, consumer advocates take what they have learned from the scientists back to their advocacy communities. This results in increased awareness of the importance of research and a stronger relationship between the scientific and consumer advocate communities. Additional information about consumer advocate participation can be found in Section I, Overview.

## Peer Review Panel Members

OCRP peer review panel members represent a renowned group of research scientists, clinicians, and consumer advocates from the ovarian cancer field. Unbiased, expert advice on the scientific and technical merit of proposals is submitted to the program by individual peer review panel members. Scientific reviewers are selected for their subject matter expertise and experience with scientific peer review. Consumer reviewers are nominated by an advocacy or support organization and are

chosen on the basis of their leadership skills; their commitment to advocacy, support, and outreach; and their interest in expanding their scientific knowledge. More than 460 clinicians, scientists, and consumer advocates have contributed their expertise to the peer review process for the OCRP. Additional information about the peer review process can be found in Section I, Overview.

“Since becoming an ovarian cancer survivor, I have met many survivors as well as many women whose lives were taken by this disease. So, when asked if I would like to serve on the 2008 DOD OCRP Career Development panel, I was ecstatic and also hopeful that this program could make a difference. I was not disappointed as I witnessed on our review panel a group of researchers, physicians, and consumer reviewers with the passion of making an impact on this disease. Our panel intensely reviewed submissions in the search for the most promising proposals submitted by young researchers aspiring to pursue independent careers in ovarian cancer research. I applaud OCRP for introducing this unique funding mechanism and playing a crucial role in eliminating this disease.”

**Debbie Miller**  
**National Ovarian Cancer Coalition**  
**FY08 Peer Reviewer**



## Integration Panel Members

Serving on the IP are innovative, prominent members of the ovarian cancer community. The IP refines the program focus and investment strategy and recommends a broad portfolio of proposals for funding that reflects the investment strategy for that particular program cycle (for more information about the advisory functions of the IP, see Section I, Overview). Thus, the recommendations of individual IP members enable the OCRP to find and fund cutting-edge research and set important program priorities aimed at eliminating ovarian cancer.

“As an ovarian cancer stage IIIc survivor, I have lobbied on Capitol Hill every year since 2002 for the Ovarian Cancer Research Program. Our efforts for 2009 have already begun, and our hope is to obtain \$25 million.

I am honored to be a member of the Integration Panel and to have a voice representing all ovarian cancer survivors when it comes to determining what research the DOD funds.”

**Karen Mason**  
**National Ovarian Cancer Coalition**  
**FY08 Integration Panel Member**



## FY08 OCRP IP Members

**Nita J. Maihle, Ph.D.** (Chair)  
*Yale University School of Medicine*

**Jeffrey Boyd, Ph.D.** (Chair Emeritus)  
*Fox Chase Cancer Center*

**Deborah Armstrong, M.D.**  
*Johns Hopkins University*

**James P. Bacion, Ph.D.**  
*Case Western Reserve University*

**Lora Hedrick Ellenson, M.D.**  
*Weill Medical College of Cornell University*

**Patricia Goldman**  
*Ovarian Cancer National Alliance*

**Thomas Hamilton, Ph.D.**  
*Fox Chase Cancer Center*

**Elise Kohn, M.D.**  
*National Cancer Institute*

**Karen Mason**  
*National Ovarian Cancer Coalition*

**Alexander Nikitin, M.D., Ph.D.**  
*Cornell University*

**Sundaram Ramakrishnan, Ph.D.**  
*University of Minnesota*

**Nyrvah Richard**  
*In My Sister's Care*

**William Rodgers, M.D., Ph.D.**  
*Lenox Hill Hospital*

**Stephen Rubin, M.D.**  
*The University of Pennsylvania Medical Center*

**Michael Seiden, M.D., Ph.D.**  
*Fox Chase Cancer Center*

## Scientific Community

With more than 180 outstanding scientists and clinicians funded by the OCRP, many of whom are highlighted in this chapter, the program is accelerating discoveries in ovarian cancer research.

“DOD funding from the OCRP Pilot grant provided the avenue to my currently funded program in ovarian cancer using the chicken model.”

**Dale Hales, Ph.D.**  
**University of Illinois at Chicago**  
**FY05 Pilot Award Recipient**

“The new paradigms session at the MRS/AACR [Metastasis Research Society/American Association for Cancer Research] meeting last week was extremely well received. I presented our quorum-sensing hypothesis in concert with talks by Matt Parsek and Mike Federle who are leaders in the fields of quorum sensing and biofilms.... It was truly groundbreaking and caught a lot of people’s interest. I would never have had this opportunity without DOD ovarian cancer funding. I am totally jazzed and determined to keep moving forward on this new paradigm.”

**Carrie Rinker-Schaeffer, Ph.D.**  
**The University of Chicago**  
**Medical Center**  
**FY05 Pilot Award Recipient**



# Accelerating Discoveries

## Thinking Differently

The OCRP has succeeded in attracting some of the brightest investigators from other research areas to ovarian cancer research. They offer unique approaches and, through their diverse disciplines, think differently about ovarian cancer.



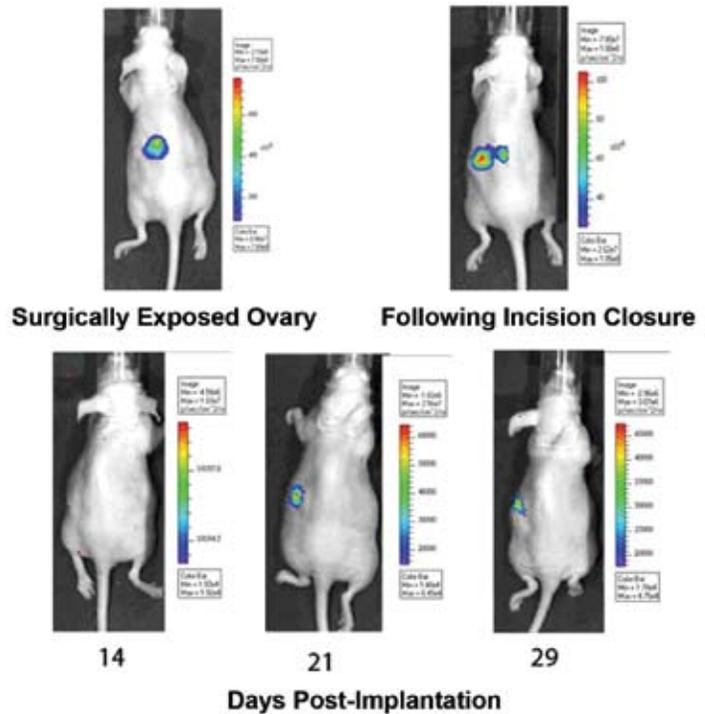
### A Venomous Attack on Ovarian Cancer

Francis Markland, Ph.D.

