SESSION 3

S5. New Approaches to Cancer Gene Discovery

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Recent advances in microfabrication, coupled with the availability of a draft of the human genome sequence, provide new opportunities for the identification of genes involved genetic susceptibility to cancer. The identification of these genes, as well as those primarily responsible for the development of sporadic cancers, also has been augmented by improvements in high throughput technologies for mutation detection and sequencing. Linkage analysis remains an option for identifying familial susceptibility genes, but traditional approaches now may be enhanced by the availability of more genetic markers (including single nucleotide polymorphisms – SNPs) or by molecular phenotyping of the tumors arising in family members. One means of sub-grouping tumors is through the use of array-based expression profiling. However this technique requires fresh/frozen tissue for the preparation of good quality tumor RNA, a reagent in short supply when considering specific families. DNA from archival material, a tumor source much easier to obtain than frozen tumor, can be evaluated for recurrent patterns of chromosomal gains and losses using a high-resolution array-based version of comparative genomic hybridization (CGH). The ability to use array CGH as part of a gene identification strategy has been significantly enhanced by the availability of the draft genome sequence, as now regions identified as deleted or amplified can be directly interrogated computationally to identify known or predicted genes that fall within the region of interest. This step eliminates the laborious and time-consuming strategies previously required to identify transcripts in candidate regions. Regions containing genes involved in sporadic tumorigenesis also can be identified with array CGH using the same approach.