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14. ABSTRACT We have accomplished all the tasks as described in the Development award and, as a result, we have successfully competed for the Consortium award in 2011. The current progress report is submitted because we requested no cost extension of the development award in order for us to utilize the carryover budget to support the Consortium ovarian cancer symposium in May 2012. All the participants from the Consortium project as well as the reviewer panelists from DoD think highly positive for the annual ovarian cancer symposium to promote communication, efficiency and collaboration among different research site investigators, and to disseminate the new knowledge to the public. Since we don't have sufficient budget in the Consortium award for this part, we therefore propose to use the carryover budget from the previous Development award to subsidize the cost of the symposium. The symposium went very well and was highly received by all participants as well as from DoD OCRP staff.					
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Introduction

We have used this Development award to successfully compete for the Consortium award in 2011 (DOD Award W81XWH-11-2-0230: “*Prevention of Ovarian High-Grade Serous Carcinoma by Elucidating Its Early Change*”). The first progress report of this W81XWH-11-2-0230 Consortium has been submitted to DoD and please see that report for details. Therefore, we will briefly summarize the progress report that is relevant during the last year and more specifically how we used the carryover budget to the develop and/or support the entire consortium.

The purpose of the Consortium are to **1)** elucidate the pathogenesis of ovarian cancer by characterizing the early lesions involved in the development of high-grade ovarian serous carcinoma, and **2)** to provide biomarkers for early ovarian cancer detection. Both goals will be facilitated by this Consortium Development plan which is a collaborative, interdisciplinary program that will establish the infrastructure to coordinate basic and translational research. Thus, the main purpose of the proposed Consortium Development project is to establish the infrastructure for supporting the subsequent Consortium research program focusing on identification and characterization of early molecular changes in ovarian cancer. The consortium is composed of four research sites and one Coordination center. The four research sites include Johns Hopkins University (JHU), Toronto University Health Network (TUHN), Memorial Sloan Kettering Cancer Center (MSKCC), and Yale University. The Coordination center will have three Cores (Administration, Biostatistics, and Pathology/Epidemiology) which will provide the essential support and integration of the projects from the research sites. JHU will be the Coordinating center with purview over the three Cores which in turn will coordinate the activities of the four research sites.

Dr. Kurman is the Director of the proposed Consortium development and will oversee the program. Dr. Kurman is currently the Director of Gynecologic Pathology at the Johns Hopkins Medical Institutions and has had a specific interest in gynecologic pathology for over 30 years. Dr. Kurman is a national and internationally recognized authority in the field of ovarian pathology and has published extensively on all types of ovarian neoplasms. Under the leadership of Dr. Kurman, the individual projects will act in a synergistic and highly integrated fashion aimed at better understanding the molecular landscape of early/precursor lesions of ovarian cancer in the subsequent consortium program project.

The scope of the Development award is briefly summarized. The Administrative Core will collect IRB protocols from all research sites, organize the Consortium symposium including the Pathology/ Epidemiology consensus meeting, setup and test the audio-video broad band electronic device for e-conference, organize the Internal Advisory Board, assemble research protocols for shared techniques. The Pathology/Epidemiology Core will define criteria for early ovarian cancer lesions (precursors) and select cases and controls, survey available cases and controls from all research sites, create one overall database for specimens with clinical and epidemiologic data, establish tissue processing and trafficking mechanisms, setup quality control procedures for DNA, RNA and protein extraction. The Biostatistics Core will establish the data collection, storage and security system, perform power calculation, sample size justification and participate in study design for each project. Each research site will establish regular research conferences, formulate research specific aims, identify expert collaborators and consultants, and collaborate with Pathology/Epidemiology Core to identify pre-existing early lesions and precursors. The completion of these tasks is considered critical for us to continue our research in the Consortium research program and, in fact, this is the case. Of note, all the tasks have been done and as a result, we have been funded by the DoD consortium study.

Body

We have brought expertise of pathology, epidemiology, molecular techniques and tissue banking to focus on studying the pathogenesis of ovarian cancer development. The main tasks (according to the Statement of Work as originally submitted) that have been accomplished in this Development phase are followings. **First**, we have successfully brought together several institutions including Johns Hopkins University (JHU), Toronto University Health Network (TUHN), Memorial Sloan Kettering Cancer Center (MSKCC), and Yale University with clinics of women at high risk of developing ovarian cancer. We have set up a collaboration network of investigators at these institutions who have had a long-term interest in ovarian tumorigenesis, particularly in the characterization of molecular events related to the development of early lesions and their early detection. **Second**, we are creating a Coordination center to facilitate the interaction, integration and cohesion of this program. This goal has been achieved by establishing three Consortium Cores (Administration, Biostatistics, and Pathology/ Epidemiology). **Third**, we have set up different levels of communication to facilitate the interactions among investigators. **Finally**, we are inviting clinicians and patients to be active participants in this Consortium and they will work with the scientists to provide clinical insights into research projects. The details of progress are summarized in Table 1. We are fortunate that our consortium has been selected as the Consortium award in 2011. We have requested the “no-cost-extension” which has been granted by US AMRMC for another year to continue the tasks related to consortium development such as support for the incoming Ovarian Cancer Symposium and purchase of containers for slides and tissue blocks, etc. We have accomplished all the tasks and as a result, we move beyond the Development phase and are fully engaged in the consortium projects in W81XWH-11-2-0230.

