PHORBOL MYRISTATE ACETATE: EFFECTS ON LYMPHOCYTES AND TUMOUR CELLS. J.Bubeník, M.Indrová and P.Perlmann. Institute of Molecular Genetics, Czechoslovak Academy of Sciences, Prague, Czechoslovakia and Department of Immunology, University of Stockholm, Stockholm, Sweden.

Admixture of phorbol myristate acetate (PMA) has been found to abolish growth-inhibitory effects of interleukin 2 (IL 2)-containing preparations on methylcholanthrene -induced mouse sarcomas in vivo. Detailed analysis of this phenomenon revealed that:

1. PMA enhances growth of transplanted sarcomas in syngeneic mice and increases ^{3}H-TDR incorporation by the sarcoma cells in vitro.
2. PMA enhances DNA synthesis and in vitro growth of cytotoxic T lymphocytes as well as the mitogenic effect of IL 2-containing preparations.
3. The former activity (1) overlaps in vivo with both the latter (2) and the tumour-inhibitory effect of IL 2-containing preparations, thus abolishing the therapeutical efficiency.

EXPRESSION OF A HUMAN OSTEOGENIC SARCOMA ANTIGEN ON MITOGEN STIMULATED PERIPHERAL BLOOD MONONUCLEAR CELLS AND HUMAN TUMOUR CELL LINES. D.G.Campbell, M.R.Price and R.W.Baldwin, Cancer Research Campaign Laboratories, University of Nottingham, Nottingham NG7 2RD, U.K.

The anti-human osteogenic sarcoma monoclonal antibody 791T/36 was determined to react with human peripheral blood mononuclear cells stimulated with phytohaemagglutinin (PHA). By flow cytofluorimetry, 791T/36 antibody reactivity was shown to be directed against a subpopulation of cells with the characteristics of PHA-blasts. Maximal antigen expression co-incided with maximal DNA synthesis in cells cultured with PHA for 3 days and up to about 2×10^5 antibody molecules were bound per blast cell at saturation.

The target antigen was identified by gel electrophoresis and autoradiographic techniques (Price et al, this meeting) and the apparent molecular weight was determined to be 72,000. This is equivalent to that of the glycoprotein antigen expressed upon the immunizing osteogenic sarcoma 791T and to that of the 791T/36 defined antigens associated with other human tumour cell lines. These include three osteogenic sarcomas (2 OS, 788T and 278T), a colon carcinoma (HcLo) and a prostate carcinoma (EB 33) all of which show serological reactivity with the 791T/36 antibody in independent tests.

The findings indicate that the 791T/36 antibody defines an antigen which is not only a major cell surface component of a number of human tumour cell lines, but also a marker for activated lymphocytes.

ONE-ELECTRON OXIDATION IN POLYCYCLIC AROMATIC HYDROCARBON (PAH) CARCINOGENESIS
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Current data point to multiple mechanisms of activation in PAH carcinogenesis. Evidence from several experimental approaches suggests that radical cations formed by one-electron oxidation are important intermediates. Development of PAH radical cation chemistry and determination of ionization potentials (IP) of a large number of PAH point to a common feature of almost all carcinogenic PAH, namely highly localized charge in the radical cation and generally low IP. Binding studies of the two carcinogenic PAH, benzo(a)pyrene (BP) and BP-6-CH_3, in mouse skin provide clear evidence for activation by one-electron oxidation. Binding of BP to DNA occurs predominantly at C-6, and binding of BP-6-CH_3 to mouse skin DNA yields a major adduct, in which the methyl group of BP-6-CH_3 is linked to the 2-amino of deoxyguanosine. Carcinogenicity studies of 18 PAH in rat mammary gland indicate that only PAH with low IP postulated to be activated by one-electron oxidation induce tumours in this target organ. These combined data indicate that one-electron oxidation of PAH is involved in the tumour-initiating process of the compounds. Supported by NCI contract NOI CP5620 and grant ROl CA25176.