

SZE

## EFFECT OF 3-METHYLCHOLANTHRENE ON NUCLEAR SUBFRACTIONS IN RAT LIVER

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The induction of microsomal aryl hydrocarbon hydroxylase activity by the polycyclic aromatic hydrocarbon 3-methylcholanthrene (3-MC) is considered to be a crucial event in the metabolic activation of these compounds to their ultimate carcinogenic forms. The inducing action of 3-MC is thought to be accomplished mainly at the epigenetic level. The present experiments were designed to study some aspects of the effect of a single dose of 3-MC on the transcriptional machinery of rat liver nuclei. Both the nucleolar and nucleoplasmic protein kinases and RNA polymerases were found to be stimulated by a single intraperitoneal injection of 3-MC. The activation of these enzymes as well as an enhancement in the *in vivo* phosphorylation of nuclear proteins were restricted to a nuclear subfraction that contains transcriptionally active chromatin. The same subfraction is the predominant  $^3\text{H}$ -3-MC binding site as well. These observations suggest that nuclear protein kinases, phosphoproteins and RNA polymerases may be involved in the realization of the inducing effect of 3-MC.

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INTRATUMORAL IMMUNOTHERAPY OF ADVANCED METASTATIC CANCER WITH PROPIONIBACTERIUM GRANULOSUM KP-45

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Propionibacterium granulosum strain KP-45 (P.g.) possesses potent immunostimulatory and immunomodulating properties with the induction of endogenous interferon, activation of macrophages and natural cytotoxic (NK) activity. Experimental investigations have demonstrated that the antineoplastic activity of P.g. is much stronger after local (intratumoral) injection than after systemic (intravenous or intraperitoneal) administration. A total of 97 patients with advanced metastatic cancers (stomach and colo-rectal - 32; prostatic - 10; breast - 50; inflammatory breast - 5) were treated with intratumoral injections of 10 mg of lyophilized killed P.g. (twice monthly for 2 months, then once monthly) given directly or through an endoscope. Patients with breast cancer were treated with P.g. combined with chemotherapy (FAC courses) and for other patients immunotherapy was a sole form of treatment. Involution of primary tumours (CR - 28%; PR - 46%) associated with longer survival times (1 - 2 yrs) was observed.

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THO

## HUMAN TUMOUR IMMUNITY AND CHARACTERIZATION OF THE PUTATIVE ANTIGEN

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Human immunity to cancer can be detected by an *in vitro* assay of leukocyte adherence inhibition (LAI), which depends on organ-specific cancer neoantigen (OSN) recognition by antibody dependent monocytes or autologous T cells and production of leukotriene-like mediators that mediate LAI by inhibiting the adherence of about 30% of all leukocyte subtypes. The immunogenic OSN molecule is enriched from spent medium by physicochemical methods and then affinity purified with a mouse monoclonal antibody (MAb). The affinity purified OSN is a 40,000 dalton (p40) molecule. Small amounts of lower molecular weight molecules are precipitated by the MAb anti-p40: p32, p25 and p13. MAb anti-p40 is directed to a framework determinant and does not bind the OSN epitope recognized by human leukocytes. The purified p40 is hydrophilic, contains no identifiable glycosylation sites, is heterogeneous with a pI of 6.3 to 7.3, and N-terminal amino acid sequence to 14 cycles has been accomplished. P40 OSN from human lung and colon cancer have been purified and shown to be antigenic in LAI by rigorous and extensive blind testing.

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