

Priorities of the GYNECOLOGIC CANCER Progress Review Group

Co-Chairs:

William Hoskins, M.D.

Nicole Urban, Sc.D.

Executive Director:

Edward C. Trimble, M.D., M.P.H.

Gynecologic cancer

Cervical, endometrial, and ovarian cancers

- **Represent 95 percent of gynecologic cancers**
 - **Burden the U.S. with over 80,000 cancer cases and 26,000 cancer deaths annually**
 - **Collectively rank fourth among women's cancers in both incidence and mortality**
 - **Account for 14% of cases and 11% of deaths from solid tumors in women**
- 

Cervical cancer

**Is well controlled *in developed countries*
because**

- **Its precursor lesion is known**
 - **Effective screening tests have been available for many years**
 - **Screening is widely disseminated**
- 

Cervical cancer

Offers an extraordinary opportunity for better control worldwide through

- **Understanding of its etiology and pathogenesis (HPV infection)**
- **Vaccine development**
 - **To prevent HPV infection**
 - **To prevent cancer among HPV-infected women**



Endometrial cancer

Hormone-dependent disease is usually treatable

- **Precursor lesion is known**
 - **Symptoms facilitate early diagnosis**
 - **Disease usually responds to treatment**
-

Endometrial cancer

Hormone-independent disease presents a greater challenge

- **Aggressive**
 - **Etiology and pathogenesis are not well understood**
 - **Similar in some ways to ovarian cancer**
-

Ovarian cancer

Poorly controlled in the U.S and worldwide

- **Precursor lesion is unknown**
 - **Etiology and pathogenesis are not well understood**
 - **Disease advanced at time of diagnosis due to**
 - Aggressive behavior
 - Absence of symptoms
 - **Response to therapy is variable**
-

Ovarian cancer

Offers an opportunity for better control through early detection and prevention

- **Serum markers**
 - **Imaging**
 - **Risk models**
- 

The GYN PRG process was iterative to build consensus

**Each member of the GYN PRG Roundtable
had the opportunity to participate in 3
breakout sessions**

- **Session I: Scientific**
- **Session II: Scientific**
- **Session III: Tumor-type**



Roundtable Session I

Scientific breakout groups: Session I

- **Angiogenesis, Metastasis, and Growth Signaling**
 - **Defining Signatures of Cancer Cells, Genomics, Proteomics & Informatics**
 - **Clinical and Molecular Genetics**
 - **Early Detection, Screening and Prevention**
 - **Genes and Environment**
 - **Health Disparities, Communication, Education & Quality of Care**
 - **Health Related Quality of life and Survivorship**
-

Roundtable Session II

Scientific breakout groups: Session II

- **Imaging**
 - **Immunology**
 - **Laboratory and Clinical Models**
 - **Radiobiology**
 - **Treatment, Clinical Trials, Gene Therapy, Staging & Surgery**
 - **Treatment and Drug Discovery**
 - **Tumor Biology, Hormone Receptors, Epithelial-Stromal Interactions & Early Activation**
-

Roundtable Session III

Tumor-type breakout groups: Session III

- Cervical
 - Endometrial
 - Ovarian
-

Interdisciplinary discussion was comprehensive

Breakout groups identified priorities

- **Gaps in knowledge**
- **Barriers to progress**
- **Action plan**
- **Resources needed**



PRG structure facilitated identification of emerging themes

**Leadership reviewed reports of the
breakout groups to identify themes for
high-impact priorities**

- **Identified consistently by most groups**
- **Cross-cutting with respect to all of the
gynecologic cancers**
- **Comprehensive with respect to disciplines and
research community interests**



Clear priorities emerged

Leadership identified 3 types of priorities

- **Essential priority (1)**
 - **High-impact priorities (3)**
 - **Scientific priorities (6)**
-

Essential priority: the VSSR

**Develop and make available to the
cancer research community a
Virtual Shared Specimen Resource
(VSSR) to support gynecologic
cancer research**



Virtual Shared Specimen Resource (VSSR)

**An initiative considered absolutely
necessary for advancing the**

- detection,**
- classification, and**
- treatment**

of gynecologic cancer



VSSR: annotated specimens available to all

**Includes high-quality, fresh-frozen tissue
and fluids**

- **Obtained at critical points in the disease process**
 - **Associated with high-quality clinical and follow-up data**
 - **Processed and stored in evolving ways**
- 