University of Southern California

Dr. Francis Markland of the Keck School of Medicine at

the University of Southern California studies the effects of snake venom on cancer growth and angiogenesis. With funding from an FY06 Idea Development Award, Dr. Markland is testing the hypothesis that vicrostatin, a synthetic protein whose structure is based on a natural protein found in snake venom, in combination with cytotoxic chemotherapy will be an effective therapy for ovarian cancer. Dr. Markland is also testing the potential usefulness of vicrostatin as an agent for imaging integrin-positive epithelial ovarian cancer.



### **Development of Orthotopic, Xenograft Ovarian Cancer Model**

Human cancer cells are injected into the surgically exposed ovary of middle-age Nu/Nu mice. The luciferase-transduced cancer cells are mixed with luciferin and injected locally into the left ovary. The upper left panel shows the exposed ovary with injected luciferase-transduced cells, and the upper right panel shows the luciferase-transduced cells after closing the incision. The lower panels show the viability and lack of morbidity in mice recovering from the survival surgery. These panels illustrate the persistence and viability of cells up to 29 days (from left to right: 14, 21, and 29 days). At day 14 the founding population of cancer cells is below a detectable limit, but on subsequent days, as the tumor grows, luciferase levels are detectable. Further study of the growth of orthotopic ovarian cancer is in progress in combination with the imaging potential of vicrostatin, the synthetic version of the snake-venom protein contortrostatin.



### Sniffing Out Ovarian Cancer

Touradj Solouki, Ph.D.

University of Maine

Dr. Touradj Solouki of the

University of Maine is a

chemist with expertise in mass

spectrometry. An FY06 Idea Development Award has allowed Dr. Solouki and his collaborators at the Pine Street Foundation (including Mr. Michael McCulloch, epidemiologist) to use their knowledge to develop an innovative approach for early detection of ovarian cancer. They hypothesize that exhaled breath condensate is a valuable source of biomarkers that can distinguish women with epithelial ovarian cancer from both healthy controls and women with endometriosis or polycystic ovarian syndrome. The research team is exploring this hypothesis by using both chemical methods (gas chromatography/Fourier transform ion cyclotron resonance mass spectrometry in the University of Maine's chemistry lab) and biological methods (trained dogs in the Pine Street Foundation's California lab). These studies could result in detection of ovarian cancer at an earlier stage than it can currently be detected through cancer antigen 125 (CA-125) and ultrasound.



### Crowd Control of Ovarian Cells

Carrie Rinker-Schaeffer, Ph.D.

University of Chicago

The pioneering studies of

Dr. Carrie Rinker-Schaeffer

are the first tests of quorum-sensing behavior in ovarian cells. She is applying the behavior of bacterial populations to ovarian cancer. Quorum sensing is a process of cell-cell communication that bacteria use to control gene expression in response to fluctuations in cell population density. Quorum sensing allows bacteria to act as individuals and participate in group activities. As a metastasis expert and recipient of an FY05 Pilot Award, Dr. Rinker-Schaeffer is testing the hypothesis that the quorum-sensing mechanism is involved in metastatic colonization in ovarian cancer.



# Major Challenges and Strategies

## Challenges in Ovarian Cancer

The difficult reality for at least two out of every three ovarian cancer patients is that they will be diagnosed at an advanced stage of disease. They will fight against recurrence, yet face 5-year survival rates of less than 30 percent. They will battle ovarian cancer as a chronic disease and likely undergo several different treatments. Therefore, there is a critical and urgent need to accelerate new discoveries and translate these discoveries to patients. Addressing the following issues is critical to making a major impact against the disease and in the lives of ovarian cancer patients:

- Discovering the initiating molecular events and target cells in ovarian cancer
- Detecting ovarian cancer at its earliest stages
- Improving the success of treatment of recurrent disease
- Improving the quality of life of patients while they are undergoing treatments

Answering questions in these seemingly straightforward areas has proved to be extremely challenging, partly because of the unique and baffling biology and natural history of ovarian cancer.

Understanding the origins of ovarian cancer is complicated, as it is composed of a heterogeneous and histologically complex group of tumors (serous, endometrioid, mucinous, clear-cell, and transitional cell). Furthermore, each of these groups consists of several subtypes. Ovarian tissues have distinct developmental features. Most epithelia of the female reproductive tract derive from the Mullerian ducts; however, the epithelium that lines the ovarian surface is a

modified mesothelium derived from the coelomic epithelium. Further biological challenges include identifying the target cell of origin of ovarian cancer. Confounding evidence has suggested that serous tumors may arise from cortical inclusion cysts, fallopian tubes, the secondary Mullerian system, or epithelial cells. Limited knowledge of the initiating events of ovarian cancer has hampered the detection of ovarian cancer at its earliest stages. Understanding these early events could lead to the development and targeting of effective therapies, as well as the development of animal models in which early pathogenic events can be studied.

Earlier detection of ovarian cancer could greatly improve survival rates, as the 5-year relative survival rate approaches 92 percent when ovarian cancers are detected at an early stage (stage I). Unfortunately, only 19 percent of all ovarian



cancers are caught early. Early detection is challenging because of the biology and natural history of the disease. Ovarian cancer cells are found on the outer surfaces of the ovaries, and there are no barriers to prevent malignant cells from reaching the abdomen. Many researchers believe that unlike tumors in most other cancers, ovarian tumors may have a very short stage II or may skip stage II entirely. Further, even a screening tool with 99% specificity and 100% sensitivity would detect only 1 in 21 women with a positive screen actually having ovarian cancer.<sup>3</sup>

Improved treatment of recurrent disease is a vital issue for ovarian cancer patients. Patients commonly receive a series of at least three to five treatment regimens, which raise quality-of-life issues such as managing side effects and cumulative toxicities. Cumulative toxicities are long-term effects on the body from exposure to chemotherapy agents. Optimizing the order, timing, and combination of existing therapies is a critical issue for patients and their doctors. However, the development of new therapeutic agents, such as targeted therapies, is perhaps even more vital. Many researchers believe that targeted therapies, especially angiogenesis inhibitors such as Avastin, will turn ovarian cancer into a chronic disease. However, new approaches to targeted therapy are needed because two important targets of available cancer drugs, epidermal growth factor receptor (EGFR) and human epidermal growth factor receptor 2 (HER2), may not be relevant for ovarian cancer. EGFR is infrequently mutated while HER2 is infrequently overexpressed in ovarian cancer.

## OCRP Strategies

### Targeting These High-Priority Research Areas

The OCRP has carefully considered these challenges and has designed a plan of attack, creating areas of research emphasis and encouragement. Specific areas of emphasis were required for grants solicited from 1997 to 2006. Topics included:

- **Etiology** (origins of ovarian cancer; interactions of ovarian cancer cells with the host microenvironment; and mechanisms of tumor growth, angiogenesis, invasion, progression, and metastasis)
- **Early detection** (screening tools)
- **Preclinical development of targeted therapeutics**
- **Molecular and vital imaging**

In FY07 and FY08, the OCRP developed areas of encouragement for solicited grant proposals. These specific areas of research focus were encouraged but not required.

