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Inhibitory effect of anti-angiogenic agent TNP-470 on lung metastasis from colon cancer

H. Oda, Y. Ogata, Y. Harada, A. Ohkita, K. Inuzuka, J. Konishi, Y. Hara, M. Kanazawa, K. Shirouzu. *First Department of surgery, Kurume University School of Medicine, Japan*

Introduction: This study was designed to determine efficacy and timing of TNP-470 administration on inhibition of pulmonary metastasis after resection of primary tumor in orthotopically inoculated colon cancer.

Methods: Five weeks aged male nude rats were used for lung metastatic model from reconstructed colon cancer. A total of 2×10^6 KM12SM cells (human colon carcinoma cell line) were inoculated on cecal wall of nude rat under ether anesthesia. Five weeks after the injection of KM12SM cells cecal tumor was resected completely, the inhibition rates of lung metastasis and the survival rates were analyzed after the administration of TNP-470 among following 4 groups. A: resection alone as a control. B: resection+ TNP-470 administration for 4 weeks immediately after the resection. (total phase) C: resection+ TNP-470 administration for 2 weeks immediately after the resection. (early phase) D: resection+ TNP-470 administration for 2 weeks from 3 weeks later the resection. (late phase)

Result: At 7 weeks after the resection of cecal tumor both the incidence and the number of lung metastasis in groups Band C was significantly lower or smaller than that in control, but that in group D was not. Also we found that the survival rate in group B and D was significantly higher than control, but that in group D was not. These results suggest that TNP-470 may no longer effect on inhibition of tumor growth after Tumor neovascularization was augmented in lung metastatic foci.

Conclusion: It is important to decide the timing of administration of anti-angiogenic agents for inhibition of distant metastasis from colon cancer.

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Restaging breast cancer after somatostatin receptor scintigraphy with [^{111}In-DTPA-Phe-1]-Octreotide

C. Giannakenas[1], E. Tzorakoleftherakis[2], H.P. Kalofonos[3], T. Petsas[4], P.J. Vassilakos[1]. [1]*Dept. of Nuclear Medicine;* [2]*Dept. of Surgery;* [3]*Dept. of Oncology;* [4]*Dept. of Radiology, Regional University Hospital, University of Patras, Patras, Greece*

Object: We evaluated ^{111}In-DTPA-Octreotide (OC) for imaging of somatostatin receptors in mammary tumors both for preoperative localization and postoperative follow-up.

Method: We studied 29 females aged 27–79 y, with verified or suspected breast tumors. All patients had findings in preceding studies with mammography and/or U/S, CAT. Planar and selectively SPECT was performed at 6*1 and at 22*2 hrs p.i after 2.3–3 mCi OC (IV). The scintigraphic findings were verified by histology (biopsy or tissue removed by surgery). Scintigraphic findings were compared to the prestudy grading.

Results: Imaging was true positive in 22/24 positive pts (sensitivity 84.6%). false positive in 1/24 and false negative in 4/24. In 8/22 true positive scans involvement of maxillary and/or thoracic lymph nodes was demonstrated. Pts were regraded accordingly.

Conclusions: OC appears to be useful for diagnostic imaging of breast cancer. Its ability to image lymphnode involvement and both local and distal recurrence has been helpful in restaging of the patients (and in particular those with stage IIIA–IIIB tumors), with the relevant clinical significance.

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Liaison® Ferritin – An automated chemiluminescent immunoassay for the determination of Ferritin

