been reported to range from very low to levels equal to those in Caucasians. We report the results of completed *BRCA1* and *BRCA2* analyses in 20 African American families at risk for breast or ovarian cancer. Families were selected on the basis of a history of breast cancer or breast and ovarian cancer and further subdivided into the following categories: high-risk (three affected first-degree relatives; ten families), moderate-risk (two affected first-degree relatives; seven families) and undetermined-risk (single affected first-degree relative, with medical information being updated). *BRCA1* and *BRCA2* germline alterations were first detected using a series of exon-specific polymerase chain reaction primers for single-strand conformation polymorphism analysis; this was followed by DNA sequencing of polymorphism variants. A limited number of *BRCA1* polymorphic intronic variants detected as a result of these studies were also analyzed for their effect on *BRCA1* mRNA splicing using an assay developed by Myriad Genetics. In this cohort we detected one protein-truncating mutation in either *BRCA1* or *BRCA2* (1/20; 5%). However, we detected splice mutations, missense mutations and several polymorphic variants in both *BRCA1* and *BRCA2,* with a much higher frequency in *BRCA2.* Many of these variants were both new and specific to African American patients; they also occurred in the absence of another disease-causing mutation. Moreover, a new *BRCA1* missense mutation in one of the high-risk families, exon 19(W1718C), seems to co-segregate with breast cancer. We will report the relative frequencies of these *BRCA1* and *BRCA2* variants in patient and control populations. These results agree with previous observations that deleterious mutations in *BRCA1* or *BRCA2* are uncommon in at-risk African American patients. They indicate that more benign variants should be further evaluated for their potential role in the disease process in these patients and that additional, as yet unidentified, genetic factors may contribute to breast cancer risk in African American families.

Baxevanis, Andreas D. [19]

An integrated approach to the extraction, storage, processing and analysis of microarray gene expression data

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A single microarray experiment provides thousands of individual pieces of data; it is therefore essential to focus on effective informatics methods in order to draw new biological conclusions efficiently and confidently. We have developed a unified software package that meets several important needs in the area of microarray data analysis. The software achieves several goals: (1) Integrating algorithms developed at the National Human Genome Research Institute into NuTec's GLEAMS software system, creating a single, integrated core platform that is capable of handling the computational aspects of complementary DNA and oligonucleotide array analysis, including imaging, signal processing, data extraction, database management and higher-order data analysis. (2) Developing new bioinformatics strategies to deduce the sequence- and structure-based relationships that are currently hidden within cDNA and oligonucleotide array data, including clustering methods and connections to gene ontologies. (3) Linking microarray data to data being amassed in clinical laboratories, to combine pedigree, phenotypic and genotypic data with gene expression data. (4) Using parallel computing to facilitate the analysis of microarray data. An overriding goal of this project is that the software be as user-friendly as possible, keeping in mind the level of computer training of most of the biologists who will be using it as well as the hardware that is typically available in most laboratories.

Beaulieu, Martin [20]

High-throughput genotyping using candidate region mismatch scanning (PCR-CRMS)

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To identify loci affecting disease susceptibility, linkage and association analyses are performed by scoring previously characterized sequence variation, such as microsatellites and single-nucleotide polymorphisms. However, such analyses can be expensive and time-consuming. Moreover, examination of particular candidate gene regions for potential new linkages and associations may be limited by the infrequent occurrence of known markers. The typing by currently available methods of a sufficiently large number of markers to achieve a robust analysis is often beyond the reach of the typical research laboratory. Various techniques that score either unknown or known sequence variation have been developed, yet none of these strategies is equally well suited for mutation detection and the scoring of genotypes. To perform both tasks, a technique should be both sensitive enough to detect all mutation types and sufficiently quantitative that the translation of the data into allele-sharing status is feasible. We investigated the possibility of replacing conventional genotyping with a mutation-detection approach. Genome mismatch scanning is a hybridization-based mutation-detection technique employing the *Escherichia coli* mismatch-detection enzymes MutHLS. It was originally developed to enrich for identical-by-descent regions between two whole genomic DNA samples. To accommodate polymerase chain reaction products of candidate regions, we have conducted a comprehensive biochemical optimization of the technique for target sizes ranging from 260 to 1,250 base pairs. Our modifications, which we now collectively designate polymerase chain reaction–candidate region mismatch scanning, have simplified the assay, rendered it quantitative and demonstrated its potential for cost-effective, high-throughput genotyping. Strategies for exploiting the method in the study of candidate regions or in genome-wide studies will be discussed.

Belbin, Thomas [21]

Molecular classification of head and neck squamous cell carcinoma using cDNA microarrays

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Head and neck squamous cell carcinoma (HNSCC) is the fifth most common cancer worldwide and accounts for 95% of the head and neck cancer cases in the Western world. Over the past three decades advancements in management have