### The FY07 areas of encouragement were:

- Imaging for early detection of ovarian cancer
- Identifying the primary lesion
- Addressing whether early and late stages of ovarian cancer are the same disease
- Monitoring quality of life associated with treatment (neuropathy, cognitive)
- Identifying and validating targets for vaccine development
- Nutritional genomics and environmental effects

### The FY08 areas of encouragement were:

- Identification of early changes associated with ovarian cancer
- Identification and characterization of ovarian cancer stem cells
- Contribution of the stroma to the tumor microenvironment in ovarian cancer

<sup>3</sup> NIH Consensus Conference. Ovarian cancer. Screening, treatment and follow-up. NIH Consensus Development Panel on Ovarian Cancer. *JAMA* 1995;273:491-7.

## Funding Cutting-Edge Research

The structure of the OCRP allows for quick yearly adjustments in funding strategies that can promote cutting-edge science. Many OCRP-funded projects are some of the first studies of their kind in ovarian cancer. Some examples of the FY07 awards include:

### Initiating Events in Ovarian Cancer

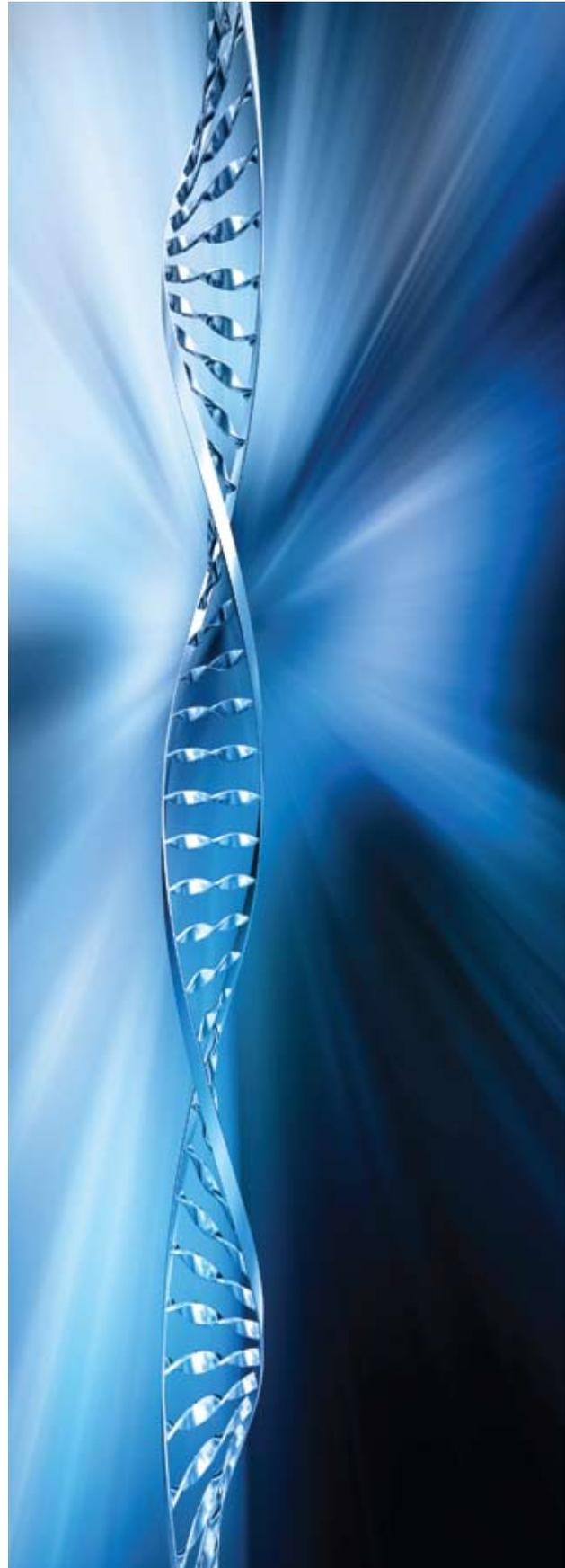
- Isolating stem cells from a new rat model of spontaneous ovarian cancer
- Developing a new generation of bioreactors containing human liver cells and proliferating metastatic ovarian tumor cells to identify the emergence of therapy-resistant stem cells
- Developing a new mouse model to test whether ovarian cancer originates in the fallopian tube

### Early Detection

- Developing a new MRI (magnetic resonance imaging) strategy that uses nanoparticle probes
- Using a hen model system, testing whether anti-ovarian antibodies in the blood precede ovarian cancer
- Testing for mutations in human microRNAs

### New Therapeutic Strategies

- Identifying microRNA therapeutic targets for chemoresistant disease
- Using epigenetic therapies to enhance the effectiveness of paclitaxel
- Developing a new drug that targets paclitaxel directly to tumor cells and stimulates the immune system
- Using the organ-rejection immune response to destroy ovarian cancers
- Using statins (cholesterol-lowering drugs) to decrease metastases and blood clots in ovarian cancer patients



## Challenging Roadblocks

During the past year, OOCR investigators have made several exciting discoveries that could lead to a better understanding of ovarian cancer etiology, improved diagnosis, and new therapeutic strategies. Improvements in these areas could greatly impact ovarian cancer patients. Several success stories are highlighted here.

### New Therapeutic Targets and Strategies for Recurrent Disease

#### Targeting the Tumor Vasculature

George Coukos, M.D., Ph.D.

University of Pennsylvania

Dr. George Coukos (pictured below) of the University of Pennsylvania is targeting tumor vasculature cells to suppress ovarian cancer growth. With funding from an FY05 Idea Development Award, Dr. Coukos' team found that the antiangiogenesis drug SU5416 in combination with low-dose paclitaxel provided therapeutic advantage in tumors with low levels of vascular endothelial growth factor (VEGF). The researchers are also targeting human tumor vascular cells through tumor endothelial marker 1 (TEM1). They developed innovative in vivo models to test human

TEM1-targeting tools in mice. Additionally, Dr. Coukos' team validated the tumor vascular markers adlican and DR6 as therapeutic targets. They found high levels of adlican in ovarian cancers but low levels in normal tissues. Furthermore, adlican protein was detected in the tumors, ascites, and sera of ovarian cancer patients but not in normal sera. DR6 was highly expressed in the vasculature of solid tumors. DR6 protein was detected at higher levels in the sera of patients with ovarian cancer than what was found in control individuals. These results suggest new strategies for targeting tumor vasculature and designing rational combinatorial therapy to treat ovarian cancer.





### Targeting PELP-1 to Overcome Resistance to Endocrine Therapies

Ratna Vadlamudi, Ph.D.

