Symposium no. 4

Biology of Tumour Invasion and Metastasis

4.001

DETERMINATION OF LAMININ P1 (LAMP1) FRAGMENT SERUM LEVELS IN METASTATIC BREAST CANCER (PRELIMINARY RESULTS).

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Laminin is a glycoprotein component of basement membranes, which could play an important role in the tumour invasion and metastatic spread of neoplastic disease. LAMP1 is a pepsin resistant fragment of laminin (molecular weight 200.000-300.000),detectable in the serum of patients with pathological conditions associated with an increase in basement membrane material.In this study we measured LAMP1 serum levels (units of LAMP1/mL)by radioimmunoassay (Behring Germany)in 30 pts with breast cancer histologically demonstrated, divided in 16 with no metastatic disease (M-),14 with presence of metastases (M+) and 10 healthy subjects (K).Our results are reported in the following table:

	K	M-	M+
Mean	1,17	1,10	1,56
Median	1,18	1,03	1,61
SD	0,10	0,16	0,43

These preliminary date indicate an increase of LAMP1 serum levels according to metastatic diffusion in breast cancer patients. Further analysis is required to establish the true value of this new laboratory test.

4.002

FACTOR X ACTIVATING ACTIVITY OF PROSTATIC TUMOURS **A Adamson, J L Francis*, O Roath*, R Witherow, M Snell.** Dept of Urology, St Mary's Hospital, London and *University Dept of Haematology, Southampton General Hospital, UK.

Fibrin is now recognised as an important component of the tumour stroma. There is also evidence to suggest that peri-tumour fibrin formation may be beneficial to the host, perhaps by limiting the shedding of malignant cells.

We have determined the factor X-activating activity (FXAA) of prostate tissue removed at transurethral surgery in a specific chromogenic assay. Using antibody inhibition tests this procoagulant was characterised as being a factor VII/tissue factor complex. FXAA activity was significantly lower ($p<0.02$) in tissue from malignant prostates (n=31) compared to benign prostatic hypertrophy tissue (n=34).

Malignant change in the prostate is associated with a reduction in FXAA activity and this may be an important factor in tumour growth and dissemination.

4.003

URINARY TISSUE FACTOR LEVELS IN GENITOURINARY CANCER. **A Adamson, J L Francis*, R Witherow, M Snell.** Departments of Urology, St Mary's Hospital London and *Haematology, Southampton University Hospitals, UK.

Expression of tissue factor by host and tumour cells may be abnormal in patients with cancer. We have determined urinary tissue factor levels (UTF) levels in patients with prostate cancer (CaP), bladder cancer (TCC), normal controls and patients with benign prostatic hypertrophy (BPH).

Patients with bone scan positive CaP had higher UTF levels than those with BPH ($p<0.001$), BS-ve ($p<0.005$) and androgen ablated metastatic CaP ($p<0.001$). Levels were also higher in TCC compared to controls ($p<0.001$). In patients undergoing check cystoscopy (n=53), those with recurrent disease (n=32) had higher levels ($p<0.01$) than those with normal examinations (n=21).

It is concluded that UTF levels are elevated in bladder and prostate cancer, reflecting active disease in the former and bone scan status in the latter and that UTF may be a useful tumour marker.

4.004

NGF-R IMMUNOREACTIVITY IN HUMAN BREAST CANCER.

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Nerve growth factor receptor (NGF-R) is known to mediate differentiation and growth inhibition of neurons and tumor cell lines. For this purpose we studied 34 breast cancer patients and 8 with normal or benign breast pathologies. Frozen tissues were stained with ME20-4 MoAb anti NGF-R (Amersham) biotin-streptavidin-DAB system (ICN). NGF-R reactivity was present in 17 of 34 patients and localized in the interstitium: adventitia of some vassels and basal membrane of some differentiated but not undifferentiated ducts. No reactivity was present in normal or adenomatosus breast ($p<0.01$). This reactivity probably represents the innervation fase of differentiated vessels and ducts growing inside or around the tumor, but is absent in normal breast and in less differentiated neoplastic tissue and probably represents another element indicating the differentiation status of neoplasia.

4.005

HIGH DAILY SERUM LEVELS OF THE PINEAL HORMONE MELATONIN ARE ASSOCIATED WITH LOW CELL KINETICS IN SOLID TUMORS.

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Tumors with high growth fraction are generally more malignant.Since pinealectomy stimulates cancer growth,we have evaluated the relation between cell kinetics and pi neal function by determining daily serum levels of melatonin(MLT),the main pineal hormone,in 62 untreated non-metastatic cancer patients(pts) (breast:28;non-small cell lung:34).Cell kinetics was detected by measuring Ki-67 labeling rate.Tumor was considered as positive for Ki-67 when the percentage of positive cells was greater than 3%. Ki-67 was positive in 15/28 breast cancer and in 16/34 lung cancer pts.Ki-67 negative pts showed signi ficantly higher MLT mean levels than the positive ones (breast:37±6 vs 15±3 pg/ml, $\bar{x} \pm$ SD, $P < 0.025$;lung:39 ± 8 vs 22 ± 3, $P < 0.05$).These results would suggest a pineal involvement in the control of cancer cell proliferation.

4.006

TYROSINE-PHOSPHORYLATION OF UROKINASE-TYPE PLASMINOGEN ACTIVATOR

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We report that urine purified human u-PA has phospho-Tyr residues as detected by immunoblotting analysis with anti-P-Tyr monoclonal antibodies and isolation of P-Tyr by HPLC following basic hydrolysis of purified u-PA . Either the 55 kDa u-PA form and the lower MW form (33 kDa), containing the proteolytic chain, are Tyr-phosphorylated. Also the u-PA produced 'in vitro' by human fibrosarcoma cells (HT-1080), as well as u-PA present in tissue extracts of tumors induced in nude mice by HT1080 cells; in these human tumor cells u-PA represents the major Tyr-phosphorylated protein. It has been shown (Mastronicola et al. FEBS 1990, 266,109) that the pro-u-PA from human epidermoid carcinoma cells (A431) have P-Ser residues, likely involved in impairing the binding of u-PA with PA inhibitor-1. All these data indicate that phosphorylation of u-PA may represent a regulatory mechanism of the plasminogen activation pathway. It will be important to assess the physiological roles, if different, of Tyr and/or Ser phosphorylation in this protease.

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