M. Mack, M. Oed, A. Kunz, R. Schlett. *Byk-Sangtec Diagnostica, D-63128 Dietzenbach, Germany*

An immunoassay utilizing chemiluminescence and paramagnetic particles has been developed for the new fully automated, random access Liaison® immunoanalyzer. The Liaison® Ferritin assay is a two-site immunolumino-metric one-step assay using two highly specific monoclonal antibodies. A specially designed unique reagent integral contains all specific reagents. The cooled reagent compartment guarantees an on-board stability of at least 4 weeks. The assay works with a 2-point calibrated mastercurve. To perform the assay, 10 μl sample is added to 300 μl tracer and 20 μl antibody-coated magnetic particles. After 10 min incubation the particles are separated, washed and the chemiluminescent signal is generated. The time to first result is only 15 min. The assay with a unique extended standard range up to 3,000 ng/ml shows no high dose hook effect up to 130,000 ng/ml (spiked sera). The cross-reactivity to human liver ferritin is 100%, to human spleen ferritin 66% and to human heart ferritin 8%. Precision (within-run <3%; between-run <5%), linearity, recovery and sensitivity (<0.2 ng/ml) are excellent. The assay shows a very good correlation to LIA-mat® Ferritin (r = 0.994). In summary the Liaison® Ferritin run on the new Liaison® immunoanalyzer and is a very rapid and accurate method rapidly providing reliable results.

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Increase of HLA-DR$^+$ T cells and decrease of CD8$^+$ CD28$^+$ putative cytotoxic cells with 'naive' phenotype (CD62L^{hi}) in cancer patients with dissemination

A. Büssing[1], M. Schietzel[2]. [1]*Krebsforschung Herdecke, Department of Applied Immunology;* [2]*Department of Radiology/Oncology, Communal Hospital Herdecke, Germany*

Introduction: In view of the critical importance of the CD28-B7 costimulatory pathway in antigen-specific T cell activation, we examined the expression of CD28 and HLA-DR molecules on the surface of peripheral T cells from patients with malignancies, systemic sclerosis (SS), HIV infection, and healthy controls.

Methods: Lymphocyte subsets of cancer patients without metastases (n = 165; breast cancer, colorectal tumors, lung cancer; all off chemotherapy or radiation), patients with dissemination (n = 28), and patients with low grade lymphoma (n = 24) were investigated by flow cytometry.

Results: Cancer patients, especially during disease progression, and lymphoma patients reveal significantly lower numbers of CD28$^+$CD8$^+$ putative cytotoxic cells with CD62L^{hi} 'naive' phenotype (probably due to an extravasation and migration to sites of anti-tumor activity as observed similarity in rheumatoid arthritis), and significantly higher amounts of HLA-DR$^+$ T cells, similar to the immune responses in patients with SS and HIV infection. High numbers of HLA-DR$^+$ T cells were associated with high numbers of CD62L^{lo} CD8$^+$ putative 'memory' cells.

Conclusion: These results suggest that (1) both the CD8$^+$ subsets and HLA-DR$^+$ T cells respond to self-peptides during disease progression, and (2) that the immune responses of these different diseases are, however, similar. Unfortunately, we do not know whether this response is of benefit for the host or not.

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VEGF expression as a prognostic factor in node-positive esophageal cancer

Y. Ogata, H. Yamana, Y. Harada, Y. Hara, H. Fujita, K. Shirouzu. *Department of Surgery, Kurume University School of Medicine, Kurume-shi, Japan*

Purpose: To clarify clinical significance of Vascular Endothelial Growth Factor (VEGF) expression in esophageal cancer, We have studied the VEGF expression clinico-pathologically.

Methods: Paraffin-embedded tumor specimens from sequential 141 esophageal cancer patients who were underwent operation between 1990 and 1994 were studied. The thin sections were examined by avidin-biotin peroxidase complex method using anti-human VEGF and anti-human Von Villebland Factor antibodies.

Results: VEGF expression by monocyte-macrophages was observed in all cases, but only a few cells were positive. In contrast the incidence of VEGF expression in the tumor cells was relatively low at 29.8% of all specimens. However, in the cases where the tumor cells were positive for VEGF, it was discovered that the main cell source of the VEGF production was the tumor cells themselves. The micro vessel count at the tumor invasive edge in the cases positive for VEGF in the tumor cells was significantly higher than that in the negative cases. The survival rate of node-positive patients with VEGF expression by tumor cells was significantly lower than that without VEGF expression.

Conclusion: VEGF may play an important role in tumor angiogenesis in esophageal cancer, and VEGF expression in tumor cells should become a prognostic factor in node-positive patients.