University of Texas Health Science Center at San Antonio

Dr. Ratna Vadlamudi, recipient of an FY05 Pilot Award, provided the first evidence for the role of proline, glutamic acid, and leucine-rich protein 1 (PELP-1) in ovarian cancer tumorigenesis and its usefulness as a therapeutic target for ovarian cancer. PELP-1 is a novel estrogen receptor coactivator protein that Dr. Vadlamudi hypothesizes may be involved in the resistance of ovarian tumors to endocrine therapies. Dr. Vadlamudi's team showed that PELP-1 functioned as a novel proto-oncogene in ovarian cancer cells and played an essential role in the activation of the c-Src and AKT pathways. Additionally, PELP-1 played a critical role in cytoskeletal reorganization and cell morphology. The researchers showed that downregulation of PELP-1 through shRNA (short-hairpin RNA) methods resulted in decreased tumorigenic potential of ovarian cancer cells in animal models. Furthermore, downregulation of PELP-1 sensitized ovarian cancer cells to carboplatin and paclitaxel, suggesting that targeting PELP-1 could enhance the potency of chemotherapeutic drugs.



### Evaluating EphA2 as a Novel Therapeutic Target

Anil Sood, M.D.

M.D. Anderson Cancer Center

Dr. Anil Sood, recipient of an FY03 Idea Development Award, is pioneering the first studies on the functional role of EphA2 in ovarian cancer growth and the evaluation of EphA2 as a therapeutic target for ovarian cancer. EphA2 is a transmembrane receptor tyrosine kinase that is paradoxically overexpressed but not phosphorylated in invasive, aggressive ovarian cancers. Dr. Sood's team showed that EphA2 overexpression is an independent predictor of poor outcome in ovarian cancer. Additionally, the combination of EphA2 overexpression and p53 null status was associated with decreased overall patient survival and increased incidence of ascites and distant metastases. The researchers also

found that EphA2 overexpression in endothelial and ovarian cancer cells was strongly associated with critical factors involved in angiogenesis and invasion—specifically, microvessel density and matrix metalloproteinase expression. Dr. Sood's team successfully demonstrated in vitro and in vivo gene silencing of EphA2 by using small interfering RNA (siRNA) and antibody approaches that were effective in reducing tumor growth. Based on the results of these preclinical studies, Dr. Sood's group is currently developing both systemically delivered siRNA and antibody approaches that target EphA2 for clinical trials in ovarian cancer patients.



### New Targets for Immunotherapy

Kevin Hogan, Ph.D.

University of Virginia

Dr. Kevin Hogan, an FY04 New Investigator Award recipient, is identifying new ovarian cancer tumor antigens that can be used in the immunotherapeutic treatment of ovarian cancer. Dr. Hogan's team found that the TAG family of cancer/testis antigens was expressed in ovarian cancer cells. The researchers identified two human leukocyte antigen (HLA)-A2-restricted epitopes in the TAG proteins and showed that cytotoxic T lymphocytes specific for each of these peptides were capable of recognizing tumor cells expressing both the corresponding class I major histocompatibility complex-encoded molecule and the TAG genes.

## New Diagnostic Targets for Earlier Detection of Ovarian Cancer



### Analyzing Mitochondrial DNA Mutations

Felix Aikhionbare, Ph.D.

Morehouse School of Medicine

Dr. Felix Aikhionbare is searching for mutations associated with early-stage ovarian cancer through a novel approach of analyzing mitochondrial DNA instead of nuclear DNA. With funding from an FY04 New Investigator Award, Dr. Aikhionbare

and his team discovered 238 new mitochondrial DNA sequence variants. The researchers identified specific mutations that distinguished the histologic subtypes (serous, endometrioid, and mucinous) of ovarian cancer. Another mutation was observed only in early-stage serous tumors. Furthermore, two mutations were observed at high frequency specifically in ovarian cancer tissues derived from African American women.



### Profiling Ovarian Serous Carcinomas

Tian-Li Wang, Ph.D.  
Johns Hopkins University  
FY04 New Investigator Award recipient, Dr. Tian-Li Wang,

performed the first comprehensive analysis of DNA copy number changes in highly pure ovarian serous carcinoma. Ovarian serous carcinoma is the most common and lethal type of ovarian cancer, but its molecular etiology is poorly understood. Dr. Wang's team found a high level of DNA copy number gain (amplification) in the CCNE1, Notch3, HBXAP/Rsf-1, AKT2, and PIK3CA gene loci in high-grade but not low-grade serous carcinomas. These results suggest distinct genomic profiles for high-grade and low-grade ovarian serous tumors. The findings indicate that these two subtypes develop along distinct molecular pathways, with high-grade serous carcinoma being characterized by pronounced chromosomal instability. The identified amplified loci could be novel targets for improving the diagnosis and treatment of ovarian serous cancers.



### First Proteomic Analysis of Ascites

Igor Jurisica, M.Sc., Ph.D.  
University Health Network  
University of Toronto

With support from an FY04 New Investigator Award, Dr. Igor Jurisica in collaboration with Dr. Thomas Kislinger performed the first high-quality, in-depth proteomics analysis of ovarian cancer ascites. Ascites fluid typically accumulates in the peritoneal cavity of patients with advanced disease, and proteomic information on ascites may be valuable for understanding the

mechanisms of chemoresistance, a significant problem in recurrent disease. Dr. Jurisica's research team analyzed ascites from ovarian cancer patients with high-grade serous carcinoma. They identified 80 putative biomarkers that were reproducibly detected in all four ovarian cancer ascites samples. Eighteen of these proteins were previously reported as secreted proteins in plasma or urine and are thus the best candidates for a diagnostic test. These proteins have important cellular functions, including growth, differentiation, and metabolism, and could potentially be used for disease surveillance and for monitoring treatment responses.

## New Discoveries of the Fundamental Mechanisms Underlying Ovarian Cancer



### New Links Between Genomic Instability and Cilia

Erica Golemis, Ph.D.  
Fox Chase Cancer Center

Dr. Erica Golemis is exploring how the human enhancer of filamentation 1 (HEF1) and Aurora A (AurA) proteins contribute to genomic instability and metastatic properties of ovarian tumors. HEF1 and AurA function by controlling centrosome stability. With funding from an FY05 Pilot Award, Dr. Golemis' team showed that HEF1-dependent AurA activation induced disassembly of cilia. Cilia are cellular projections that act as antennae to sense stimuli and induce appropriate responses. The team found that HEF1 and AurA mediated ciliary disassembly through activation of histone deacetylase 6 (HDAC6). The researchers found that small-molecule inhibitors of AurA and HDAC6 selectively stabilized cilia from regulated resorption cues, suggesting a novel mode of action for these clinical agents. These findings have clinical implications for ovarian cancer patients, as they suggest that AurA- or HDAC-targeted drugs may have in vivo effects involving cilia that may contribute to the efficacy and side effects of these agents.



