

Section VI.
***OVARIAN CANCER
RESEARCH
PROGRAM***



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Ovarian Cancer Research Program

Vision: To prevent ovarian cancer

Mission: To support innovative, integrated, multidisciplinary research efforts that will lead to a better understanding, control, and prevention of ovarian cancer.

Congressional Appropriations for Peer-Reviewed Research
\$17.5M in FY97–98, \$10M in FY99, and \$12M in FY00

Award Summary

8 Program Projects in FY97–98

18 awards from the FY99 appropriation

~14 awards anticipated from the FY00 appropriation

Outcomes of Eight FY97–98 Grantees

Publications (includes
manuscripts in press) 15

Abstracts/Presentations 43

Ovarian cancer is often not associated with any obvious signs or symptoms until late in its development. Signs and symptoms of ovarian cancer may include:

- ☞ General abdominal discomfort and/or pain (gas, indigestion, pressure, swelling, bloating, cramps);
- ☞ Nausea, diarrhea, constipation, or frequent urination;
- ☞ Loss of appetite;
- ☞ Feeling of fullness even after a light meal;
- ☞ Weight gain or loss with no known reason; and
- ☞ Abnormal bleeding from the vagina.

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

The Disease

Ovarian cancer ranks first among gynecological cancers in the number of new deaths it causes in the United States each year. An estimated 23,100 women will be diagnosed with and 14,000 will die from ovarian cancer in 2000 in the United States.¹ Ovarian cancer is often without overt or specific symptoms until late in the disease process. The overall 5-year survival rate is 46%. However, women with earlier stages of the disease have better survival rates than those with more advanced disease.

History of the Ovarian Cancer Research Program

—Program Background

The Department of Defense (DOD) Ovarian Cancer Research Program (OCRP) was established in fiscal year 1997 (FY97) by Appropriations Conference Committee Report No. 104–863, which provided \$7.5M for research in ovarian cancer. At that time, the U.S. Army Medical Research and Materiel Command convened a meeting of expert scientists, clinicians, and consumer advocates in the field of ovarian cancer to define the goals and areas of emphasis of the program. Participants were drawn from academia, military, oncology societies and associations, consumer advocacy organizations, and cancer research funding agencies to identify underrepresented avenues of research and novel applications of existing technologies and to avoid duplicative research efforts. The overall mission of the DOD OCRP is to support innovative research efforts leading to a better understanding, control, and prevention of ovarian cancer.

¹ American Cancer Society – Cancer Facts and Figures 2000.

—Congressional Appropriation and Funding History

From FY97–00, Congress appropriated a total of \$39.5M to fund peer-reviewed ovarian cancer research through the OCRP. A total of 26 awards have been made in three award mechanisms: Program Project Awards, Idea Awards, and New Investigator Awards. Each fiscal year’s investment strategy is consistent with congressional language and reflects the program’s vision to prevent ovarian cancer. Appendix B, Table B–4, summarizes the directions from Congress for the OCRP appropriations, the program’s withholds and management costs, and the investment strategy executed by the OCRP for FY99–00. Additional details of the FY97–98 programs may be found in the DOD CDMRP Annual Report, September 1999.

FY99 Program

Congress appropriated \$10M in FY99 to continue funding peer-reviewed ovarian cancer research through the OCRP. The FY99 program sought submissions in two award mechanisms, Idea Awards and New Investigator Awards, to complement the research initiatives of other funding agencies. The intent of Idea Awards was to encourage innovative approaches to ovarian cancer research. The aim of New Investigator Awards was to prepare new, independent investigators for careers in ovarian cancer and to attract more senior investigators new to the ovarian cancer field. The FY99 program emphasis areas were etiology, prevention, diagnosis, and quality of life.

Table VI–1 reflects the funding summary for the FY99 OCRP. Figure VI–1 reflects research areas funded in the FY99 OCRP.

