MOLECULAR ANALYSIS SHOWS A COMMON DELETION IN THE MAJOR TYPES OF LUNG CANCER

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Chromosome studies of 5 SCLC cell lines revealed a common deletion of chromosome 3 with bands p21-p23 as the shortest region of overlap. Hybridization with a polymorphic 3p21 probe (minor allele frequency almost 0.5) revealed no heterozygosity in 15 SCLC cell lines. All those SCLC patients who were found to be heterozygous for this probe in blood DNA gave homozygous patterns when their tumour DNA was analyzed. Hybridization of DNA from 17 squamous- and 6 adenocarcinomas revealed 13 and 3 cases, rspectively, with only one band in the autoradiograph. The others showed two bands of unequal intensities. For 12 heterozygous control DNAs, the intensity ratios of the two bands varied between 1.20 and 0.80. For all tumours, except for one squamous- and one adenocarcinoma, the ratio was significantly outside this range. The presence of low intensity bands can be attributed to an admixture of normal tissue with the tumour, as was confirmed by histologic examination. The common occurrence of the 3p21 deletion in all lung cancers suggests that it is one of the essential events in the development of this tumour.

BIOLOGICAL CHARACTERISTICS OF HUMAN MALIGNANT MELANOMA CELL LINES AND ITS POSSIBLE CLINICAL APPLICATION

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Cellular heterogeneity of human tumours is considered responsible for different sensitivity to chemotherapeutic drugs; a characteristic which has great clinical significance. In order to achieve an accurate study of the biological properties of histologically verified human cutaneous melanoma, four cell lines were characterized using antimelanoma monoclonal antibodies, examined morphologically and by karyotype analysis. Different degrees of immunofluorescent staining have been detected in primary tumour continuous cell lines compared to cloned cell lines obtained from the same primary culture by colony selection or micromanipulation. Metastaic melanoma cell line from the same patient differed in immunofluorescence from primary and cloned cell lines. Morphological analysis showed variability within the primary, as well as metastatic cell culture, while cloned cell lines were morphologically more uniform. Chromosome analysis revealed abnormalities in ploidy, different rearrangments and three shared characteristic markers. Such characterization of tumour cell lines could be used in planning therapy for individual patient with single or metastatic tumours.

9-AMINOACRIDINE-4-CARBOXYAMIDES INDUCE COVALENT INTERSTRAND DNA CROSS-LINKING IN TUMOUR CELLS

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We have shown previously that such classical intercalators as 1-nitroacridines exert their cytotoxic and antitumour activity by covalent DNA cross-linking which occurs after metabolic activation in the cell. On this basis, we anticipated that some other highly active antitumour drugs which are believed to act via intercalation might, in fact, cross-link cellular DNA. This hypothesis has been confirmed in our laboratory for some anthracyclines and anthracenediones. Recently, we have also found that 9-aminoacridine-4-carboxyamides, a new class of antitumour compounds synthesized at the Univeristy of Auckland, New Zealand, induce interstrand cross-links in DNA of tumour cells in dose-dependent manner. The ability to form interstrand DNA cross-links depends on both cytotoxic activity of the compounds studied and their chemical structure.

HUMAN LYMPHOMA XENOGRAFTS IN DRUG SCREENING

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Three human non-Hodgkin lymphomas (B-cell origin) were established as transplantable xenografts in artificially immune-suppressed CBA mice. (None of the samples from Hodgkin-lymphomas had taken.)