### New Links Between Homeobox Genes and Angiogenesis

Honami Naora, Ph.D.  
M.D. Anderson Cancer Center

Dr. Honami Naora hypothesized that an ovarian surface epithelium has an embryonic-like phenotype that resembles that of hematopoietic progenitor cells and, therefore, could also be highly susceptible to the effects of aberrant homeobox gene activation. An FY05 Idea Development Award has allowed Dr. Naora and her team to focus on the DLX4/BP1 homeobox gene, which is located on chromosome 17q in a region whose amplification correlates with poor prognosis in ovarian cancer. These researchers found that DLX4 was not expressed in normal ovaries and cystadenomas, but that its expression in ovarian carcinomas was significantly associated with high tumor grade and advanced disease stage. Imaging of mice bearing intraperitoneal ovarian tumors revealed that DLX4 overexpression substantially increased tumor burden and tumor vascularization. Furthermore, DLX4 induced expression of vascular endothelial growth factor as well as intracellular and secreted isoforms of fibroblast growth factor-2. These findings show a novel, proangiogenic, growth stimulatory mechanism for a homeobox gene in promoting ovarian tumorigenesis and suggest new therapeutic targets and strategies for ovarian cancer.



### Effects of MUC16 (CA-125) on Immune Cells

Manish Patankar, Ph.D.

University of Wisconsin-Madison

FY03 Idea Development Award recipient, Dr. Manish Patankar, is studying novel functions of MUC16, a large-molecular-weight glycoprotein that is overproduced by epithelial ovarian tumor cells. The diagnostic marker, CA-125, is a peptide epitope present on MUC16. Ovarian cancer cells express MUC16 on the cell surface, and it is shed in the surrounding milieu. Dr. Patankar's group has shown that the shed MUC16 binds to immune cells and inhibits their anti-tumor cytolytic responses. Cell-surface-bound MUC16, because of its large size, shields tumors and prevents immune cells from efficiently interacting with cancer cells. The net result of the actions of shed and cell-surface-bound MUC16 is evasion of immune responses by cancer cells. In addition to its immune modulating functions, MUC16 plays an important role in facilitating peritoneal metastasis of ovarian cancer cells. The molecular definition of the biological role of MUC16 helped devise strategies for the detection and treatment of ovarian cancer. Dr. Patankar is building on these findings

by developing a new diagnostic test based on bound forms of MUC16 to monitor regression and recurrence of ovarian cancer.

# Leveraging Research Tools

An important goal of the OCRP is to establish sustainable shared resources for studying ovarian cancer. OCRP investigators generated several resources including tissue repositories, databases, biomarkers, computational tools, and a decision-making guide for women at high risk of developing ovarian cancer as shown in Table V-1. Success stories include the generation of new animal models that are valuable tools for understanding the etiology of ovarian cancer, developing improved diagnostic tools, assessing chemopreventive agents, and testing therapies in preclinical studies.

*Table V-1. OCRP-Supported Research Resources*

Principal Investigator	Research Resource
Dr. Nicole Urban	Repository with over 6,000 individually identified ovarian tissue specimens
Dr. David Bowtell	Multicenter population-based resource of linked epidemiologic and clinical data and biospecimens from 1,000 cases and 1,200 matched controls
Dr. Beth Karlan	Human ovarian tissue and clinical database containing ovarian carcinomas (152) and benign ovaries (110)
Dr. Samuel Mok	New biomarkers for early-stage ovarian cancer
Dr. Igor Jurisica	Computational tools and methods for analysis of complex biochemical, biological, and clinical data on epithelial ovarian cancer at no cost to the public
Drs. Gus Rodriguez and Patricia Johnson	Chicken models of ovarian cancer
Dr. Tyler Jacks	Mouse model of ovarian cancer associated with endometriosis
Dr. Louis Dubeau	Mouse model with homozygous BRCA1 knockout restricted to ovarian granulosa cells
Dr. Mary Daly	Book, "Ovarian Cancer Risk-Reducing Surgery: A Decision-Making Resource" (available to the public at no cost)
Dr. Santo Nicosia	Ovarian cancer tissue repository with more than 600 samples
Drs. Kathleen Cho and Rong Wu	Mouse model of OEA (ovine enzootic abortion)
Dr. David Gershenson	Nonhuman primate model
Dr. Xiangxi (Mike) Xu	Mouse model for postmenopausal ovarian cancer risk



David Gershenson, M.D.

Molly Brewer, M.D.

University of Texas M.D.

Anderson Cancer Center

Drs. David Gershenson and Molly

Brewer chose to investigate

rhesus macaques in chemoprevention studies.

With support from an FY98 Program Project

Award, they treated the monkeys with oral

contraceptives and a synthetic vitamin A or retinoid

and examined biomarkers in ovarian biopsies for

model assessment. The team found that these

nonhuman primates served as excellent models for

ovarian cancer chemoprevention due to their drug

tolerance, the ease of surgical intervention, the

monkeys' close genetic relationship to humans, and

their availability.

Gustavo Rodriguez, M.D.

Evanston Northwestern Healthcare Research Institute

An FY99 Idea Award enabled Dr. Gustavo

Rodriguez to further characterize the domestic

laying chicken as an animal model for ovarian

cancer prevention research. Readily available,

these hens spontaneously develop ovarian cancer

at a high rate. Since they ovulate frequently

(almost daily), it is possible that the pathogenesis

of these cancers may mimic the pathogenesis of

ovarian cancer in women, which is characterized

by increasing risk associated with an increased

number of lifetime ovulatory events. Furthermore,

studies have demonstrated that the clinical and

molecular features of ovarian cancer in chickens

and women are similar in a number of important

areas, including molecular pathways, biomarkers,

and pattern of metastatic dissemination. Thus,

Dr. Rodriguez believes that the chicken model

has considerable value for comparative studies of

ovarian cancer progression and should be more

widely considered and used.



Rong Wu, M.D. (top)

Kathleen R. Cho, M.D. (bottom)

University of Michigan

Drs. Rong Wu and Kathleen R.

Cho have established a novel mouse model of endometrioid carcinoma induced by

conditional inactivation of tumor suppressor genes (Apc and Pten) in the mouse ovarian surface epithelium. The tumors were

grossly apparent within 6 weeks of the induction and resembled

human tumors morphologically and genetically.

After initial funding from an FY03 New Investigator Award, the research team continues developing this model to be used as a tool for preclinical testing of novel therapeutics targeting Apc and Pten signal transduction pathways.

Tyler E. Jacks, Ph.D.

Massachusetts Institute of Technology

Another mouse model for both endometriosis and ovarian cancer has been successfully developed by Dr. Tyler E. Jacks, recipient of an FY04 Idea Development Award. The hallmark of the new model is the use of oncogenic K-ras in combination with inactivated Pten. The model will serve as an invaluable tool for the in vivo testing of molecularly targeted chemotherapy as well as conventional anticancer agents.



