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BPC3 Update to the Steering Committee: Pete Kraft

History and Accomplishments

The Breast and Prostate Cancer Cohort Consortium (BPC3) began in 2003 and was first funded to conduct collaborative studies of hormone-related gene variants and environmental factors involved in the development of breast and prostate cancer. This research involved 10 cohorts and pooled data on 8,850 patients with prostate cancer and 6,160 patients with breast cancer. The goal was to characterize common variations in about 55 candidate genes that mediate the steroid hormone metabolism and insulin-like growth factor signaling pathways, and associate these variations with cancer risk. By pooling cases and controls across the BPC3 studies, the investigators were able to achieve greater statistical power, and therefore rule out or confirm associations that had been reported from individual studies.

In 2007, the BPC3 Consortium expanded the number of cases/controls to 14,000 and 16,000 for breast and prostate cancer, respectively. This second phase of BPC3 had three major goals: 1) to utilize a genome-wide association approach to identify genetic variants associated with estrogen receptor negative (ER-) breast cancer, as well as aggressive forms of prostate cancer; 2) to serve as a rapid verification test set for SNPs identified in other genetic scans; and 3) to examine gene-environment interactions in the SNPs identified in CGEMS and other studies as being associated with breast and prostate cancer.

The BPC3 Consortium has been remarkably productive and published over 100 studies. View BPC3 publications on the Cohort Consortium website. However, recognizing the need for even greater statistical power to identify gene variants with low to moderate penetrance and moderate prevalence in the population than could be achieved by pooling the data from the 10 cohorts in BPC3, the BPC3 cohorts joined the Breast Cancer Associations Consortium (BCAC) which includes data from more than 100,000 breast cancer cases and 100,000 controls, and the Prostate Cancer Association Group to Investigate Cancer Associated Alterations (PRACTICAL) Consortium which includes data from more than 65,000 prostate cancer cases and 65,000 controls. Thus, the data from BPC3 continue to contribute to efforts to provide reliable assessment of the risks associated with genetic variation, and to validate new findings.

The BPC3 published between 80 and 100 papers over the last 12 years. These achievements took a mix of epidemiologists, geneticists, and statisticians, a mix of junior and senior investigators, all working together.

The BPC3 demonstrated that cohorts from multiple institutions could collaborate on a common, planned project. The BPC3 was the first funded project to come out of the Cohort Consortium, and its success inspired others. Moreover, the collaboration proved nimble, moving from candidate genes to genome-wide association studies and beyond to (proposed) exome-chip and (funded) targeted sequencing studies as the science required.

The BPC3 trained a generation of early-career investigators from multiple institutions, who are now themselves independent principal investigators.

Challenges

The evolving needs of the science (genotyping costs, sequencing costs) required more resources than could be provided by a typical R01 mechanism. Independent funding proposals focused on important special problems—often focused on analysis of existing data. While many of these were funded, they did not include funds to maintain a coordinating infrastructure. Regular meetings to share progress and challenges and discuss future opportunities ceased, and the centralized, harmonized genotype, phenotype and covariate data bases could not be updated. In light of this, and in order to encourage initiative and flexibility in future collaborations among BPC3 cohorts and other studies—we did not want to send the signal that an additional step of formal approval from consortium was needed for collaborations among subsets of cohorts—the BPC3 was formally disbanded in 2016.