

Cohort Consortium Flourishing as It Enters Ninth Year

In November, more than 100 investigators from 12 countries gathered in Bethesda for the eighth annual meeting of the NCI Cohort Consortium. Created in 2000, this extramural/intramural consortium addresses critical areas of cancer etiology research in which large-scale collaborations with sufficient data and biospecimens are needed to study gene-gene and gene-environment interactions. DCEG and the Division of Cancer Control and Population Sciences (DCCPS) have initiated, fostered, and supported this important research collaborative.

The consortium has grown steadily since its inception, attracting new cohorts and new investigators. In 2008, the consortium was joined by the DCEG U.S. Radiologic Technologists Study; the Canadian Study of Diet, Lifestyle, and Health; and the Swedish Women's Lifestyle and Health Study. These new members bring the total number of cohorts to 37, representing about 4 million study subjects, with some cohorts still accruing participants.

Consortium research projects are tackling some of the most challenging questions in the cancer field, which have been difficult to answer with existing studies. The large number of study subjects in the consortium permits the detection of modest genetic effects, such as those found by studying single nucleotide polymorphisms in genome-wide association studies (GWAS). Moreover, many of the cohort studies possess prediagnostic epidemiologic and biochemical data, which provide the opportunity to determine whether exposures, such as dietary intake, occurred before the onset of the cancer. For less common cancers, the consortium fosters the extensive collaborations necessary to gather a sufficient number of cases and statistical power to answer etiologic questions.

Consortium projects are in various stages of development, with some reporting results, others conducting analyses, and others newly forming. Among the early teams was the Breast and Prostate Cancer Cohort Consortium (BPC3), which identified a prostate cancer risk locus at chromosome 8q24. The BPC3 team also recently published a new GWAS report demonstrating multiple novel loci associated with prostate cancer (*Nat Genet* 2008;40:310–315). Such observations provide critical new insights into the underlying determinants of cancer, which may lead to better risk prediction models, improved screening and detection tools, and new therapeutic directions.

PanScan, a project team composed of 12 prospective epidemiologic cohorts, is making strides in its search for pancreatic cancer susceptibility genes. In 2008, the PanScan study team completed a whole-genome scan of 2,000 pancreatic cancer cases, which is currently being analyzed.

Also under way is the Vitamin D Pooling Project (VDPP). Epidemiologic evidence suggests that vitamin D deficiency is associated with increased risks of certain types of cancer, especially colorectal cancer. VDPP seeks to understand the relationship of vitamin D with the development of less common cancers, such as renal, gastric and esophageal, endometrial, ovarian, and pancreatic tumors as well as the lymphomas. Recently, assays measuring 25-hydroxyvitamin D [25(OH)D] on more than 11,000 samples from 10 participating cohorts were completed, and the findings will soon be published.

Although assembled with a focus on cancer, the consortium has the ability to study non-cancer outcomes as well. A project to take advantage of this data resource is the body mass index (BMI) pooling project. The BMI project contains data on several million Caucasian subjects from 26 cohorts; a parallel project will pool data on BMI and mortality in Asian cohorts. With large numbers of subjects, investigators hope to better clarify the relationship between being overweight and death rates for many conditions.

"The consortium meetings create the synergy and enthusiasm necessary to solve complex research questions," remarked Dr. Deborah Winn, Deputy Director of DCCPS. "The past, current, and future discoveries coming from the consortial projects will have major public health impacts."

A new project team focusing on breast cancer among African American women convened for the first time at the 2008 annual meeting. The investigators plan to conduct GWAS to clarify why African American women are more likely to be diagnosed with aggressive, high-grade, and estrogen- and progesterone-receptor–negative breast cancers.

The consortium is also supporting a newly formed brain cancer study group. The team will focus on glioma, an often-fatal cancer of unknown etiology, although many studies suggest a familial component. Investigators hope that GWAS of this tumor using the 2,000 cases available within the consortium will yield important clues. The meeting also provided an opportunity for small group discussions focusing on several other cancers, including non-Hodgkin lymphoma and cancers of the upper gastrointestinal tract, liver, and endometrium.

Cross-cutting workshops are another key component of the annual consortium meetings. Dr. Julie Palmer from Boston University chaired a working group that discussed methodologic challenges, including a presentation by **Gabriella Andreotti, Ph.D.**, Occupational and Environmental Epidemiology Branch, on the collection of environmental samples. **Lindsay M. Morton, Ph.D.**, Radiation Epidemiology Branch, chaired a session on second

cancers, while **Yikyung Park, Sc.D.**, Nutritional Epidemiology Branch, led a session on using cancer registries to ascertain cancer outcomes.

Strategic planning is vital as the consortium looks to the future. “One of the most exciting things about working with the consortium is to see the creativity and energy that the investigators are putting in to develop new directions and projects,” observed **Patricia Hartge, Sc.D.**, Deputy Director of the Epidemiology and Biostatistics Program (EBP). “It is this momentum which continues to move the consortium forward.” This year, 10 new project proposals were submitted for consideration to the consortium.

“One of the most satisfying parts of being involved with the creation and ongoing development of the consortium has been seeing investigators from all biomedical disciplines come together to work out these pressing research questions,” noted **Robert N. Hoover, M.D., Sc.D.**, Director of EBP. As the consortium matures, investigators remain excited about the crucial and distinctive foundation it provides to foster studies that illuminate the causes of cancer using the power of collaboration, large sample sizes, and the unique properties of the cohort study design.

For more on the Cohort Consortium, visit <http://epi.grants.cancer.gov/Consortia/cohort.html>.

—Maria Sgambati, M.D.