Louis Dubeau, M.D.

University of Southern California

FY03 Idea Development Award

recipient, Dr. Louis Dubeau,

developed a mouse model with the inactivated BRCA1 gene

specifically in ovarian granulosa cells. Granulosa cells normally produce sex hormones that regulate the ovulatory cycle and influence cell growth.

Two-thirds of these animals developed serous adenomas in the ovaries and uterine horns.

Findings from this model indicated an important

new role for BRCA1 in the etiology of ovarian cancer—specifically, that granulosa cells in the ovary are the critical cells affected by

BRCA1 inactivation.



Xiangxi (Mike) Xu, Ph.D.

Fox Chase Cancer Center

Dr. Xiangxi (Mike) Xu (and who is now continuing the project at the University of Miami Sylvester

Cancer Center) developed new mouse models for studying postmenopausal ovarian cancer risk.

With funding from an FY05 Idea Development

Award, Dr. Xu's team used the germ cell-deficient Wv mice to study the etiology of ovarian cancer risk. These mice mimic postmenopausal biology

phenotypes and develop benign ovarian tumors. The researchers crossed these mice with mice

lacking the p53, p27, or Pten tumor suppressor genes to generate mice with both germ cell

depletion and oncogenic mutations. These mice showed alterations in the ovarian surface

epithelium and increased malignant phenotypes of the ovarian tumors. From these models, Dr. Xu's

team hopes to gain insights into the etiology of ovarian cancer related to reproductive factors.

## Development and Commercialization

The goal of the CDMRP Technology Transfer Initiative (TTI) is to facilitate the continuation of advanced, clinically relevant CDMRP-funded research projects beyond preclinical and early-phase clinical trials. The TTI seeks to bridge partnerships between CDMRP-funded investigators and the medical research and development community so that additional clinical research, manufacturing, and commercialization can bring to market the results of CDMRP-funded discoveries, leading to new medicines, devices, and therapies for the patient community.

The OCRP strives to develop and commercialize products that will impact ovarian cancer patients. OCRP-funded research has led to several exciting findings with commercial potential. Twenty-three patents or patent applications have resulted from 12 awards. Two examples of issued patents are “Mutant Endostatin: Promising Antiangiogenic Therapeutic Agent for Ovarian Cancer” (Dr. Sundaram Ramakrishnan) and “Methods for the Early Diagnosis of Ovarian Cancer” (Dr. Martin J. Cannon).



### Identification of Biomarkers for the Detection of Early-Stage Ovarian Cancer

Zhen Zhang, Ph.D.

Johns Hopkins University

FY03 Idea Development

Award recipient, Dr. Zhen Zhang, employed bioinformatics tools and proteomic expression profiles of human sera to identify and validate five potential biomarkers—ApoA1, TTR, ITIH4, hepcidin, and CTAP3/NAP2—for detection of epithelial ovarian cancer. In addition to ApoA1, TTR, and ITIH4, the investigators have filed patents on the two newly discovered biomarkers hepcidin and CTAP3. Studies revealed that CTAP3 serum levels were significantly higher in stage I/II ovarian cancer patients compared with healthy controls. Hepcidin variants were elevated in cancer patients pretreatment, receded after surgery, and elevated again after cancer recurrence. The investigator will further validate these biomarkers in clinical studies.



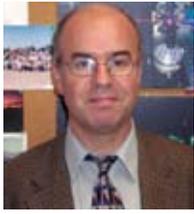
### Computational Biology Approach to Marker Selection for Early Detection of Epithelial Ovarian Cancer

Igor Jurisica, M.Sc., Ph.D.

University Health Network

University of Toronto

Dr. Igor Jurisica’s research team developed a sensitive computational biology tool, the Online Predicted Human Interactive Database (OPHID). OPHID is a database of predicted and known human protein–protein interactions. This technology integrates and analyzes existing and emerging data sets of altered gene and protein expression in epithelial ovarian cancer and other cancers. This project has created companion graphic visualization software, called NAViGaTOR (Network Analysis, Visualization, and Graphing TORonto), which stores, analyzes, and visualizes protein–protein interactions to better interpret molecular profiles of cancer.



### Early Detection and Diagnosis of Ovarian Cancer Using Novel Sensitive Optical Techniques

Nouredine Melikechi, Ph.D.  
Delaware State University

Dr. Nouredine Melikechi and his team have developed sensitive laser optical techniques to identify blood biomarkers aimed at the early detection of epithelial ovarian cancer. An FY05 HBCU/MI Collaborative Research Award enabled the team to study laser-induced breakdown spectroscopy, Fourier transform infrared spectroscopy, absorption spectroscopy, and photothermal lens spectroscopy methods for their promise to ascertain minute differences in cancer protein biomarkers in biosamples such as blood, plasma, and sera. These optical lasers were able to distinguish differences in spectra signatures between blood samples from a wild-type and a tumor-prone mouse model. The ovarian cancer mouse model was supplied by collaborators at Fox Chase Cancer Center.



### Cancer-Specific Compounds Developed for Therapy and Diagnosis of Ovarian Cancer

Janina Baranowska-Kortylewicz, Ph.D.  
University of Nebraska

Ovarian cancer tumors that have a higher fraction of cells in cell cycle S-phase are regarded as more difficult to treat and are considered to be predictive of poor prognosis. FY03 Idea Development Award recipient, Dr. Janina

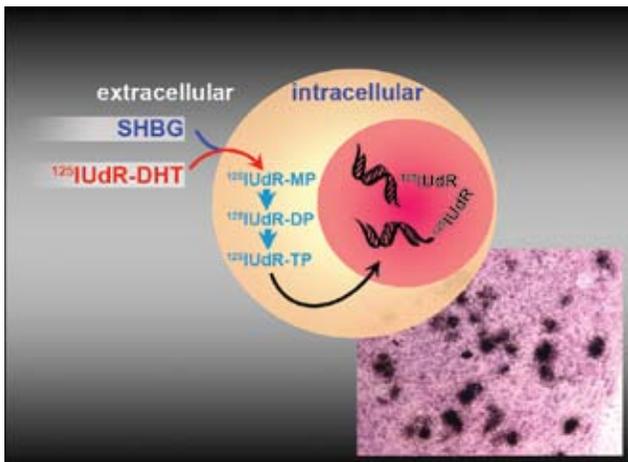
Baranowska-Kortylewicz, developed new classes of radiopharmaceutical drugs that are ovarian cancer specific and will preferentially kill aggressively growing tumors. The targeted delivery system uses two agents: dihydrotestosterone (DHT) as the receptor-based tumor-seeking moiety and the cell cycle-dependent drug 5-radioiodo-2'-deoxyuridine ( $^{125}\text{I}$ UdR). This drug combination has a higher uptake into the DNA of tumor cells that are both androgen receptor positive and have higher S-phase fractions. Both in vitro and in vivo studies have confirmed the efficacy of this new class of drugs.



