Symposium no. 4: Biology of Tumour Invasion and Metastasis

4.025

EFFECT OF LECTINS ON ONCOGENE ACTION

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Previously we have described the proliferativ effect of lectin treatment, in vivo. We proved this effect by the mean of flow cytometry.

Now, we have examinded DNA and RNA of PHA treated animals./spleen, liver, thymus, lymph nodes/. There is an elevated expression of N-ras oncogene after treatment 24 hrs and six days. Elevated expression of c-myc oncogene could be detected on sixth day of treatment.

On DNA level we have founded stronger signal by N-ras oncogene probe after sixth days of PHA treatment in spleen and thymus. For these experiments we used EC-labelled inserts.

4.026

IS SERUM CARBOXYTERMINAL PROPEPTIDE OF TYPE I PROCOLLAGEN A USEFUL MARKER IN PATIENTS WITH BONE METASTASES?

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Type I collagen is the sole collagen type found in bones and tendons. Carboxyterminal propeptide deriving and cleaved from type I procollagen (PICP) during collagen synthesis is liberated into blood where it can be measured. Elevated serum levels of PICP in patients with Paget's disease compared with normal subjects and correlated with serum alkaline phosphatase (Alk.Ph.) have been previously described. Thus it might be a valuable marker of bone formation. We investigated the significance of PICP and serum osteocalcin (OC), serum Alk.Ph. and 24 hr urinary excretion of hydroxyproline (HOP) in 29 cancer patients with bone lesions (12 prostatic, 1 myeloma, 1 renal, 3 lung and 12 breast). The higher levels of PICP in patients with osteoblastic or mixed metastases, and a statistically significant correlation between PICP and OC ($r = 0.57$ $p < 0.05$) were seen, while no correlation between PICP and Alk.Ph. and HOP was found. These results show that serum PICP levels could be a specific marker of osteoblastic activity.

4.027

OSTEOCALCIN SERUM LEVEL IS AN INDEX OF OSTEOBLASTIC ACTIVITY

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Osteocalcin (BGP) is considered a good marker of osteoblastic activity, but high concentrations have also been found when osteoblasts are not apparently involved. 167 patients, divided into 5 groups, were studied: Paget's disease of bone (n=35); primary hyperparathyroidism (n=18); mixed bone metastases (n=46); osteolytic metastases with hypercalcemia (n=7) and without hypercalcemia (n=61). In all patients serum BGP, serum alkaline phosphatase (Alk.Ph.) and 24 hr urinary hydroxyproline (HOP) were measured.

High levels of BGP were found in primary hyperparathyroidism, polyostotic Paget's disease, osteoblastic and mixed bone metastases and in 6 cases of osteolytic bone metastases (3 with hypercalcemia). Low-normal BGP levels were observed in the other patients. A statistically significant correlation was found between BGP and Alk.Ph. but not between BGP and HOP. These data indicate that BGP is produced in high concentration during elevated osteoblastic activity and, together with AlK.Ph. production, is linked to bone formation.

4.028

SERUM SOLUBLE INTERLEUKIN-2 RECEPTOR (sIL-2r) LEVELS IN DIFFERENTIATED THYROID CANCER (DTC)

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Increased serum sIL-2r levels have been found in several metastatic solid tumors, but no information is available for thyroid carcinoma. Aim of this study was to evaluate circulating sIL-2r in patients with DTC submitted to total thyroidectomy before and after L-Thyroxine (L-T4) therapy. sIL-2r was significantly decreased (273±152 U/ml, $p<0.0001$) when compared to healthy euthyroid controls (490±248 U/ml) in 53 patients with DTC without metastases or local recurrency (group A); when compared to group A, sIL-2r was significantly increased (491±520, $p<0.02$) in 9 patients with lymph-node metastases (group B) and in 17 patients (985±1286, $p<0.001$) with distant metastases (group C). A significant correlation was found between serum thyroglobulin (Tg) and sIL-2r in all groups ($r=0.348, p<0.002$). Administration of L-T4 was associated with significant increase of sIL-2r in group A (592±330 U/ml, $p<0.001$), but not in groups B (441±203 U/ml) and C (842±567 U/ml). However, when patients of groups B and C were examined individually, sIL-2r levels consistently decreased on L-T4 in those with basal levels >1000 U/ml and this decrease paralleled that of serum Tg. In contrast, sIL-2r did not change or even increased on L-T4 in patients with lower basal serum sIL-2r, independently of serum Tg changes. In conclusion, the present study suggests that thyroid status and disease activity independently modulate circulating sIL-2r concentrations in DTC. Further studies are needed to clarify the clinical and biological relevance of this finding.

4.029

ANTIGENIC COMMUNITY OF TWO MULTIFUNCTIONAL ADHESIVE PROTEINS BETWEEN *CANDIDA ALBICANS* AND TUMOR CELLS

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Adherence properties are considered as crucial in the pathogenic potentiality of many microorganisms as well as in metastatic ability of tumor cells.

We looked for similarities in adhesion phenomenon between tumor cells and *Candida albicans* germ tubes since germ tubes appear to be closely associated with pathogenicity and express on their surface receptors for components such as Laminin and Fibrinogen.

We showed previously* that a monoclonal antibody (Mab 15C9), obtained from Balb/C mice immunized with *Candida albicans* germ tubes, reacts with a protein at the surface of tumor cells (molecular weights : 45 and 33 kDa for the yeast and 78-64-60 kDa for the tumor cells). The expression of this protein can be related, in Western Blotting, to the metastatic behaviour and adherence properties of different tumor cells. Its role and nature are studied and it is found to closely interact with Fibrinogen and Laminin. On tumor cells, both Laminin and Mab 15 C9 react with 78 kDa antigen, while both Fibrinogen and Mab 15 C9 react with the doublet 64-60 kDa. Moreover Mab 15 C9 reacts with Bβ and γ Fibrinogen chains.

Mab 15 C9 seems to recognize a multifunctional adhesive protein common to the yeast and to the tumor cells, or a peptide which belongs both to Laminin and Fibrinogen receptors, since molecular weights of antigens differ one from the other.

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4.030

METASTASIS AND NEUROENDOCRINE SYSTEM IN STRESSED MICE.

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Evidence exists that psychological stressors affect tumor incidence and progression in laboratory animals. The aim of the present work has been that of determining the effects of the application of different defined paradigms of psychological stress on primary tumor growth and spontaneous metastasis in syngeneic mice kept in a low stress environment, and implanted with Lewis lung carcinoma. The nature of the mediators operative in the effects of a stressor examined (spatial disorientation) has been examined by direct assay or administration of specific neuro-endocrine effectors. In these conditions, the participation of plasmatic glucocorticoids appears to be insignificant, that of β-endorphins is significant, whereas the adrenergic system appears principally involved. Melatonin seems to possess a protective role in metastatic spread, as confirm measuring its urinary excretion. These findings indicate that psychological stressors may influence tumor metastasis via host's antitumor resistance factors through neuro-endocrine mechanisms, which have been presently preliminarily identified and which are currently under further investigation.