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NORMAL VALUES OF SERUM TUMOR MARKER LEVELS IN RELATION TO AGE

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Seven serum tumor markers of carbohydrate or mucinous origin (CA 125, CA M26, CA M29, CA 15.3, MCA, CA 19.9 and CA 72.4) were measured in a collective of 780 healthy women, gynaecologically fully controlled, by anamnesis and ultra-sound, from 37 to 76 years of age. For each tumormarker mean, median and S.D.in relation to age were calculated.

Age related serum levels of seven tumor markers in healthy controls:

Group	< 45 yr		45-49 yr		50-54 yr		55-59 yr		≥ 60 yr	
N=	224		251		163		93		49	
Marker:	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
CA 125	17	14	18	14	12	6	11	5	11	6
CA M26	32	35	27	28	22	23	14	15	25	27
CA M29	7	3	8	4	8	3	8	3	11	9
CA 15.3	19	8	19	7	19	7	20	8	23	11
MCA	9	5	9	5	9	6	9	7	11	7
CA 19.9	12	11	12	11	11	10	13	11	14	15
CA 72.4	2	2	2	3	2	1	2	2	2	2

These results indicate that for some markers a generalized normal value (cut off level) may be used safely but for others, the choice of the cohort of "normal healthy volunteers" with respect to age, may be decisive for the false-positive score of the test, and hence its applicability.

11.110

THE HUMORAL IMMUNITY OF STOMACH CANCER PATIENTS

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To investigate the humoral immune response of patients with stomach carcinomas lymphocytes from spleens and lymphnodes were fused with the heteromyeloma HAB-1. Ig-positive clones were tested against the autologous tumor cells and a pannel of malignant and normal tissues. Out of more than twenty investigated cases it was found that the majority of the tumorreactive human monoclonal antibodies are of the IgM-type and show crossreactivity with normal structures or embryonal tissues. No tumorspecific reactivity could be observed. Interestingly one of the isolated antibodies derives from a CD 5 positive lymphocyte, which have been shown to play a major role in the early polyreactive T-cell independent defence against viral and bacterial infections. This could indicate that these CD 5 positive lymphocytes are also involved in an early immune reaction against cancer cells.

11.111

Liposome mediated tranfer of human TNF cDNA

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The use of liposomes for the gene transfer into eucaryotic cells is an alternative method to other techniques, e.g. calciumphosphate precipitation. For the encapsulation of the tumor necrosis factor (TNF) DNA reverse phase evaporation vesicles were employed. The human TNF cDNA was cloned in two variants into the MoMuLV derived retroviral expression vector m3 neo. The first variant of TNF carries a modified signal sequence of the IgG heavy chain (SP-TNF) and the second variant does not contain the authentic signal sequence of TNF (NS-TNF).
The liposome mediated gene transfer was carried out on NIH 3T3 cells and human colon carcinoma cell lines too. In first experiments it was shown that the liposomal gene transfer resulted in a significant higher transfection efficiancy compared to the calcium phosphate technique. Southern and Western blot analysis gave evidence of stable integration and high expression of the foreign gene, which lasted for more than four months. Furthermore growth assays indicated growth inhibitory effects of the liposomal transduced two TNF variants.

11.112

THE RADIOIMMUNOLOCALIZATION OF McAb LC-1 AND ITS FRAGAMENT IN NUDE MICE BEARING LUNG ADENOCACINOMA

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Purified McAb LC-1 (IgM type) was cleaved into 118 K fragment by DTT treatment. This 118K fragment of LC-1 was retained its immnoreactivity when incubated with target cells by ELISA. Both purified McAb LC-1 and its fragment were labelled with ^{131}I or ^{99m}Tc, nude mice bearing human lung adenocarcinoma LAX-83 were used. The results showed that strong accumulation of ^{131}I-labelled LC-1 IgM within the lung tumor area, and the control human stomach cancer SGC-7901 area showed no accumulation. The biological distribution in nude mice showed similar result. The cpm on lung cancer cells is at least 7 times higher than the cpm on stomach cancer cells, when LC-1 IgM and its fragment were labelled with ^{99m}Tc, and injected into nude mice bearing lung adenocarcinoma, significant tumor localization shown by gamma photoscanning.

11.113

ANTITUMOR EFFECT OF McAb LC-1 AND TRICHOSANTHIN CONJUGATION

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McAb anti human lung cancer LC-1 IgM was purified by hypotonic and chromatography. The conjugate of LC-1 and trichosanthin was prepared by SPDP and confirmed by SDS-PAGE and HPLC. Their Molar ratio was 1:3. The Ab activity retained in conjugat was demonstrated by ELISA. The cytotoxicity in vitro of the conjugate to target cells was about 80%. ^{131}I labelled conjugate showed clear image in nude mice bearing lung cancer but not in stomach cancer. The result of in vivo immunotherapy in nude mice bearing lung cancer indicated that the inhibition percentage was 33.1 compared to all the control groups ($p<0.05$).

11.114

METOCLOPRAMIDE DOES NOT ENHANCE THE EFFECT OF IONIZING RADIATION ON NORMAL TISSUE.

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We have previoulsy shown (1) that metoclopramide (MCA), a benzamide derivative, potentiates the effect of ionizing radiation (RT) on xenografted squamous cell carcinoma of the H&N. The therapeutic gain of this is dependent on whether the normal tissue damage also increase when MCA and RT are combined.

Materials & Methods: Acute skin reactions were studied in female 129-type mice. Oxygen breathing mice were given MCA i.p. 1 hour before irradiation of the hind leg. There were two study groups, one given one fraction and one group given two fractions with 24 hr interval. Skin reactions were scored over a 23 day period. LD50/30 were studied in BALB/c nu/+ mice. They were given whole body irradiation one hour after MCA i.p.

Results: MCA did not affect neither the RT induced acute skin reactions nor the LD50/30.

Conclusion: The abcense of potentiation of radiation damage to normal tissue in this animal study increases the possibility of clinical benifit from MCA as a potentiatior of RT and encourages further clinical evaluation.

(1)Lybak S et al. *Int J Rad onc Biol Phys*, 1990;19:1419-24