### Double-Targeted Macromolecular Therapeutics for the Treatment of Ovarian Cancer

Jindrich (Henry) Kopecek, Ph.D., D.Sc.  
University of Utah

With funding from an FY04 Idea Development Award, Dr. Jindrich Kopecek and colleagues designed macromolecular therapeutics capable of delivering drugs not only to tumor sites but also to a particular subcellular compartment within tumor cells. Photosensitizers (PSs) bound to targetable water-soluble polymer carriers via enzymatically cleavable oligopeptide or reducible disulfide spacers release PSs intracellularly. Improved efficacy of such conjugates has been achieved by specifically targeting the nucleus and mitochondria, two subcellular compartments vulnerable to photochemical damage. The novel strategy to achieve tumor and subcellular targeting could be applied successfully to other therapeutic agents and tumors.



## Unique Partnerships

The key initiative of the Translational Research Partnership Award offered in both FY07 and FY08 is to encourage a research partnership between a clinician and a laboratory scientist that accelerates the movement of promising ideas in ovarian cancer into clinical applications. This award is designed to support collaborations between two independent investigators who have unique skills and have made unique contributions to address a central problem or question in ovarian cancer in a manner that would be less readily achievable through separate efforts.

New for FY08 is an optional Non-Traditional Partnership Award to leverage resources in the ovarian cancer research community by providing intellectual input and contributing research resources and/or financial resources. The optional Non-Traditional Partnership may be between an academic institution/government agency and a biotechnology/pharmaceutical company; between an academic institution/government agency and a foundation; or between a biotechnology/pharmaceutical company and a foundation.



## Promising Scientists

The OCRP supports the development of independent researchers in ovarian cancer research. Since the program's inception, the OCRP has worked toward recruiting and retaining promising ovarian cancer scientists. In previous years, the OCRP has offered the New Investigator Award and the HBCU/MI<sup>4</sup> Fellowship Award. For FY08, the Career Development Award (Phase I) was introduced. Pending congressional appropriations, a Phase II Career Development Award to sustain these investigators' research will be offered in 2011. This award provides training opportunities and supports individuals in the early stages of their careers by offering the chance to obtain the funding and experience necessary to pursue an independent career at the forefront of ovarian cancer research.



*Kathleen R. Cho, M.D.*

*University of Michigan*

In FY00, Dr. Cho of the University of Michigan received a New Investigator Award. During this award, she validated and used a restriction landmark genome scanning analysis and its informatics tool (virtual genome scan) to predict regions of gene amplification. With this methodology, she demonstrated that the L-MYC gene is amplified in a subset of ovarian carcinomas and that the fibroblast growth factor 9 gene is overexpressed in ovarian carcinomas as well. Dr. Cho worked as a collaborator on Dr. Rong Wu's FY03 New Investigator Award that developed an ApcloxP/loxP; PTENloxP/loxP mouse model of ovarian endometrioid adenocarcinoma. Further studies on this mouse model and other ovarian cancer mouse models will continue under Dr. Cho's recently funded FY07 Translational Research Partnership Award. Dr. Cho and her partner, Dr. Alnawaz Rehemtulla, will study ovarian cancer biology and test for novel therapeutic paradigms using these genetically engineered mouse models with human ovarian cancer.



*Denise C. Connolly, Ph.D.*

*Fox Chase Cancer Center*

Dr. Denise Connolly of the Fox Chase Cancer Center received a New Investigator Award in FY03. She developed a mouse model of human epithelial ovarian cancer with inactivated BRCA1 and p53 genes. Dr. Connolly found ovarian and non-ovarian neoplasms in mice that had undergone conditional inactivation of the loxP-flanked alleles of the BRCA1 and p53 genes and that received intrabursal injections of adenovirus-cre recombinase. From one of the ovarian leiomyosarcomas, she was able to establish tumor cell lines as well. A 2006 Concept Award continues her investigation into BRCA1 and transformation-related protein 53 (Trp53) inactivation. In that study, Dr. Connolly is investigating the effects of the genes' inactivation in the ovarian stroma on the epithelial cell growth and neoplastic transformation in mouse ovarian surface epithelial cells (MOSE).

<sup>4</sup> Historically Black Colleges and Universities/  
Minority Institutions

Early results show that MOSE cells with the mutant form of the Trp allele have a growth advantage over those cells with wild-type Trp53. In addition to her own work, Dr. Connolly is a primary collaborator on Dr. Nouredine Melikechi's (see page V-24) HBCU/MI Collaborative Research Award. As Dr. Melikechi's mentor, she is providing blood samples from normal and epithelial ovarian cancer-prone mice to further the development of sensitive optical techniques for the detection of ovarian cancer.



Jin Q. Cheng, M.D., Ph.D.

University of South Florida

Dr. Jin Cheng of the University of South Florida was first funded by the OCRP in FY99 with a New Investigator Award that looked at the phosphoinositide 3-kinase/AKT1 pathway and ovarian cancer. In addition, he was a Principal Investigator for two of the research projects under Dr. Santo Nicosia's FY01 Program Project Award. In one project, he found elevated AKT2 protein levels in more than 40 percent of tumors, most of which were stage III or stage IV grade. Dr. Cheng also found that farnesyltransferase inhibitor (FTI) and cisplatin caused apoptosis in cells at a significantly higher rate than cisplatin alone. In AKT2-induced cisplatin-resistant epithelial ovarian cancer cells, FTI and a geranylgeranyl transferase I inhibitor (GGTI-298) stimulated apoptosis. In the second project, Dr. Cheng showed that ascorbyl stearate (vitamin C) brought about apoptosis in several ovarian cancer cell lines and decreased phosphorylated AKT expression. In FY05, Dr. Cheng received an Idea Development Award studying the Aurora-A oncogene. Thus far, he has observed that Aurora-A expression overrides cisplatin-induced apoptosis as well as gamma-irradiation-generated cell cycle arrest by targeting p53. Cells that were transfected to express Aurora-A were resistant to apoptosis produced by cisplatin, Taxol, and etoposide. Currently, Dr. Cheng has an FY07 Concept Award that will examine the role that micro RNAs have in ovarian cancer resistance to cisplatin and Taxol.



Patricia Kruk, Ph.D.

