Gangi, Lisa [62]

Gene expression in prostate cancer: microarray analysis of tumor specimens from African American and Caucasian patients

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Adenocarcinoma of the prostate is the most frequently diagnosed cancer and the second leading cause of cancer deaths among American men. Prostate cancer has an even more devastating impact on the African American community: African American men have the highest incidence of prostate cancer in the world. At diagnosis, these patients are significantly younger in age and demonstrate a more advanced stage of the disease than Caucasian men. The mortality rate of prostate cancer is approximately 50% higher among African American men than among Caucasian men. Although there is mounting clinical evidence that the etiology of prostate cancer in African American men differs from that in Caucasian men, there is little understanding of the underlying molecular mechanisms. Complementary DNA microarrays allow the simultaneous assessment of thousands of genes in order to determine if there is a differential gene expression pattern that consistently segregates according to race and tumor grade. This microarray study compares total RNA samples extracted from histologically graded and Gleason-scored tumor prostectomy specimens from 20 African American and 10 Caucasian cancer patients.

Gavin, Mark [63]

Control of exit from G1 and S phases of the cell cycle by histone deacetylase–Rb-hSWI/SNF and Rb-hSWI/SNF repressor complexes

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The retinoblastoma protein (Rb) has traditionally been associated with regulating the progression of cells through the G1 restriction checkpoint of the cell cycle. There is increasing evidence that Rb is also involved in controlling the progression of cells through S phase. We have evidence that Rb combines with a histone deacetylase and the ATP-dependent chromatin remodeler, hSWI/SNF, to form a complex that arrests cells in G1. After phosphorylation of Rb by cyclin D1/cdk4/6, the histone deacetylase dissociates from this complex, leaving the Rb-hSWI/SNF complex to regulate exit from S phase. We suggest that these complexes regulate cell cycle progression by controlling the order of expression of cyclins E and A.

Giannella-Neto, Daniel [64]

Identification of protein-tyrosine kinase catalytic domain conserved sequences in the ORF expressed sequence tags database

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Given the importance of protein-tyrosine kinases (PTKs) in the signaling pathways that lead to cell proliferation, it is not surprising that they have been implicated in the onset and proliferation of cancers, diabetic retinopathy, atherosclerosis and psoriasis. We have selected 328 conserved sequences grouped into PTK families comprising 13 amino acids that include the Asp-Phe-Gly motif of PTK catalytic domains. We have searched approximately 700,000 complementary DNAs representing partial expressed gene sequences biased toward the central coding regions (ORF expressed sequence tags [ORESTES]) of the resulting human transcripts of a variety of human tumors. A compilation of the searched sequences was obtained from Human Cancer Genome Project data available on line at http//:www.ludwig.org.br. We have identified 150 different translated ORESTES containing the Asp-Phe-Gly motif, representing 31 PTK families, mostly related to Eph/Elk/Eck orphan receptors (7/13 no-matched sequences in GeneBank), HGF (5/9 no-matched), cyclin-dependent kinases (CDKs) and close relatives (8/9 no-matched), DAG-activated, phospholipid-dependent PKs (2/9 no-matched), the PDGFR family (1/8 no-matched), DDR/TKT (1/7 no-matched), MEK/STE7 (0/7 no-matched), PAK/STE20 (0/6 no-matched), epidermal growth factor receptor (0/5 no-matched), SRC (3/5 no-matched), RAC(AKT) protein kinase (2/5 no-matched), and RAF (0/5 no-matched). Twelve other PTK families were also matched with fewer than than four ORESTES. Searching for PTK catalytic domains in the ORESTES database could provide a source for new sequences partially coding PTKs that could play a role in the progression of human cancer and reveal potential targets for PTK inhibitors.

Gieseg, Michael [65]

Expression profiling renal tumors as a first step in the evaluation of tumor models

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Tumor models are poorly predictive of the efficacy of anticancer drugs on human neoplasms. Expression profiling technology presents a rational approach to identifying and unraveling the complex environmental and genetic differences that exist between models and human disease. As a first step in identifying these differences, we are building an expression database of renal cell carcinomas, comparing messenger RNA levels of primary tumors with those of normal kidney cortex from the same patient removed during surgical resection. Four tumor/normal kidney pairs were analyzed using the Affymetrix HuGeneFL array to determine if this approach could functionally separate subtypes of renal cell carcinoma. Two carcinomas were a clear-cell type and two were chromophobe carcinomas. Analysis of the mRNA expression results revealed that the normal samples clustered separate-