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EXPRESSION OF MARKERS OF DIFFERENTIATION IN NORMAL BRONCHIAL EPITHELIUM AND BRONCHIAL DYSPLASIA Pendleton N, Dixon GR, Green JA, Myskow MW Clatterbridge Cancer Research Trust Laboratories, Merseyside, L63 4JY. Dept Histopathology, Broadgreen Hospital, Liverpool, UK.

A series of 39 bronchial dysplasias (severe 27: moderate 10: mild 2) have been studied with markers of differentiation. The antigens studied by a standard immunocytochemical technique were simple epithelial cytokeratins (CK) 7,8,18 and 19, stratified epithelial cytokeratins 6,10,13 and 14, and stratification associated antigens involucrin and peanut agglutinin binding lectin (PNA). The normal bronchial epithelium expressed CK's 4,6,7,8,18 and 19 in all cases, CK13 in 13 cases and PNA in 7 cases, but not CK's 10 and 14. In the dysplastic bronchial biopsies epithelial staining was observed with epithelial CK's 7,8,18 and 19 in all cases, CK13 was seen in 26 cases, CK 14 in 13 cases, CK 6 in 11 cases and CK 10 in 5 cases. Involucrin expression was observed in 17 dysplastic biopsies and PNA in twelve. A significant association between non-severe histological grade of dysplasia and CK 6 expression ($p=0.018$) was found. Correlations were found between the loss of CK6 expression ($p<0.0001$), the expression of CK 14 ($p=0.008$) and involucurin expression ($p=0.0018$) with bronchial dysplasia. We conclude that the pattern of differentiation antigen expression in bronchial dysplasia is significantly different to that of the normal bronchial epithelium.

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EVALUATION OF CYFRA 21-1 AS TUMOR MARKER AT THE DIAGNOSIS STEP IN THE PRIMARY LUNG CANCER

Rastel D. *, Ramaioli A.**, Clément M.*, Thirion B.*
* CIS bio international, Gif sur Yvette - France. ** Unité de Statistiques Médicales - Centre A. Lacassagne - Nice - France.

Cytokeratin 19 (Ck 19) is a specific protein of simple epitheliums and expressed mostly in lung cancer tissues. The study was designed to find out whether it could be used as a seric tumor marker in lung cancer.
Immunoradiometric assay was made with two monoclonal antibodies reactive to specific epitopes of Ck 19 and referred to CYFRA 21-1.
2250 sera were retrospectively tested by 11 investigators in 5 different countries. In a 711 healthy population of blood donors 99.8 % were below 1.2 ng/ml. Cumulative Distribution Analysis were used to confirm the 3.3 ng/ml cutoff which showed 96 % specificity in a non-malignant lung disease group (n=546). At this cut off the sensitivity among small cell lung cancer is 16.2 % (n=74) and 41 % for non small cell lung cancers (NSCLC) (n=547). The sensitivity in the WHO histological subtypes is 56.7 % for squamous, 34 % for large cells and 27 % for adenocarcinomas. The level of CYFRA 21-1 is significantly correlated with the tumor size and UICC stages. The sensitivity of other tumor markers among squamous type is 30 % for SCC , 25 % for CEA and 46 % for TPA compared on the same population at 96 % specificity for all markers. In conclusion CYFRA 21-1 appears to be a relevant tumor marker for NSCLC particularly sensitive for squamous type and would be valuable in monitoring treatment and in detection of recurrences.

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PARAMETERS OF THE IMMUNE REACTION AS PROGNOSTIC FACTORS IN LUNG CANCER.

Body J.J, Sculier JP, Paesmans M, Libert P, Richez M, Bureau G, Van Cutsem O, Thiriaux J, Berchier MC and Klastersky J for the Eur L C Working Party, Inst J Bordet, Brussels, Belgium.

We have measured the serum levels of soluble receptors for interleukin-2 (IL-2R) and the soluble antigen from suppressor/cytotoxic T-lymphocytes (T8; T-cell Sciences, USA), before chemotherapy in 55 patients (pts) with small cell lung cancer (SCLC) and 94 pts with non-SCLC (NSCLC). Compared to the 95th percentiles determined in 153 healthy subjects, IL-2R levels were increased (> 931 U/ml) in 26% of pts with SCLC and 43% of pts with NSCLC, whereas T8 levels were increased (> 502 U/ml) in 11% and 14%, respectively. In NSCLC, but not in SCLC, objective responders had lower IL-2R levels than non-responders, 845±442 (SD) vs 1288±887 U/ml ($P<0.05$). IL-2R was also a predictive factor for survival in NSCLC: the 47 pts with IL-2R levels below the median value (857 U/ml) had a median survival time of 42 wks vs 22 wks for the 47 other pts ($P<0.001$;logrank test). Using a Cox model, PS was the most important prognostic factor ($P=0.0001$) followed by IL-2R levels ($P=0.009$) and disease extent ($P=0.01$). In summary, serum IL-2R appears to be a new and independent adverse prognostic factor for patients with NSCLC.

