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Original Paper

Expression of drug pathway proteins is independent of tumour type

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Abstract

Current clinicopathological staging systems have the advantage of standardized criteria for assessing tumour stage, and a relationship between advancing tumour stage and poor prognosis has been established for most cancers. However, these tools have not led to clear criteria for therapy selection in individual patients. Indeed, the concept of therapy based on anatomical location seems quaint. Therefore, a representative drug pathway (irinotecan) was evaluated across common tumour types to test the hypothesis that pharmacological proteins are expressed independent of anatomical location. Many enzymes are involved in controlling the disposition of irinotecan, including the cellular target (TOP1), metabolism enzymes (CES2, UGT1A1, CYP3A4, CYP3A5), and cellular transporters of the anti-cancer agent (ABCB1, ABCC1, ABCC2, ABCC3, ABCC5, ABCG2). These 11 proteins were evaluated in tissue microarrays containing colon, breast, prostate, ovary, and lung cancers; brain tumours; melanoma; lymphoma; and selected normal tissues. A total of 255 tumours and 37 normal tissue samples were evaluable for all proteins. Linear discriminant analysis designed to predict the tissue type from the protein expression levels revealed a 49.6% misclassification rate, indicating that protein expression of this drug pathway is not associated with tissue type. Cluster analysis identified a variety of tumours with the same pharmacological profile. The anatomy independence of drug pathways stimulates efforts to move away from our traditional approaches to the selection of cancer therapy. Copyright © 2006 Pathological Society of Great Britain and Ireland. Published by John Wiley & Sons, Ltd.

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