Table 1. Tasks proposed in the Development phase and the status of accomplishment.

Tasks proposed	Accomplished
Administration Core (JHU)	• Organize the Consortium symposium including the Pathology/Epidemiology consensus meeting; • Setup and test the audio-video broad band electronic device for e-conferences; • Organize the Internal Advisory Board;
Pathology and Epidemiology Core (JHU)	• Define criteria for early ovarian cancer lesions (precursors) and select cases and controls through the consensus meeting; • Survey available cases and controls from all research sites; • Establish tissue processing and trafficking mechanisms; • Set up quality control procedures for DNA, RNA and protein extraction
Biostatistics Core (JHU)	• Establish the data collection, storage and security systems; • Perform power calculation and sample size justification for each project; • Participate in study design of individual projects
Research sites (JHU, TUHN, MSKCC, Yale)	• Establish regular research conferences at each site; • Formulate research specific aims; • Identify expert collaborators and consultants; • Collaborate with Pathology/Epidemiology Core to identify pre-existing early lesions and precursors;

	Investigators have attended the DoD pre-award meeting at Fredrick
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Key Research Accomplishments

We use the carryover budget to support in part of the 3rd Johns Hopkins Ovarian Cancer Symposium and the details are summarized below.

During 3rd Johns Hopkins Ovarian Cancer Symposium two meetings were held.

- 1st Meeting DoD Grant Officers, DoD PIs and the Research Advisory Committee, May 17th, 2012 12p-1p

At this meeting, DoD Grant Officers, DoD PIs and the Research Advisory Committee members were present. After Dr. Kurman's introduction, all five PI's briefly summarized their projects. In addition to these summaries, Dr. Schildkraut commented on p5 questionnaire, Path Core, tissue collection, MTA and IRB issues. Input for how sampling should be done was discussed. Dr. Soslow asked how to evaluate endometrial serous cancers if there is a lesion in the tubes and if peritoneal carcinoma was predominant. Dr. Sherman added that in general tubes have been mishandled, inside the tubes are changed during fixation, histology was not optimized, no set rules for tube processing, serious contamination issues, etc. All participants agree with the need of rigorous evaluation of the tubes.

- 2nd Meeting all PI's; on May 17th, 2012 4:30p

It was decided that all five project PIs and administrative core agreed to establish the Steering Committee in research project and dealing with authorship. A decision was made about how the sampling for tumor and prophylactic cases should be done. Also the proposed slide labeling system was accepted for sample registry. A pilot study for inking ovary parts closest to the fimbriae was suggested by Dr. Soslow.

Reportable Outcomes

- The Consortium Development award has built up the necessary infrastructure to mature into a full Consortium program project which focuses on characterizing the early ovarian cancer lesions and precursors.
- This consortium has been selected for the second phase Ovarian Cancer Consortium award.
- As stated in the application, we have established the website for researchers and patients:
<http://www.ovariancancerprevention.org/>
- Publication from the Development award:
 - Visvanathan K, Vang R, Shaw P, Gross A, Soslow R, Parkash V, Shih IM, Kurman RJ. Diagnosis of serous tubal intraepithelial carcinoma (STIC) based on morphologic and immunohistochemical features- a reproducibility study. *Am J Surg Pathol*, 35:1766-1775, 2011. PMID: 21989347
 - Kuhn E, Kurman RJ, Shih IM. Ovarian cancer is an imported disease- fact or fiction? *Current Ob Gyn Report*, 1:1-9, 2012. PMID: 22506137
 - Kuhn E, Kurman RJ, Vang R, Sehdev AS, Han G, Soslow R, Wang TL, Shih IM. TP53 mutations in serous tubal intraepithelial carcinoma (STIC) and concurrent pelvic high-grade serous carcinoma- evidence supporting their clonal relationship. *J Pathol*, 226:421-426, 2012. PMID:21990067
 - Kurman RJ, Shih IM. Molecular pathogenesis and extraovarian origin of epithelial ovarian cancer: Shifting the paradigm. *Hum Pathol*, 42:918-931, 2011. PMID: 21683865

5. Kuhn, E, Meeker A, Visvanathan K, Gross AL, Wang TL, Kurman RJ, Shih IM. Telomere length in different histologic types of epithelial ovarian cancer with emphasis on clear cell carcinoma. Mod Pathol, 24:1139-1145, 2011. PMID: 21499239

Conclusion

The Consortium Development award has provided us the ground that is necessary to assembly a highly productive team consisting of many enthusiastic researchers from different initiations for ovarian cancer research. This can be only made possible through this DoD Development grant mechanism which turns out to be highly effective and rewarding. In fact, we have taken this advantage of Development award to obtain the Consortium award.

References

None.

Appendices

None.