Table VI–1. Funding Summary for FY99 OCRP Awards

Award Mechanism	Number of Proposals Received	Number of Awards	Investment
Idea Awards	139	12	\$5.8M
New Investigator Awards	55	6	\$2.4M

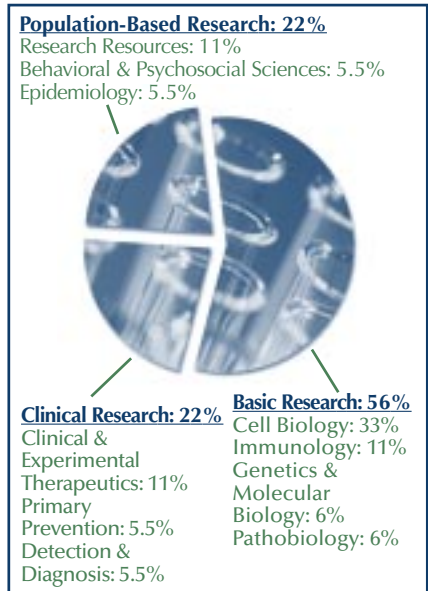


Figure VI–1. FY99 OCRP Portfolio by Research Area



“Ovarian cancer has the highest case-fatality rate of all gynecologic cancers and is a major source of mortality and morbidity for women. Unfortunately, the effective treatment and prevention of ovarian cancer will remain difficult since we do not understand its molecular origins. Historically, little funding has been available for research directed at ovarian cancer. That is now beginning to change, and the DOD OCRP has led the way. Given the nature of the program, the DOD OCRP funds high-risk but potentially large impact research efforts. I do not think it is an exaggeration to say the DOD OCRP has started an effort which fosters translation of recent discoveries on the molecular basis of cancer into the cure and prevention of this dreaded disease.”

*Michael Birrer, M.D., Ph.D.
 Chair, Integration Panel*

Enhancing Synergism among Disciplines

In FY97, FY98, and again in FY00, the OCRP made a concerted effort to enhance ovarian cancer research infrastructure via the Program Project Award mechanism. This mechanism encouraged experts from multiple disciplines to establish ovarian cancer research programs that would advance investigations in the field. In addition, these awards included both an Idea research project (designed to stimulate and reward particularly novel ideas) and a New Investigator research project (designed to support both young investigators as well as more established investigators with different research backgrounds to pursue research in ovarian cancer. One of these Program Projects, conducted at the Fred Hutchinson Cancer Research Center, is designed to develop a cost-effective screening strategy for early detection of ovarian cancer. This work is a collaboration among experts in molecular biology, immunology, pathology, oncology, and statistics at three institutions. Molecular biologists are using novel techniques to compare gene expression in normal and malignant tissue. Laboratory-based clinical immunologists and oncologists are employing other approaches by looking in blood for antibodies to ovarian cancer-related proteins and by comparing the test results in women with cancer, benign ovarian disease, and no ovarian disease.

As part of the OCRP's concerted effort to build infrastructure, the FY00 OCRP has also solicited innovative, multidisciplinary, and synergistic Program Project proposals integrated around one or more program emphasis area (i.e., etiology, early detection/diagnosis, preclinical therapeutics, and quality of life). Program Projects funded by the OCRP will foster an environment conducive to groundbreaking research and ensure the continuance of excellent ovarian cancer research. ♦

“One of the unique aspects of the OCRP is the investment the program makes in consumers and the resulting contributions made by the consumer community in advancing medical research. By participating at every level of planning and review, consumers gain a profound understanding of the research world. This program has enabled ovarian cancer survivors to become well-informed, credible advocates for strengthening the research that is so vital to unlocking the mystery of ovarian cancer and ultimately to saving women's lives.”

Ann Kolker

Consumer, Integration Panel Member

FY00 Program

The program's success encouraged Congress to appropriate an additional \$12M in FY00 for the OCRP. The FY00 programmatic vision encompassed two award mechanisms, Program Project Awards and New Investigator Awards. The Program Project Award mechanism was designed to enhance ovarian cancer research infrastructure by engaging experts from multiple disciplines to establish ovarian cancer research programs that would advance investigations in the field. The intent of New Investigator Awards was similar to the aim of the FY99 OCRP Awards. The FY00 program emphasis areas were etiology, early detection/diagnosis, preclinical therapeutics, and quality of life. A Program Announcement was released on April 28, 2000. A total of 118 proposals was submitted to the program. Peer review will be in November 2000, and programmatic review will be completed in January 2001.