VSSR: a “virtual” resource

**The resource is developed *by and for* the
gynecologic research community**

- **information describing the specimens is managed centrally, but**
 - **the specimens themselves are collected by and reside in various institutions**
-

VSSR: essential features

Features of the VSSR include

- specific scientific goals,
- a coordinating center, and
- an advisory committee to ensure
 - efficiency, equity, quality, and inventory control in
 - specimen collection, management, and distribution



VSSR: scientific oversight

Design, coordination and monitoring will ensure

- **Sharing of specimens to enable investigators to collaborate across disciplines and institutions**
 - **Prospective, tailored specimen collection as well as banking of specimens**
 - **Incentives structured to promote collaboration**
 - **Policies developed regarding consortia members' rights and responsibilities**
 - **Input from advocates and industry**
- 

VSSR: a cooperative effort

**The time is right to accelerate progress in
gynecologic cancer research**

- **Partnership among research institutions, facilitated by the NCI**
 - **Builds on NCI/NIH initiatives**
 - **Human Genome Project**
 - **Director's Challenge**
 - **SPORE program**
 - **Early Detection Research Network**
 - **Tissue Procurement Network**
- 

VSSR: addresses current barriers to progress

Banked specimens often are not

- **Processed or stored appropriately for current scientific needs**
- **Obtained at the appropriate time in the course of disease**
- **Representative of the needed tissue types**



VSSR: addresses current barriers to progress

Banked specimens often are not

- **Linked to adequate clinical data, including**
 - demographics
 - risk factors
 - therapy
 - follow-up



VSSR: ensures that the best scientists have access to the right specimens

Even when banked specimens are otherwise appropriate,

- **Lack of incentives to share specimens inhibits their widespread use**
 - **Informed consent obtained from tissue donors limits their utility for current scientific needs**
- 

VSSR: supports needed experiments

**Will enable the gynecologic research
community to**

- **Exploit emerging genomics, proteomics and informatics technologies**
 - **Identify gynecologic cancers early in the disease process**
 - **Discover new targets for prevention and treatment**
- 

VSSR: supports needed experiments

Experiments often require

- **Serial collection of specimens: before, during and after treatment, and at any recurrence**
- **Control specimens including**
 - **normal tissue from the same woman**
 - **normal comparable tissue from women with**
 - **benign gynecologic conditions and/or**
 - **no evidence of any malignant disease**



VSSR: allows investigators to address critical questions

Answers have been elusive:

- **How can women at high risk for gynecologic cancers be identified?**
 - **How can ovarian and endometrial cancers be detected early?**
 - **What strategies can be developed to prevent gynecologic cancers?**
 - **What new approaches can be developed to better treat gynecologic cancers?**
- 

VSSR: recommended actions

- **NCI should provide resources to develop a VSSR for gynecologic cancer research**
 - **An advisory committee should oversee the progress of the resource and its research**
 - **Multiple institutions should collaborate in the development and use of the VSSR**
 - **NCI-based commission should facilitate resolution of privacy issues**
- 

Three high-impact scientific priorities emerged

Opportunities were identified for significant progress in:

- **Identification of markers of risk, early detection and targets for treatment**
- **Development of human papillomavirus vaccines**
- **Research to improve patients' quality of life and reduce disparities related to care**



Identify markers of risk, early detection and targets for treatment

Exploit emerging technologies to identify

- **Precursor lesions**
- **Markers of risk**
- **Markers for early detection**
- **Molecular disease classifications**
- **Prognostic indicators**
- **Targets for prevention and treatment**
- **Proteomics in ovarian cancer detection**



Technology (with specimens) can yield answers to critical questions

- **What are the precursor lesions associated with epithelial ovarian cancer and high-risk endometrial cancer?**
- **What biomarkers, measurable in easily accessible fluids, are associated with**
 - **these precursor lesions?**
 - **invasive gynecologic cancers, especially ovarian and high-risk endometrial cancer?**
 - **response or non-response to therapy?**



Understanding molecular signatures will yield targeted therapies

- **What is a clinically relevant molecular classification and staging system for invasive gynecologic cancers?**
- **What new targets can be identified for which directed therapies can be developed to improve survival from the gynecologic cancers?**



