Carr, Kristen [32]

Relationship between gene expression profile and clinical outcome in malignant melanoma

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Cutaneous melanoma is the most serious form of skin cancer and one of the most common cancers in young adults. Its incidence is increasing at a significant rate, and the long-term survival rate for patients with melanoma has not improved markedly since the 1970s. Our laboratory identified unexpected subtypes of human cutaneous melanoma and observed a unique pattern of gene expression in highly invasive melanomas[1]. However, the study design for this initial report did not allow a direct correlation of gene expression profiles with disease progression or response to therapy. We have begun to address the relationship between gene expression profile and clinical outcome by collecting and analyzing a set of melanoma tumor biopsy samples with known clinical outcome. We have supplemented this set of samples with a melanoma tissue microarray. The examination of gene expression patterns of melanoma tumors will provide a unique opportunity to study a homogeneous group of patients and determine whether gene expression patterns can assist in predicting disease progression or therapeutic response.

1. Carr, K. *et al. Nature* **406**, 535 (2000).

Chen, Danian [33]

Genomic amplification in retinoblastoma narrowed to 1.2 Mb on chromosome 6p containing a novel kinesin-like gene, *RBKIN*

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Retinoblastoma is a rare tumor that arise in human retina when both RB gene alleles are mutated. All retinoblastoma have additional genomic changes evident on karyotype and comparative genomic hybridization. We have previously shown a high frequency of the i(6p) marker chromosome and gain of 6p22 in retinoblastoma. We now report a minimal region of 6p22 gain in retinoblastoma that spans 1.2 Mb detected by quantitative multiplex PCR. Using public databases, we determined that the sequence of this region was contained in three contigs. The STS marker with the highest frequency of genomic gain was contained within one fully sequenced PAC AL023807. Exon prediction indicates three unigene clusters within this PAC, one with 19 cDNA sequences in the dbEST. By analysis of those sequences we predicted a partial cDNA sequence, which has homology to the motor domain of the kinesin gene family. We generated several nested PCR primer pairs for rapid amplification of cDNA ends (RACE) and obtained from a retinal cDNA library a previously uncloned kinesin family gene, *RBKIN*, expressed in retina and included in the region of genomic gain in retinoblastoma. *RBKIN* is 5,850 bp and is homologous with mouse *Kif13a*. It is expressed in all adult human tissues tested including retina, as well as retinoblastoma, but its expresion level is very low in most fetal tissues. *RBKIN* and/or another gene in the same 1.2 Mb of 6p22 are likely to be oncogenes that contribute to initiation and malignant progression of retinoblastoma.

Chen, Sei-Yu [34]

Genomics-based strategies for the identification of lung cancer diagnostic targets

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Lung cancer is the most common cancer in men and women. In 2000 it caused an estimated 156,000 deaths, accounting for 28% of all cancer-related deaths. We have screened for differentially expressed genes in lung cancer using complementary DNA database mining and suppression subtractive hybridization based on the polymerase chain reaction. These genomics methods have been used to identify lung cancer genes that are tissue-specific, lung cancer–specific or both. We generated eight subtracted libraries using different subtraction combinations and sequenced 10,000 clones from each library. To confirm the differential expression of the candidate genes obtained, we used the real-time polymerase chain reaction with Taqman fluorescent probe assays. We generated gene expression profiles for some of these genes on different anatomical sites and in different disease states. We used this validation strategy to analyze 46 potential candidates. The RNA expression for 7 of these 46 genes was tested in more than 120 tissue samples. All genes showed high tissue-specific expression and overexpression in 45–67% of the lung cancer samples compared with the expression in normal adjacent tissues from the same individual. Full-length cloning, gene expression in bacteria and antibody production for these genes are under way. Once all the reagents are obtained, we will develop immunoassays to evaluate their utility as biomarkers for lung cancer. These genes, either individually or grouped in panels, could be of potential use as new tumor markers for early detection, differential diagnosis, prognosis, disease monitoring or cancer surveillance. They could also be useful as new therapeutic targets.

Chen, Yidong [35]

cDNA microarray analysis using both gene expression ratios and intensities

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In typical complementary DNA microarray experiments, two fluorescently labeled RNAs are hybridized to an array of cDNA probes on a glass slide, and their rela-