Scientific Achievements

Funded research is anticipated to provide the relatively young OCRP with the infrastructure to effect contemporary and future scientific discoveries in ovarian cancer. Eight centers across the nation (see Figure VI-2) were funded in FY97 and FY98 to establish ovarian cancer research initiatives focusing on collaborative efforts across many research disciplines to advance understanding of ovarian cancer etiology and prevention. These centers are: Fred Hutchinson Cancer Research Center in Seattle, Washington; Duke University Medical Center in Raleigh-Durham, North Carolina; Fox Chase Cancer Center in Philadelphia,



Figure VI-2. FY97-98 OCRP Program Project Awards Distribution

Pennsylvania; The University of Texas M.D. Anderson Cancer Center in Houston, Texas; the Jonsson Comprehensive Cancer Center at the University of California at Los Angeles in Los Angeles, California; Brigham and Women's Hospital in Boston, Massachusetts; University of Minnesota in Minneapolis, Minnesota; and the Mayo Foundation in Rochester, Minnesota.

Investigators funded in FY97 and FY98 have disseminated their research results and presented their latest research advances by reporting 15 publications in prestigious science journals and presenting 43 abstracts/presentations at national and international forums. The establishment of 12 core facilities (e.g., cell and tissue repositories and laboratory core facilities) that support the funded research also provides resources that will sustain future biomedical research on ovarian cancer. Moreover, the M.D. Anderson Cancer Center, Fred Hutchinson Cancer Research Center, and Fox Chase Cancer Center were awarded NCI SPORE grants to support translational research approaches that may have an immediate impact on improving ovarian cancer care and prevention. In addition, between FY98 and FY99, a total of 11 new investigators have been recruited to the research field of ovarian cancer. Altogether, investigators funded by the OCRP have intensified the fight against ovarian cancer. Their work will be presented in an upcoming meeting sponsored by the Congressionally Directed Medical Research Programs (CDMRP), the *Ovarian Cancer Investigators' Forum*, which will bring together FY97 and FY98 OCRP grantees to share and discuss their work with Integration Panel members, CDMRP Staff, and each other.

Three out of the eight funded Program Projects are described below. These represent some of the most exciting advances in ovarian cancer research already made in the first 2 years of funding:

Use of Novel Techniques to Identify and Investigate Molecular Markers for Ovarian Cancer Screening and Prevention: To detect ovarian cancer before it spreads outside the ovary, researchers at the Fred Hutchinson Cancer Research Center, the University of Washington, and Virginia Mason Research Center in Seattle are studying novel human genes that carry the code for products (proteins) that may serve as potential

“The funding we received from the OCRP has been critical to the development of an ovarian cancer research program at the Fred Hutchinson Cancer Research Center and the University of Washington. However, the work that was done in preparation for submission of [this] grant proposal, together with progress that was made during our first year of OCRP funding, made it possible for us to compete successfully for an ovarian cancer National Cancer Institute Specialized Program of Research Excellence grant. We now have a critical mass of senior and junior investigators from a consortium of research institutions working together to find ways to reduce the morbidity and mortality attributable to ovarian cancer.”

Nicole Urban, Sc.D.
Head, Ovarian Cancer Research Program
OCRP Award Recipient





“As an oncologist who treats women with ovarian cancer, I am very pleased with the approach taken by the DOD OCRP. We need strong basic science to move us forward to developing early detection and ultimately prevention strategies. Patients want us to find ways to detect this disease earlier, when cure rates would be much more likely. Ovarian cancer research should benefit from the explosive knowledge building in molecular biology and genetics. We can be proud that these areas are considered high priority by the research community and look to continued progress in that sphere. We should continue to attract the best and brightest researchers to join us in the search for basic understanding of ovarian cancer biology, which in turn will lead to advances in treatment options.”