Genomics, proteomics and informatics will enable prevention

- **What models of risk, incorporating biomarkers as well as family history, environmental exposures, and reproductive history, can predict future development of epithelial ovarian cancer and endometrial cancer?**
- **What new approaches can be identified for prevention of the gynecologic cancers?**



Resources required

- **VSSR: Tissue to support marker and target identification and validation**
 - **Repositories of fluids such as blood samples**
 - serial specimens from women without cancer at entry and with good follow-up data for cancer endpoints, such as the Prostate, Lung, Colorectal, and Ovarian Cancer Screening (PLCO) Trial resource
 - criteria for access to very valuable specimens, such as these, need to be developed
- 

Resources required

- **Statistical and bioinformatics infrastructure must be developed**
 - to allow for adequate analysis and interpretation of the findings from molecular and validation studies
 - to ensure that the best strategies are selected for testing in trials



HPV Vaccines

- **High Impact Priority # 2**
 - **Develop effective human papillomavirus (HPV) vaccines to prevent biotransmission and development of neoplasia**



HPV Vaccines

- **Rationale**

- **cervical cancer is the leading cause of death from gynecologic cancer in the world**
- **Although the incidence of invasive cervical cancer is relatively low in the United States because of cytologic screening, the cost of evaluating and treating abnormal pap smears in the United States exceeds 6 billion dollars annually**



HPV Vaccines

- **Rationale (continued)**
 - **HPV vaccine research has been underway for some time but no effective prophylactic or therapeutic vaccine has been developed**
 - **No framework for comprehensive clinical evaluation of vaccines**
 - **Clinical trials are hampered by a fragmentation of efforts**
 - **Few partnerships exist between scientists, industry and government**



HPV Vaccines

- **Key issues to be addressed**
 - **Role of mucosal and humoral immunity**
 - **Impact of endogenous (hormones) and exogenous (other pathogens and smoking) factors on the risk of developing cervical neoplasia**
 - **More efficacious vaccine strategies**
 - **Immunologic biomarkers that might be used to clinically evaluate vaccines**
- 

HPV Vaccines

- **Recommended actions**
 - **Encourage studies to improve our basic understanding of mucosal immunity**
 - **Understand the initiation of effective mucosal immunity**
 - **Studying who develops chronic HPV infection and in whom it can be eradicated**



HPV Vaccines

- **Resources needed**
 - **Core laboratories for viral and immunologic evaluation of specimens from clinical trials**
 - **World wide network for clinical trials**
 - **Expanded cadre of individuals with interest and expertise in HPV immunology**
 - **Partnerships between scientists, industry and government**
 - **Integration of research efforts worldwide**
- 

QOL and Health Disparities

- **High Impact Priority # 3**
 - **Conduct research to:**
 - **Understand and improve quality of life**
 - **Reduce or eliminate disparities related to care among patients with gynecologic cancers**



QOL and Health Disparities

- **Rationale**

- **Cure rates for gynecologic cancers are cervical 72%, endometrial 86%, and ovarian 50% resulting in a large number of gynecologic cancer survivors**
 - **Research in to quality of life for women undergoing therapy and these cancer survivors has been very limited**
- 

