

## Symposium no. 11: New Approaches to Cancer Diagnosis and Management

11.013

## STUDY OF TUMOR SEEKERS for BORON NEUTRON CAPTURE THERAPY (BNCT) of LIVER TUMORS

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BNCT is a new concepts of highly selective radiotherapy based on the external activation, by a neutron beam, of boron-10, specifically localized in tumor cells. Boron 10 captures a slow neutron emitting high Let-short ranged fragments.

BNCT has been investigated specially for brain tumors and melanomas. We present our results, in rats with intrahepatic Walker carcinoma, with BSH and BPA, the most common boron compounds for gliomas and melanomas and with the porphyrine TPPS. With these compounds we found a tumor/liver and tumor/blood ratio  $> 2$ .

11.015

## ROLE OF THE PINEAL GLAND AND MELATONIN INDUCED-IMMUNO-OPIOIDS (MIO) IN LEUKEMOGENESIS.

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We demonstrated that the pineal hormone melatonin (MLT) have an immunomodulatory role. In particular, melatonin acts on CD4+, T helper lymphocytes stimulating the release of MIO. In the present work we investigated the role of the pineal gland, MLT and MIO in leukemogenesis. Leukemia was induced in female and male mice by inoculating intrathymically (i.t.) at day 0 a radiation leukemia virus (A-Rad LV). From day 10, mice were treated chronically till animals death, injecting s.c. MLT 5 mg/Kg b.w./day, Naltrexone 1 mg/Kg.b.w./day and PBS. In another experimental model mice were: A) surgical pinealectomized at day -14, B) kept under constant environmental lighting (24:24 light cycle) and C) sham pinealectomized. Each group of mice was kept undisturbed until inoculation of A-Rad LV (day 0). The results show that exogenous MLT accelerated ( $p<0.001$ ) while surgical or functional pinealectomy delayed ( $p<0.005$ ) the disease course. Moreover, this MLT action was blocked by naltrexone indicating the involvement of MIO. These results indicate that: 1) the pineal gland and MIO promote leukemogenesis. 2) these findings might be helpful in providing new strategies for clinical interventions.

11.017

## EBV-ANTIBODIES WITH ADDITIONAL PATTERN IN INDONESIAN NASOPHARYNGEAL CARCINOMA. E Tjokrosetio, SB Kresno, S Cornain, A Syafril, AN Kurniawan, N Rifki, F Oesman

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Both the Epstein Barr Virus (EBV) expression and the immunological response in nasopharyngeal carcinoma (NPC) might be influenced by ethnic difference. Most data studied in Asia were from Chinese. We therefore investigated Indonesian native NPC patients. Thirty four new NPC cases were tested for their EBV-antibodies by immunofluorescence on acetone-fixed lymphocytic cells / NC37. Twenty other malignancies of the head & neck and twenty ENT non-neoplastic cases were used as controls. The results showed VCA-IgA antibodies in almost all (32/34) NPC cases. The titer varied: 10-20 in 10, 40-80 in 11 and 160-320 in 12 cases. The only two with WHO type-1 reacted weakly while the rest with type-3 showed weak to strong reactions. 4/20 other malignancies and none of non-neoplastic cases were positive. It is of great interest that in addition to relatively strong EA-IgG reactions our NPC sera contain antibodies which revealed patchy ring fluorescence besides the D pattern.

11.014

## ESTROGEN RECEPTOR CONTENT IS INVERSELY RELATED TO ANTIGEN CA 15-3 LEVEL IN BREAST CANCER PATIENTS

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Cytosol ER content and serum CA 15-3 level were measured immunochemically in 34 breast cancer patients at the time of mastectomy. A significant inverse correlation was found between the cytosol ER content and serum CA 15-3 level (correlation coef. =  $-0.345$ ,  $p<0.05$ ). In addition, patients with a high level of CA 15-3 ( $>25$  U/ml) had significantly lower ER content ( $17.9 \pm 18.1$  fmol/mg) than those with a low serum antigen level (ER content  $77.4 \pm 94.4$  fmol/mg,  $p<0.01$ ). The possible explanations of these results are discussed in context of well known prognostic value of ER status. The antigen CA 15-3 may represent a tumor cell component down-regulated by estrogen, and could be used as a prognostic factor and probably as a predictor of effectiveness of endocrine therapy of breast cancer.

11.016

## EFFECT OF IL-1 AND ITS INHIBITOR ON ARACHIDONIC ACID CASCADE

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Cytokines have the capacity to stimulate arachidonic acid metabolites. Arachidonic acid products are mediators that produce many biologic effects as for example, leukocyte aggregation which leads to a depletion of white cells, decrease in systemic arterial pressure, hemorrhage, edema, etc. Prostaglandins and leukotriene can be released by disrupting the phospholipid membrane after stimulation by many agents and some lymphokines. The disorganized membrane gives way to the formation of phospholipase which forms arachidonic acid. The effect of human recombinant interleukin-1 receptor antagonist (IL-1ra) on leukotriene B4 (LTB4) release was investigated in activated human monocyte cultures. To stimulate LTB4 production two agonists were used: calcium ionophore A23187 and FMLP. Preincubation of monocytes with cytochalasin B (CB) (5 µg/ml), for 15 min, augmented the release of LTB4 when FMLP, not calcium ionophore A23187, was used. The cells were treated with various concentrations of A23187 (0.05 - 50 µM) and FMLP (5 x 10<sup>-9</sup> - 5 x 10<sup>-5</sup> M) for different periods of time. The greater LTB4 stimulation was found at A23187, 5 µM, and FMLP (5 x 10<sup>-6</sup> M) for 10 min incubation time. When human monocytes were pretreated for 1 hr with hrIL-1ra at different concentrations (0.25 - 250 ng/ml) and then treated with A23187 (5 µM) or CB + FMLP (5 x 10<sup>-6</sup> M) for 10 min, a dose-dependent inhibition was found. The inhibition of LTB4 may suggest an important modulatory role for this new monokine in inflammation and immunity.

11.018

## MORPHOLOGICAL &amp; IMMUNOHISTOCHEMICAL SUPPORT FOR THE INTERSTITIAL CELL ORIGIN OF ESTROGEN-INDUCED KIDNEY TUMORS IN THE SYRIAN GOLDEN HAMSTER

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Diethylstilbestrol induced kidney tumors in castrated Syrian Golden Hamster were studied at morphological, immunohistochemical & electron microscopical levels. Several hyperplastic, preneoplastic & early tumors (tumors) were identified & classified by histological subtypes. Epithelial & mesenchymal tumoral patterns were dominant, but other histological varieties (endocrinoid, neuroectodermic) were present. A new histological classification with 7 subtypes is proposed, supported with electron microscopy & immunohistochemical results, in which neural secretion & neural markers were found. Cytotypes were obtained in several tumors with no cytogenetic abnormalities. Moreover a correlation was found between estrogen receptors & morphology of the tumors. Present results lend further support to the interstitial cell origin of these neoplasms, arising from remnants of metanephric undifferentiated elements located in the interstitial tissue of the mature kidney.