Journal of Cellular Biochemistry, Supplement 16I:72 (1992)

OVERVIEW

Detection

Epidemiological evidence indicates that in the United States, nearly all cases of bladder tumor initially present as superficial papillary neoplasms with limited potential for invasion; however, the incidence of recurrence after resection is very high (70–80%) and the detection of new lesions which have increased in grade or stage is difficult. Particularly difficult is the detection of premalignant lesions with a high risk of progression, *i.e.*, transitional cell carcinoma *in situ*, where traditional methods of detection (optical) are not useful. A growing body of evidence suggests that many, if not most, invasive carcinomas arise from flat carcinoma *in situ*. The multifocal character of bladder carcinoma makes it a particularly attractive target for the study of biomarkers which characterize the various grades and stages of both primary and recurrent episodes of cancer.

The presentations in the session "Detection" focused on the molecular and morphological changes which occur within the different stages of bladder cancer. Careful cytological examination of exfoliated cells can be used to help classify an individual's risk for carcinoma. Chromosomal aberrations and genetic changes can similarly be used to classify or detect the presence or progression of tumors.

Myron R. Melamed, MD (New York Medical College) presented his findings on the use of exfoliative cytology for the detection and grading of bladder neoplasms in patients at risk for incipient or recurrent carcinoma. Cells of benign papillary tumors cannot be differentiated from normal urothelial cells, but cytological sensitivity for carcinoma increases with increasing grade and multiple examinations over time.

The detection of non-random, cytogenetic abnormalities by conventional techniques and their investigation by fluorescent *in situ* hybridization (FISH) studies were discussed by Dr. Avery A. Sandberg (Southwest Biomedical Research Institute and Genetrix, Inc). Although no specific chromosome changes have been established for either early or fully developed bladder cancer, certain chromosomal aberrations are consistently encountered in bladder carcinogenesis; namely, loss of all or part of chromosome 9 (–9); trisomy 7 (+7); and loss of the Y chromosome. Loss of the Y chromosome may indicate an advanced stage of bladder cancer, whereas –9 and +7 signal early cytogenetic events. Cytogenetic changes coupled with molecular genetic abnormalities may serve to differentiate earlier from later cancer stages.

An evaluation of DNA flow cytometry (DNA FCM) as a screening tool for bladder cancer was presented by Dr. Ralph W. deVere White (University of California, Davis). Inherent limitations in this technique render it inappropriate as a screening tool for initial episodes of cancer in populations with no history of bladder cancer. DNA FCM can, however, be used very successfully to detect abnormalities in the DNA content of cancer cells from bladder irrigation specimens, and thus provide a very sensitive method for predicting disease recurrence. Dr. deVere White also presented a simple method for preserving exfoliated cells for shipment to central laboratories for DNA FCM testing.

Dr. Yves Fradet (Laval University Cancer Research Center) discussed the results of his research with monoclonal antibodies directed against tumor-associated antigens specific to various tumor subtypes and with distinct clinical behaviors. Certain markers, *e.g.*, surface antigen T138, are associated with recurrent tumors with high metastatic potential and can be used to identify high-risk patients. Other markers characterize papillomas with little or no malignant potential. The use of HPV 16 DNA sequences and p53 mutations as a basis for chemoprevention strategies was also discussed.

The final report in this session was given by Dr. George P. Hemstreet, III (University of Oklahoma) on the use of intermediate endpoint biomarkers for chemoprevention. Dr. Hemstreet described the clinical evaluation of F actin in patients with varying degrees of risk for bladder cancer. He proposed a battery of biomarkers to assess an individual patient's risk, *e.g.*, F- and G actin and EGF-R, to complement morphology in monitoring the progression of the oncogenic process in patients with bladder tumors.

Myron R. Melamed, MD
Department of Pathology
New York Medical College
Valhalla, NY 10595