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OVERVIEW

Genetic Surrogate Endpoint Biomarkers in Early Breast Neoplasia

Edison Liu (University of North Carolina) discussed the relationship of oncogenes and breast cancer. Specifically, he described much of the recent work with HER-2/*neu*, PRAD1, and p53. Some of these genetic lesions appear early in the breast cancer process and are stable as the tumors become invasive and metastasize. Dr. Liu also presented a short summary of the work on germline mutations such as BRCA1 and *H-ras* variable number of terminal repeats. He expressed the viewpoint that the most rational use of genetics may be to identify women at high risk for the development of breast cancer and to enroll them in future chemoprevention trials.

Robert Callahan (National Cancer Institute) presented the results of a systematic study of primary human breast tumor DNA designed to identify and characterize frequently occurring somatic mutations, particularly loss of heterozygosity (LOH) mutations on chromosome 17. Dr. Callahan's laboratory is focusing on five regions of chromosome 17 which are independently affected by LOH; two on the short arm (one of which is p53, the other still unidentified) and three on the long arm (*nme*1 and two other unidentified genes). Results from these studies suggest that there may be potential tumor suppressor genes both centromeric and teleomeric to the *nme*1 gene on chromosome 17.

David Tarin (Oxford University) described his work identifying splice variants of the CD44 gene as markers of progression in a variety of human tumors. CD44 codes for a family of heavily glycosylated cell surface proteins which are involved in many important cellular functions. Disturbances in the expression pattern of CD44 begin very early in the neoplastic process and can be detected either non-invasively using exfoliated cells or by very small biopsy samples. The potential for early diagnosis and screening are readily apparent and were discussed along with the implications for therapeutic decisions, clinical practice, and future research.

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