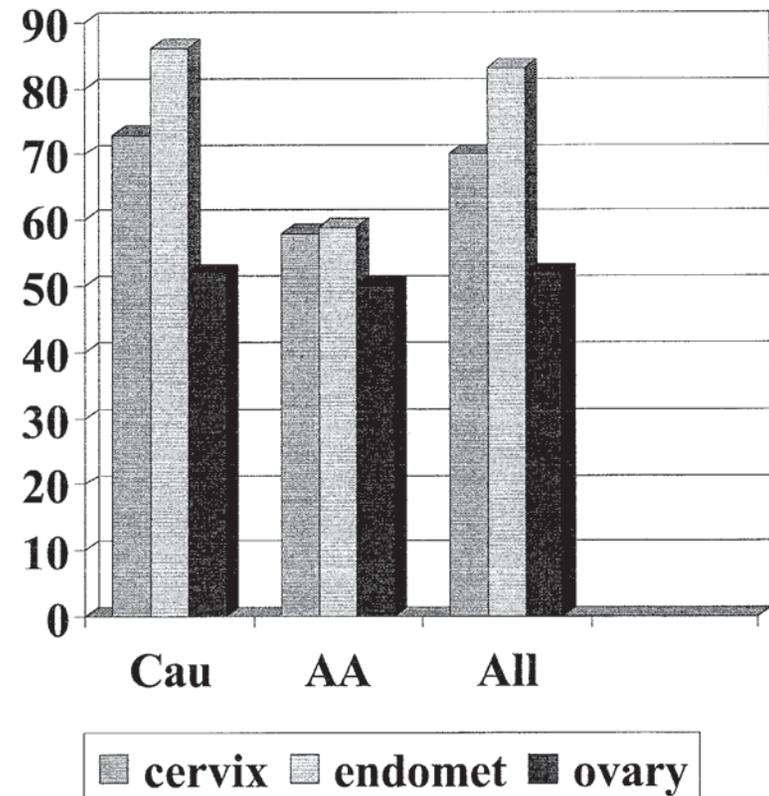
QOL and Health Disparities

- **Rationale (continued)**

- **Treatment for gynecologic cancer often results in changes of hormonal function, sexual function, sense of self worth and social maladjustment**
 - **With 20% of all female cancer survivors having had, cervical, endometrial or ovarian cancer, studies of quality of life are very important**
- 

QOL and Health Disparities

- **Rationale (continued)**
 - There are striking differences in survival for gynecologic cancer survivors by race and economic status



QOL and Health Disparities

- **Recommended actions**

- **Perform large observational cohort studies of patients with newly diagnosed and previously diagnosed gynecologic cancer to:**
 - **Investigate the impact of targeted interventions on patient-centered outcomes**
 - **Identify the influence of modifiable risk factors on gynecologic cancers**
 - **Discover options to eliminate disparities in the delivery of high quality health care**



QOL and Health Disparities

- **Recommended actions**
 - **We need to study reasons for health disparities**
 - Identify barriers
 - Identify genetic or age related differences
 - **We need to design interventions to correct disparities**
- 

QOL and Health Disparities

- **Recommended actions**
 - **QOL and health disparities research can be performed through the Cancer Care Outcomes Research and Surveillance Consortium (CanCORS), Clinical Trials Cooperative Groups, Cancer Centers and individual investigators**
 - **QOL and health disparities interventional research can be performed through Clinical Trials Cooperative Groups, Cancer Centers or individual investigators**
- 

QOL and Health Disparities

- **Resources required**

- **Develop collaborative projects and consortia to conduct large cohort studies in gynecologic cancer**
 - **Develop collaborations among investigators with expertise in gynecologic oncology, epidemiology, health services research, health communication and health psychology**
 - **Develop a cadre of new and existing investigators in the fields of communication, health psychology, health-related quality of life**
- 

Scientific Opportunities

- **Characterize the hormonal, immunologic, and epithelial-stromal interactions that result in the development of gynecologic cancers**
 - **Develop imaging techniques to evaluate tumor biology, molecular signatures, and therapeutic response**
- 

Scientific Opportunities

- **Develop relevant preclinical models for gynecologic cancers**
- **Find ways to overcome resistance to chemotherapy and radiotherapy**



Scientific Opportunities

- **Develop individualized and optimized radiation therapy techniques in conjunction with other treatment modalities**
 - **Encourage increased participation in clinical trials in gynecologic cancer**
- 

Conclusion

- **The Gynecology Progress Review Group has identified**
 - **One Essential Priority**
 - **Three High-impact priorities**
 - **Six Scientific opportunities**
 - **Implementation of these 10 priorities is essential if, in the next five years, we are to contribute in a significant manner towards the cure of gynecologic cancer**
- 

Conclusion

- **We have taken elements of all 14 breakout groups, as well as the 3 tumor type groups**
 - **The final 10 priorities represent a synthesis of these reports into a research map for the next five years**
 - **Please read the reports in Appendix C**
- 

Conclusion

- **This report is the work of +/-100 of the best minds in gynecologic cancer research (basic and clinical), gynecologic cancer therapy, industry and advocacy**
- **We cannot stress enough the importance to women of the world of your implementation of these recommendations**



Conclusion

- **Nicole, Ted and I appreciate this opportunity**
- **We are grateful to the entire PRG and to the participants in the roundtable**
- **A special thanks to the NCI staff from the Office of Science Planning and Assessment (OSPA) for all of their hard work and guidance**

