

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

11.097

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IL-1 and TNF PRODUCTION BY HUMAN TRANSFORMED  
MONOCYTOID CELLS  
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LPS-activated human monocytoïd cell lines U-937, THP-1 and HL-60 produced IL-1 $\beta$  which was determined immunocytochemically within the cellular cytoplasm. A discrepancy between IL-1 $\beta$  mRNA accumulation and protein synthesis was found for THP-1 cells. TNF $\alpha$  was not induced by LPS stimulation but after activation for 48 hours with PMA and then with LPS all studied cell lines were found to produce both IL-1 $\beta$  and TNF $\alpha$ . Human rIL-1 $\beta$  increased while rTNF $\alpha$  inhibited U-937 cell line proliferation. Using simultaneous autoradiographic study of cells pulse labelled with  $^3$ H-thymidine and immunoperoxidase staining with MAB to IL-1 $\beta$  it was shown that the proliferating U-937 cells do not synthesize IL-1 $\beta$ .

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SIMULTANEOUS ESTIMATION OF QUANTITATIVE EGFR-S AND  
STEROID RECEPTORS IN BREAST TUMORS

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It is well-known that there are some tumors which are hormone dependent. This has been well shown for breast cancer. Steroid receptor assay in this malignancy is important in selecting patients for endocrine therapy. In regard to this data we aimed our work on determining whether the estrogen and progesterone quantitative receptor values (endocrine parameters) are related to quantitative values of epidermal growth factor receptors (autocrine/paracrine parameters). In breast cancers steroid receptors (ER/PR) and epidermal growth factor receptors were determined on 109 breast cancers by classical saturation binding assays. In this study we noted an inverse relationship between the expression of EGF-R and ER and PR.

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Cancer chemotherapy potentiation and sensitization by non-toxic pretreatment with combined vitamin C and K3. H.S. Taper and M. Roberfroid. Unité de Biochimie Toxicologique et Cancérologique. UCL 7369. Av. Mounier 73 - 1200 Bruxelles, Belgium.

Combined administration of vitamin C and K3 had a growth inhibiting action on 3 types of human neoplastic cell lines cultivated in vitro at 10 to 50 times lower concentration than when both vitamins were given separately. Combined vitamin C and K3 administrated i.p. before single dose of 6 different cytotoxic drugs commonly used in human cancer therapy produced a distinct chemotherapy potentiating effect in ascitic liver tumor bearing mice. This pretreatment sensitized to a single i.p. dose of vincristine sulfate this ascitic tumor which was completely resistant to this drug. This potentiating-sensitizing action did not increase the general and organ toxicity. It was suppressed by catalase pretreatment, thus suggesting an excessive production of hydrogen peroxide with subsequent oxidative stress and its consequences as a possible mechanism involved in above action of combined vitamins C and K3.

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Interleukin-1 production in patients with  
acute leukemia and myelodysplastic syndrome

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We have studied the IL-1 production by isolated mononuclear blood cells and IL-1 serum levels in patients with myelodysplastic syndrome and acute nonlymphocytic leukemia. High IL-1 production levels have been found in patients with acute myelomonocytic leukemia and chronic myelomonocytic leukemia. In some cases the induced IL-1 production was absent. There was no correlation between the IL-1 level in serum and IL-1 production by adherent cells in vitro. In 1 of 12 patients IL-1 was revealed in blast cells immunocytochemically. The IL-1 production level did not influence survival.

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TRANS-ARTERIAL CHEMOEMBOLIZATION IN PATIENTS AFFECTED BY HEPATOCELLULAR CARCINOMA  
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In patient affected by unresectable hepatocellular carcinoma (HCC) encouraging results were obtained by trans-arterial embolization (TAE) alone or associated with chemotherapy (TACE). Our experience consists of 45 patients (40 male and 5 female, by age from 22 to 81) affected by HCC treated with TACE. 21 of them were Okuda's stage I and 24 stage II. We have excluded patients with serious liver failure (Child-Pugh's class C) and/or kidney failure, haemorrhagic syndrome, portal thrombosis and patients with massive HCC. The treatment consisted in the administration of Adriablastin (20-80 mg) and Lipiodol (5-10 ml) followed by arterial embolization with Spongel; a total of 62 treatments were carried out. Almost all patients presented fever and abdominal pain that generally disappeared in 1-2 days. In the 30 % of cases we had no side effects, while in the 65 % we observed one or more heavier early side effects as fever, pain, ascites, jaundice, acute cholecystitis turned out quickly with medical therapy. Finally, one patient presented transient hemobilia and another died two months after TACE for subphrenic abscess. The efficacy of therapy, evaluated by means of avidity for Lipiodol due to HCC with echography and TC was complete in the 25 % of patients, good ( ) 50 % of the tumour) in 45 %, insufficient ( < 50 %) in 25 % and useless in 2 patients. After TACE, 5 patients underwent to surgery. Of 40 patients treated by TACE alone, 15 died after a mean survival of 16.4 months; 11 of them died for cirrhosis complications, while only 4 died for tumour progression. The others 25 patients are still living with an actuarial survival of 18-21 months (3-33). On the ground of this experience, TACE appears an efficient therapy in patients affected by HCC, with a relatively low incidence of heavy side effects.

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Ki-67 LABELLING INDEX AND EGFR GENE AMPLIFICATION IN  
HUMAN GLIOBLASTOMAS AND THEIR PROGNOSTIC  
IMPLICATIONS

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Twenty human glioblastomas (GBM) were examined for Ki-67 labelling index (Ki-67 LI) and amplification of the epidermal growth factor receptor (EGFR) gene. 8/20 GBM contained an amplified EGFR gene. The median value for Ki-67 LI for all GBM was 1.9 (range 0.2-24.6). The median value of Ki-67 LI for GBM with amplified EGFR gene was 4.2 (range 0.4-24.4) and for GBM with normal EGFR gene the median value was 0.8 (range 0.2-11.8) (not statistically significant, 0.05 < p < 0.1, Mann-Whitney test). Kaplan-Meier estimates revealed shorter survival for GBM patients with Ki-67 LI > 1.5 than those with Ki-67 LI < 1.5 (statistically significant, p < 0.05, log rank test). GBM patients with amplified EGFR gene had shorter survival than those with normal EGFR gene (not statistically significant, p > 0.05, log rank test). Ki-67 LI and EGFR gene amplification may provide useful prognostic information, but larger studies are needed to ascertain these observations.