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THE PREOPERATIVE AND FOLLOW-UP VALUES OF MCA IN BREAST CANCER

G-PASTRANA F., HERRERO M., ABARCA L., RIOS M., OETTEL J.M., CALERO F.
GYNECOLOGY DEPARTMENT. HOSPITAL MATERNAL "LA PAZ". MADRID. SPAIN.

Tumor marker MCA was used to study in the preoperative and follow-up of 1515 breast cancer patients, during three years.
Marker was measured in serum, with monoclonal antibody B-12, using commercial kits MCA-EIA. We assumed as cutoff for MCA < 15 U/ml. Sensibility is 46% and specificity is 97%, both similar to tumor marker Ca 15.3.
We correlate MCA with two main risk factors: lymphadenopathies and hormonal receptors (ER and PR) in postoperative patients. From 643 patients with positive lymphadenopathies, 77 (11,9%), were MCA positive, and 576 (88%), were MCA negatives. . The hormonal status was known as ER positive in 480 patients, 71 (14,7%) were MCA positive, and 409 (85,2%) were MCA negative. The correlation between MCA and tumor mass (T1-T4), and histology was also made.
The overall survival rate was 82%. In patients MCA negative was 85%, and in those MCA positives was 48% ($p=0.00001$). Overall free of disease rate was 70%. In MCA negative group was 85% and in MCA positive group was 40% ($p=0.00001$). These data show considerable consistency to correlate or (good correlation) between patient evolution and serum level of MCA in different times of disease.
In conclusion, MCA test, with sensibility and specificity similar to Ca 15.3 and tested in a big amount of patients (1515), supply much information about the evolution of disease, survival detection of relapses and follow-up of distant lesions.

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OVEREXPRESSION OF BETA2-INTEGRINS IN INVASIVE BREAST CARCINOMAS.

Guriec N.[1], Feugeas O[1-2]., Marcellin L[2]., Wilk A.[2], Rouyer N.[2], Oberling .F[1-2]. Institut d'hématologie et Hopitaux Universitaires de Strasbourg, France.

Introduction : An important step in metastasis is the transendothelial migration of cells from the primary tumor to blood vessels. Recently, the part of cell adhesion molecules (CAMs) in the mechanisms of wide-spread lymphoid metastasis have been studied using T cell hybridomas. Beta2 integrins, particularly CD11a and CD11b, seem to be required for efficient metastasis.
Material and methods : We have studied by quantitative PCR the levels of expression of these CAMs in normal breasts (25), mammary fibroadenomas (10), invasive breast carcinomas (20). Expression is assessed in comparison to an internal standard.
Results : No significant expression was observed on normal breasts or fibroadenomas while invasive breast carcinomas **overexpress** CD11a and CD11b.
Discussion and conclusion : The increased levels of these molecules might aid the scattering of breast tumor cells. Expression of others adhesion molecules as CD11c, CD18, CD44... is currently studied. The results will be discussed.

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SOLUBLE INTERCELLULAR ADHESION MOLECULE 1 (sICAM-1) IN VARIOUS STAGES OF BREAST CANCER (BC)

S Shapira[1], T Klein[2], H Lurie[3], J Lehmann[4], B Klein[5], [1]Oncology Unit, Meir Hosp, Kfar Saba [2]Dept of Oncology, [3]Tissue Typing Lab, Beilinson Med Center, Petah Tiqva; [5]Oncology Unit, [4]Surgery B, Golda Med Center, Petah Tiqva, Israel

ICAM-1 is a member of the immunoglobulin super-family of adhesion receptors and an important early marker of immune activation and response. sICAM-1 level was measured in 143 BC pts and 43 controls. The pts were divided into: Group (grp) A - 71 newly diagnosed pts after surgery; grp B - 33 pts on long-term follow-up without active disease; and grp C - 39 pts with metastatic disease. In all pts, mean±SD sICAM (479ng/nl±110) was significantly higher ($p<0.001$) than that of controls (150ng/nl±51).Mean±SD of grp A was 573ng/nl±60, grp B 177ng/nl±100 and grp C 686 ng/nl±120. The levels of both grps A and C differed significantly from that of B ($p<0.001$),which was similar to the control level. No differences were observed in grp A between stages I, II and III. These data suggest that high levels of sICAM-1 indicate enhanced host-cell mediated immunoresponse and may have relevance in immunotherapy.