Journal of Cellular Biochemistry, Supplement 17F:205 (1993)

OVERVIEW

Genetic Biomarkers

The session on Genetic Biomarkers addressed one of the most crucial and promising aspects of chemoprevention research. Recent developments indicate that specific and consistent genetic changes may be identified in the various steps of aerodigestive tract carcinogenesis. These abnormalities can be interpreted as biomarkers of cumulative genetic damage from environmental exposure, as well as the expression of individual susceptibilities to cancer.

Micronuclei analysis of exfoliated epithelial cells represents an example of a non-specific marker of DNA damage which has undergone a thorough reevaluation for its potential use in chemoprevention.

Detection of chromosomal rearrangements has developed from sporadic observation in cultured cell lines into a systematic investigation of fresh tumor specimens, providing the basis for correlation with relevant clinical features. Specific deletions, translocations or polysomies are recognized with higher frequencies on certain chromosomes, and may be easily investigated on tissue blocks by *in situ* hybridization techniques.

In molecular biology, the new methodologies have shown both activation of dominant oncogenes (*myc*, *ras*, EGFR, NEU) and inhibition of tumor suppressor genes (RB1, TP53, RAR-β), with a remarkable degree of consistent chromosomal changes. The development of specific monoclonal antibodies, suitable for testing paraffin embedded material, will enable large scale retrospective analyses of clinical data. The prognostic value of blood group antigens in head and neck or lung cancer is just an example of the potential role of biomarkers in the classification and staging of invasive cancer.

Some of the above genetic changes have been described in dysplastic or premalignant lesions of the upper aerodigestive tract, as well as in macroscopically normal mucosa, thus providing a biological basis for identification of subjects at higher risk of cancer.

These data suggest that genetic biomarkers may be used in the near future not only to identify optimal candidates for chemoprevention programs, but also to monitor the results of intervention in the short and intermediate term.

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