Etiologic Heterogeneity of Cancers and the Improved Search for Risk Factors

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Abstract

Our knowledge of cancer risk has evolved over the past several decades from countless epidemiological studies of cancers of specific anatomical sites. Much recent clinical research has been devoted to identifying tumor sub-types that are clinically distinct, using for example cluster analyses of genome-wide somatic characteristics of tumors. Efforts to establish the etiologic heterogeneity of tumor sub-types has been limited to comparisons of the risk profiles of candidate sub-types, usually on the basis of individual somatic characteristics. In this talk it will be shown that studies of double primary malignancies can be uniquely informative about cancer risk heterogeneity. The magnitude of the odds ratio linking two tumor subtypes among double malignancies is inversely related to the inherent concordance of the risk profiles in the subtypes. Consequently, it is possible, in principle, to establish tumor subtypes with the maximum degree of etiologic heterogeneity without knowledge of the risk factors that give rise to the heterogeneity. This offers the prospect of strategies to provide greater statistical power for the identification of new risk factors, and to improve risk prediction. The presentation will be illustrated with data from studies of breast cancer and melanoma.

Keywords: Etiologic heterogeneity; Cancer risk; Tumor sub-types.

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