Exploration of new HCC biomarkers

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Analysis of plasma/serum for levels of viral antigens or antibodies to viral proteins has been used extensively as an early biomarker of potential risk of HCC. In addition, detection of elevated levels of alpha-fetoprotein is commonly used for early identification of HCC. Unfortunately, both of these approaches are not highly sensitive or specific. As a result, there is continuing investigation to identify additional biomarkers that may help in the early identification of cases. The use of DNA isolated from plasma or serum for detection of gene specific methylation has been discussed previously. In addition, tumor DNA isolated from blood has been analyzed for the presence of p53 mutations and found in a subset of cases to be present years prior to diagnosis as for methylated DNA. The general level of DNA present in blood has also been suggested as a potential biomarker of cancer.

Among the newer methods being tested are the detection of specific mutations in HBV. In many cases of HCC in China and Africa a double mutation, an A to T transversion at nucleotide 1762 and a G to A transition at nucleotide 1764 (1762T/1764A) have been found. These mutations have been associated with increased severity of HBV infection and cirrhosis suggesting that they might be a useful biomarker for high risk subjects.

The field of proteomics also holds promise for the development of new biomarkers. A number of groups are developing mass spectrometry methods for the identification of serum/plasma proteomic patterns that will distinguish bloods of HCC cases from those of controls. While some interesting preliminary data have been developed for several cancers, much additional work needs to be done in this area. Another approach is the use of platforms that contain an array of large numbers of proteins that can be used to screen plasma/serum samples for the presence of antibodies to specific proteins as a diagnostic marker of disease. Early studies detected antibodies to p53 protein in the blood of about 25% of cases with bladder, lung, colon and oral cancer but in <2% of control studies. The hope is that assaying for multiple antibodies will enhance the sensitivity and specificity of this approach.

Another approach being used is gene expression studies to identify new molecular markers for HCC. Microarray techniques can determine differences in the expression profiles of HCC cell lines compared to control lines and in HCC tissues compared to control tissues. The identification of candidate genes that are overexpressed in HCC could lead to the establishment of serum assays for the corresponding proteins in blood samples.

The IARC TP53 mutation database: a resource for studying the significance of TP53 mutations in human cancers

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The tumor suppressor gene TP53 is frequently inactivated by gene mutations in many types of human sporadic cancers, and inherited TP53 mutations predispose to a wide spectrum of early-onset tumors (Li-Fraumeni et Li-Fraumeni-like Syndromes). All TP53 gene variations (somatic and germline mutations, as well as polymorphisms) that are reported in the scientific literature or in SNP databases are compiled in the IARC TP53 Database. This database provides structured data and analysis tools to study mutation patterns in human cancers and cell-lines and to investigate the clinical impact of mutations. It contains annotations related to the clinical and pathological characteristics of tumors, as well as the demographics and carcinogen exposure of patients. The IARC TP53 web site (http:/