University of South Florida

As a New Investigator awardee in FY99, Dr. Patricia Kruk of the University of South Florida discovered that telomerase activity was regulated in a P13-K-dependent manner. She found that JNK (Jun N-terminal kinase) is a prime target for telomerase regulation. Through the P13-K/JNK pathway, the cytoplasmic tyrosine kinase Pyk2 also has a function in telomerase activity. Dr. Kruk was also one of the investigators working on Dr. Santo Nicosia's FY01 Program Project Award. She confirmed that telomerase reactivation can reduce apoptosis and that VEGF and lysophosphatidic acid upregulated telomerase in a transcription-dependent manner. Interestingly, vitamin E suppressed telomerase activity in ovarian cancer cells and enhanced cisplatin-mediated cytotoxicity. Another notable finding included a 73 percent decrease in telomerase activity when the c-Myc and Sp1 pathways were blocked with siRNA. In other experiments, the siRNA appeared to be a promising cisplatin cotreatment. Dr. Kruk also examined the protein Bcl-2 in urine and found that more than 70 percent of ovarian cancer patients had detectable levels of Bcl-2 in their urine samples. These preliminary findings led to Dr. Kruk's FY06 Idea Development Award that is focusing on Bcl-2 as a urinary biomarker for ovarian cancer. Early results indicate that elevated urinary Bcl-2 levels are detectable by enzyme-linked immunosorbent assay.



# The Program Today

## FY07 Summary

A congressional appropriation of \$10M continued the OCRP in FY07. The program defined its niche within the ovarian cancer field by offering two original award mechanisms, the HBCU/MI Fellowship Award and the Translational Research Partnership Award. Additionally, Concept Awards continued to support unconventional research ideas pertaining to ovarian cancer. A total of 331 proposals were received across the 3 award mechanisms, as illustrated in Table V-2, and 40 awards were made. The portfolio of funded projects in FY07 encompassed basic research, clinical research, population-based research, and research resources, as shown in Figure V-2.

Due to the overwhelming response to the OCRP award mechanisms, a pre-proposal screening phase was initiated for select mechanisms. In FY07, pre-proposals were required for two mechanisms. One-third of the pre-proposals received resulted in full proposals. All pre-proposals were screened by the Integration Panel members, the same individuals who establish the goals and vision for the OCRP.

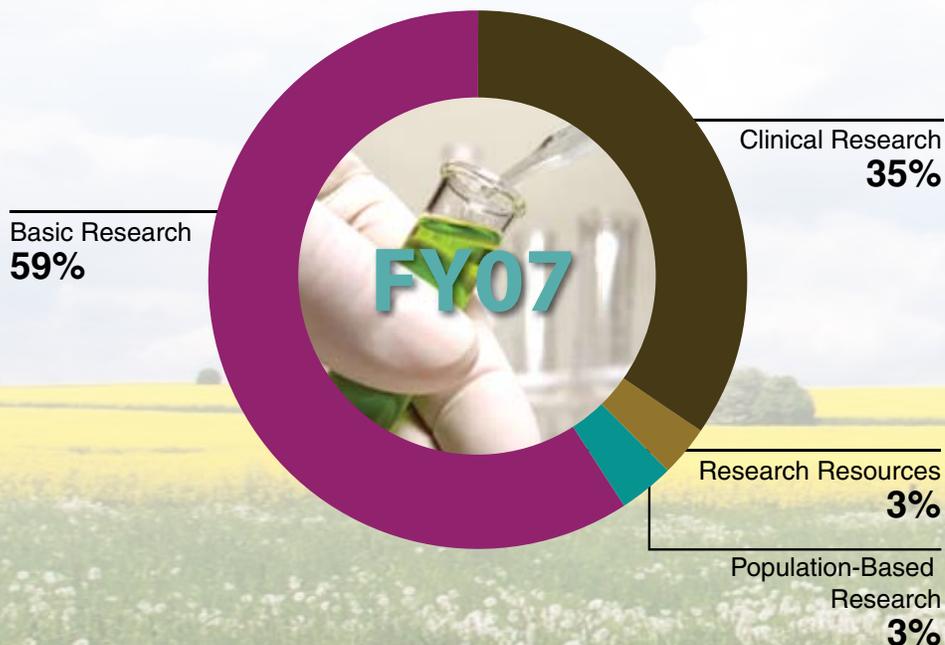


Figure V-2. FY07 OCRP Portfolio by Research Area

Table V-2. Funding Summary for the FY07 OCRP

Categories and Award Mechanisms	Proposals Received	Awards	Investment
<i>Innovative Research</i>			
Concept	281	28	\$3.2M
Translational Research Partnership	46	10	\$5.0M
<i>Training/Recruitment</i>			
HBCU/MI Fellowship	4	2	\$0.7M
<b>TOTAL</b>	<b>331</b>	<b>40</b>	<b>\$8.9M</b>

331  
Proposals  
Received

40  
Awards

\$8.9M  
Investment

**The OCRP Team**

**Patricia Modrow, Ph.D.**  
Program Manager

**Theresa Miller, Ph.D.**  
Grants Manager

**Patricia Roth, M.S.**  
Program Specialist, Azimuth

**Stephanie Ford-Molvik, M.P.H.**  
Program Coordinator, SAIC

**Bridget McKenzie-Fogle, M.S.**  
Biomedical Scientist, SAIC

**Ron Hostutler, M.B.A., Ph.D.**  
Peer Review Coordinator  
SRA International

## The Vision for FY08

As in previous fiscal years, Congress appropriated \$10M to the OCRP in FY08. With these funds, the OCRP has provided support for innovative research (Idea Development Award), research training opportunities (Career Development Award), partnerships between clinicians and laboratory scientists to fuel promising ideas into clinical applications (Translational Research Partnership Award), and partnerships to identify and characterize the early changes associated with ovarian cancer (Consortium Development Award).

- ❖ The Translational Research Partnership Award targets research collaborations between laboratory scientists and clinicians to address a central problem or question in ovarian cancer in a manner that would be less readily achievable through approaches based in a single laboratory.
- ❖ The Idea Development Award supports high-impact, innovative research that will drive the field forward in all areas of ovarian cancer research.
- ❖ The Career Development Award is intended to support research training opportunities for individuals in the early stages of their careers who wish to pursue an independent career at the forefront of ovarian cancer research.
- ❖ The Consortium Development Award seeks to promote a major multi-institutional research effort conducted by leading ovarian cancer researchers that specifically focuses on identifying and characterizing early changes of disease associated with ovarian cancer.

*Table V-3. Award Mechanisms Offered and Proposals Received for the FY08 OCRP*

Categories and Award Mechanisms	Proposals Received
<b>Clinical Research</b>	
Translational Research Partnership	43
<b>Innovative Research</b>	
Idea Development	65
<b>Training/Recruitment</b>	
Career Development	36
<b>Multi-Institutional Research</b>	
Consortium Development	4
<b>TOTAL</b>	<b>148</b>

Similar to FY07, a pre-proposal screening phase was initiated for select mechanisms. Three of the four mechanisms required pre-proposals. More than 40 percent of the pre-proposals received resulted in full proposals. A total of 148 full proposals were received across the 4 award mechanisms and approximately 15 awards are predicted, as shown in Table V-3. Appendix B, Table B-4, summarizes congressional appropriations and the investment strategy executed by the OCRP for FY07 through FY08.