*Judith Kaur, M.D.
Chair Emeritus, Integration Panel*

markers of ovarian cancer. This Program Project aims to assemble a panel of known and novel ovarian tumor markers that may form the basis of a cost-effective blood test that can be used to screen for early stage ovarian cancer. Two exciting technologies are being employed to identify the best markers. One technique identifies the genes that are overrepresented in ovarian cancer tissue compared to normal tissue. The other technique identifies gene products in ovarian cancers. So far, 13 genes and 19 gene products have been identified as potential candidates for this panel of markers. Investigators feel that these markers may be useful not only for the detection of early stage ovarian cancer but also for the evaluation of the risk of the disease.

Biological Basis from Multiple Disciplines of Chemoprevention of Ovarian

Cancer: A group of ovarian cancer investigators at Duke University Medical Center is studying the etiology of ovarian cancer with the intent of translating this knowledge into effective preventive strategies. Three research projects are included in this Program Project. Project 1 studies the association between high lifetime ovulatory exposure and alterations in p53, a tumor suppressor gene. This association may be of critical importance in developing prevention strategies because the optimal means of prevention may vary between different cancers. Project 2 looks at the role of genetic susceptibility in ovarian cancer. The identification of genetic variations associated with susceptibility to ovarian cancer will allow researchers to identify effective prevention strategies. Project 3 seeks to uncover the molecular mechanisms involved with potential use of the hormone progestin as an ovarian cancer chemopreventive agent. In addition, the ability of levonorgestrel (a progestin component in contraceptives) to induce cell death and inhibit the development of ovarian cancer in the spontaneous ovarian adenocarcinoma model is being investigated. Recently, a prevention trial in this model demonstrated that chickens treated with progestins contained 35% fewer ovarian and fallopian tube tumors than the control. As characterization of the animal model of ovarian cancer continues, molecular studies and a human clinical pilot study on levonorgestrel's protective effects are being pursued.

Ovarian Cancer Prevention Program: Researchers at the Fox Chase Cancer Center have formed a consortium of institutions to recruit women at high familial risk for ovarian cancer. The scientists are focusing their efforts on prevention of familial ovarian cancer. Investigators will evaluate the DNA of volunteers for common genetic abnormalities. In addition, an ovarian cancer symptom checklist is being developed to help health care professionals recognize and evaluate ovarian cancer symptoms. Researchers are exploring the psychological factors that influence the decision of women at risk for ovarian cancer to undergo a prophylactic oophorectomy (surgical removal of the ovaries). To date, results show that perceived risk and perceived benefits of the procedure are positively associated with intentions to undergo preventive surgery. Researchers intend to develop a decision-making profile that will be used to design and enhance counseling interventions. Patients who have elected prophylactic oophorectomy will participate in a clinical trial designed to evaluate the effects of the chemopreventive agent fenretinide on indications of ovarian neoplasms.

Summary

The DOD OCRP is supporting innovative, integrated multidisciplinary research efforts to understand and prevent ovarian cancer. This young program has a diverse portfolio of funded research that is making important contributions to understanding ovarian cancer etiology, early detection/diagnosis, prevention, preclinical therapeutics, and quality of life. Projects funded by the OCRP are strengthening ovarian cancer research efforts through the building of infrastructure and, thus, are aiding in the national health effort to impact the well-being of all women. Congress has directed the DOD to continue supporting peer-reviewed ovarian cancer research and has appropriated \$12M for the OCRP for FY01.

FY00 Integration Panel Members

Chair, Michael Birrer, M.D., Ph.D.: Chief, Molecular Mechanisms Section, Department of Cell and Cancer Biology, Division of Clinical Sciences, NCI, National Institutes of Health. Assistant Professor, Uniformed Services University of the Health Sciences.

