INTRODUCTION

A series of genetic mutations in somatic cell results in cancer. The cells of malignant tumor have the ability to acclimate to the microenvironmental changes. This can be attributed to the nature of tumor cell biology, i.e., based on effectual molecular signaling events. Such a level of intricacy with multiple cell types and variables thus demands an effective investigation of many variables at a time. Exploring our knowledge of the mechanism of malignancy and of aversion to therapy at the molecular level is paramount in designing successful treatment.

Cancer has a substantial heritable component. Understanding of the inherited prospect of cancer is an essential integrant of preventive oncology.

In the past decade, development of a range of deoxyribonucleic acid (DNA) and protein array technologies has enabled a meteoric progress in the fields of experimental and clinical oncology. Changeover of the conventional methods of cancer detection to microfabricated format approaches at increasing both perseverance of analysis and sampling throughput. Our increasing knowledge about the human genome and recent advances in gene typing has made genome-wide association studies (GWAS) of human diseases within bounds. Such studies have discerned many silent loci of genetic variation coupled with high risk of cancer. The GWAS have meaningfully increased our knowledge about cancers by revealing unique relationship of germline genetic disparities [single-nucleotide polymorphisms (SNPs)] with cancer susceptibility. In addition, GWAS successfully pointed out several genetic variants that are notably linked with cancer. However, a scission has appeared between the propensity to identify these associations and the propensity to significantly shed light on their biologic importance. Also, the identification of the genetic determinants of complex diseases like cancer by GWAS has been impeded by use of several other genotyping principles, often on limited collections of cases and controls.

To facilitate an across-the-board assessment of predisposition to various cancers, a consortium has been formed that included researchers from Genetic Associations and Mechanisms of Oncology, the Breast Cancer Case Control Consortium, the Consortium of Investigators of Modifiers of BRCA1/2 (CIMBA), Personalized Risk Stratification for Prevention and Early Detection of Breast Cancer, ATHENA Breast Health Network and the NIEHS Sisters studies, the Breast and Prostate Cancer Cohort Consortium (BPC3), the Prostate Cancer Association Group to Investigate Cancer Associated Alterations in the Genome, and Ovarian Cancer Case-control Consortium. The overall objective of this consortium is to attain a novel conception about the genomic design and mechanisms that underlie common cancers, by establishing a new genotyping array, the OncoArray, and to utilize it in genotyping a large number of cases with cancers of breast, lung, ovary, endometrium, colon, or prostate as well as genetically prone individuals; e.g., BRCA1 and BRCA2 mutation carriers. Also, joint genotyping across cancer sites permits sharing of controls and a
more comprehensive assessment of genetic risk. The assortment integrates fine-scale mapping of about 150 recognized cancer susceptibility regions.

Collaborative Oncological Gene-environment Study (iCOGS) is a custom illumina iSelect genotyping array, i.e., intended as a part of COGS, to analyze genetic variations correlated to cancers of breast, ovary, and prostate that are hormone associated. It included four consortia to get down to detailed genetic investigations of these hormone-related cancers. The project aimed at recognizing common variants that contribute to susceptibility to each of these cancers, and also variants related with several pertinent disease subtypes. The project included custom iSelect arrays that allowed genotyping of over 200,000 SNPs on a single array in 12 sample format. Inclusion of a large number of SNPs on iCOGS array not only replicates suggestive associations from GWAS but also helps to investigate a wide variety of phenotypes. The iCOGS array itself has now been retired, but a second-generation chip is designed.

GAME-ON is a cancer institute of national level consisting of five associating groups pursuing propitious scientific leads from previously generated cancer GWAS and coordinate and accelerate integrative post GWAS discovery research. The five associating groups include Discovery, Biology, and Risk of Inherited Variants in Breast Cancer (DRIVE), Transdisciplinary Research in Cancer of the Lung, Follow-up of Ovarian Cancer Genetic Association and Interaction Studies (FOCI), Elucidating Loci Involved in Prostate Cancer Susceptibility, and Colo-Rectal Transdisciplinary Study. Using particulars from The Cancer Genome Atlas to execute eQTL analyses, conducting methylation and copy number expression analyses, and developing and implicating certain novel methods for gene interaction and pathway analysis, the researchers have developed a GAME-ON oncochip.

The oncochip has an approach very similar to iCOGS, but it can be used on an even larger scale. The chip comprises nearly 600,000 SNPs developed for assessing genetic susceptibility for five specific cancers: Breast, ovarian, prostate, colorectal, and lung. Also, it includes fine mapping of all the new susceptible regions identified with iCOGS array, as well as associated variants identified through whole-genome, whole-exome, or targeted sequencing studies.

Oral cancer is one of the leading causes of increased mortality rate globally. This can be partly attributed to its delayed diagnosis due to lack of our knowledge about modern diagnostic aids. Diagnosing oral cancers at an early stage permits conservative therapeutic approaches and a more favorable prognosis. Advanced knowledge in the field of molecular biology and implication of newer diagnostic aids will transfigure our conventional perspective toward the management of oral cancers. Advanced technologies for cancer detection like DNA microarrays and chips provide more detailed genetic information at a relatively shorter period of time.

The use of an oncochip, an initiative within the GAME-ON consortium, renders a distinctive opportunity to further assess the genetic susceptibility of oral cancers. Though the GAME-ON oncochip is designed to evaluate genetic susceptibility of five cancers, it will be highly admissible for assessing oral cancers also. The chip comprises approximately 600,000 SNPs that allow further evaluation of the oral cancer that results from GWAS in great depth. Also, the chip gives a provision to explore the overlapping susceptibility between different cancers in much detail. With the use of oncochip, risk profiling of oral cancer can become very easy.

REFERENCES

6. COGS project and design of the iCOGS array. Orli Bahcall.