

Bioinformatics for the Cancer Gene Expression Profiling Studies

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DNA microarray technology is transforming the way of discovering cancer-related genes. The expression profiles of tens of thousand genes can be monitored in parallel and sophisticated statistical methods help to identify genes showing distinct expression patterns over tumor vs non-tumor groups or tumor sub-groups. Nevertheless, any objective biological interpretation of several hundred genes identified as dysregulated in cancer is a formidable task. In this talk, we will share our experience of analyzing gastric and liver cancer datasets generated from 21C Frontier Program on Functional Analysis of Human Genome. Prior to any experimental validation of the expression pattern, we employ bioinformatic analysis to categorize and prioritize the gene list. For this step, we have employed some databases and tools. The examples are:

1. Mapping genes onto BioCarta or KEGG pathway
2. Mapping genes onto GenMapp Gene Ontology
3. Utilization of expression databases such as SOURCE
4. Utilization of virtual Northern or SAGE pattern from CGAP

Microarray-based Integrated Genomic Technique to Discover Biomarkers of Colon Cancer

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Using cDNA microarrays to determine patterns of gene expression in Colon cancer we designed two independent experiments; 1) Indirect comparison, 2) Pair-wise direct comparison. Through indirect comparison of non-tumor and tumor tissues with common reference, respectively, we identified consistent differences between the expression patterns in colon cancer compared with those in non-tumor colon tissues. Some features of the gene expression pattern were related with phenotypic and genotypic characteristics of the tumors including differentiation and p53 overexpression. Direct comparison of tumor with non-tumor tissue confirmed that the consistent difference in gene expression are readily comparable with those of indirect comparison. Recently, cDNA-Array Comparable Genomic Hybridization (array CGH) revealed that a remarkable degree to which variation in gene copy number contributes to variation in gene expression (PNAS USA 2002; 99:12963-8). Herein, we utilized array-CGH analysis to investigate the overall patterns of DNA amplification and deletion during carcinogenesis of the colon cancer. In addition, we established promoter-methylation assay using DNA-array containing probes covering promoter sequences of methylation-associated genes and applied into Colon cancer study. Both analyzed data will be also discussed at meeting.