Chair-Elect, William Hoskins, M.D.: Deputy Physician-in-Chief, Disease Management; Chief, Gynecology Service, Department of Surgery; and Avon Chair of Gynecologic Oncology Research, Memorial Sloan-Kettering Cancer Center. Professor, Department of Obstetrics and Gynecology, Cornell University Weill Medical College.

Chair Emeritus, Judith Kaur, M.D.: Associate Professor of Oncology, Division of Medical Oncology, Mayo Medical School.

Holly Gallion, M.D.: Professor, Department of Obstetrics and Gynecology, University of Kentucky.

David Gershenson, M.D.: Director, Blanton-Davis Ovarian Cancer Research Program; Ann Rife Cox Chair in Gynecology; and Professor and Chair, Department of Gynecologic Oncology, The University of Texas M.D. Anderson Cancer Center.

Thomas Hamilton, Ph.D.: Senior Member, Department of Medical Oncology, and Leader, Ovarian Cancer Program, Fox Chase Cancer Center. Adjunct Professor, Department of Chemistry, Lehigh University.

Enrique Hernandez, M.D.: Director, Division of Gynecologic Oncology, and Professor of Obstetrics and Gynecology and of Pathology, Temple University School of Medicine.

Hedvig Hricak, M.D., Ph.D.: Chairman, Department of Radiology, Memorial Sloan-Kettering Cancer Center. Carroll and Milton Petrie Chair, and Professor of Radiology, Cornell University.

Beth Karlan, M.D.: Director, Division of Gynecologic Oncology and the Gilda Radner Ovarian Cancer Program, Department of Obstetrics and Gynecology, Cedars-Sinai Medical Center. Associate Professor, Department of Obstetrics and Gynecology, University of California, Los Angeles.

Ann Kolker, J.D.: Consumer, Executive Director, Ovarian Cancer National Alliance.

“In addition to funding high-quality research, the DOD OCRP seeks to develop sustainable infrastructure. Different funding mechanisms designed by the OCRP leverage off each other to synergistically support infrastructure. I hope to see graduate students and instructors associated with Program Projects develop new ideas and pursue their own research interests in ovarian cancer.”

*Steven Krosnick, M.D.
Ovarian Cancer Research
Program Manager, CDMRP*



Robert Kurman, M.D.: Richard W. TeLinde Distinguished Professor of Gynecologic Pathology, Departments of Gynecology, Obstetrics, and Pathology, The Johns Hopkins School of Medicine. Director of Gynecologic Pathology, The Johns Hopkins Hospital.

Maurie Markman, M.D.: Director, Cleveland Clinic Taussig Cancer Center. Chairman, Department of Hematology/Medical Oncology, and The Lee and Jerome Burkons Research Chair in Oncology, The Cleveland Clinic Foundation.

Cindy Melancon, R.N., M.N.: Consumer, Editor, monthly newsletter *Conversations: The International Ovarian Cancer Connection*. Founding Member of the National Ovarian Cancer Coalition, Boca Raton, Florida. Founding Board Member and Vice President of the Ovarian Cancer National Alliance, Washington, DC.

Geraldine Padilla, Ph.D.: Vice President, Cancer Control, American Cancer Society California Division.

Eddie Reed, M.D.: Director, Mary Babb Randolph Cancer Center, West Virginia University.

Harvey Risch, M.D., Ph.D.: Associate Professor of Epidemiology and Public Health, Yale University School of Medicine.

Elwood Robinson, Ph.D.: Professor and Chair, Department of Psychology, North Carolina Central University.

Mary Scroggins, M.A.: Consumer, Member of the Board of Directors of the Ovarian Cancer National Alliance. Founder and publisher of *SisterCircle* newsletter.

Michael Steller, M.D.: Director of Research, Program in Women's Oncology, Women and Infants' Hospital; Associate Professor, Department of Obstetrics and Gynecology, Brown University School of Medicine.

Robert Young, M.D.: President, Fox Chase Cancer Center. Year 2001 President-Elect of the American Cancer Society.

For more information about the OCRP and other programs managed by the CDMRP, visit <http://cdmrp.army.mil>