S6-01

Genetic aberrations detected by chromosomal and array CGH analysis in human solid tumors

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A hypothesis is widely accepted that a tumor is derived from a single cell with a series of genetic changes. With tumor progression, further genetic alterations are successively amassed due to genetic instability inherent to malignant tumors, and eventually tumors may demonstrate many genetic changes. Even among tumors with similar histologic appearance, genetic alterations frequently different. Since some of genetic alterations greatly affect biological characteristics of the tumor, genome-wide screening is necessary for not only elucidating cancer-related genes but also estimating biological behavior of each tumor. We have examined genetic alterations in approximately 2,000 human solid tumors in our laboratory using a method of comparative genomic hybridization(CGH) which is a sophisticated molecular cytogenetic technology that allows the identification of regions of chromosomal imbalances (DNA copy number aberrations). The impact of CGH analysis of malignant tumors is enhanced when CGH data are combined with clinical information including the status of lymph node metastasis and patient survival time. Some genetic aberrations represent nodal status and some are linked with patient prognosis. In general, the number of aberrations increases with tumor progression, namely it is higher in advanced tumors than in early ones. Genetic aberrations detected in early cancers are frequently found in advanced tumors. However, chromosomal loci with frequent aberrations in DNA copy number are considerably different among organs and types of carcinoma, and some are detected exclusively in a given type of cancer. The pattern of genetic aberrations varies from organ to organ and from tumor type to tumor type.

S6-02

Identification of the marker-genes for dioxin-induced immune dysfunction by using the high-density oligonucleotide microarray in mice blood.

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In mammals, TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) produces cancer, endocrine alteration, immunological change, and birth defects. The stem cell activity and the global expression profiles were studied in peripheral blood cells of male C57BL/6N mice after an intraperitoneal injection of 1ug TCDD/kg body weight at various time intervals: gestation 6.5 day, 13.5 day, 18.5 day, and postnatal 3 and 6 weeks. At postnatal 10 week, the proliferation activities of bone marrow stem cell were more attenuated ranging from 35%(P6W) to 55%(G6.5D) on colony forming assay.The expression patterns of the whole genes were analyzed by SOMs. The gene expression profiles that represent the 1 ug/kg TCDD during the development could be identified as follows; C5 for G6.5D, C22 for G13.5D, C10/C11/C14 for G18.5D, C7 for P3W, C17 for P6W. When the marker candidates were restricted for the genes of which expression level was greater than 2-fold, they were 115 genes that are involved in cell physiology and cell functions such as cell proliferation and immune function. Among them, we selected the genes that could be found in the stage - specific SOMs: two genes (SOM C22: ferritin heavy chain gene, adenovirus e1b 19 kda-interacting protein 3-like gene) for G13.5D, one gene (C10: cdna clone eukary translat elongation factor 1 alpha 1 gene) for G18.5D, 18 genes (C7: ribosomal protein l6 genes and 17 others) for P3W. The above genes are proposed to be a potential use of biomarker for dioxin exposure in the case of immume dysfunctions.