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THE EFFECT OF HUMAN GRANULOCYTE AND GRANULOCYTE MACROPHAGE - COLONY STIMULATING FACTORS ON NEUTROPHIL CHEMILUMINESCE.

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One of the most important causes of mortality in patients treated for cancer is secondary infections related to neutropenia. Granulocyte - Colony Stimulating Factor (G-CSF) and Granulocyte Macrophage - Colony Stimulating Factor (GM-CSF) are cytokines purified and produced during the past few years. They either prevent neutropenia or shorten the neutropenic phase which decreases cancer mortality and morbidity. Consequently, these factors permits clinicians to use more effective therapeutic medications. The normalization of function in an immune effector cell subset, does not necessarily overlap with the normalization of the cell number as observed in natural killer activity after bone marrow transplantation. A luminol-dependent chemiluminescence assay was developed to evaluate whether the repair in neutropenia accompanies the neutrophil ability to function. The effect of G-CSF and GM-CSF on neutrophil respiratory burst was examined.The optimal enhancing effect of recombinant human G-CSF and GM-CSF on neutrophil oxidative burst was dose dependent, obtained at a 180-240 ng/mL and 120-180 ng/mL dose interval , respectively. The preincubation of cells with G-CSF enhanced the neutrophil oxidative burst to serum opsonized zymosan, in contrast preincubation with GM-CSF could not. Zymosan interacts with CR3 (type 3 complement receptors). These results suggest that GM-CSF which acts on progenitor cells more close to stem cells does not have any synergistic activity with complement receptor type 3, while G-CSF might be related in such synergism. Thus, G-CSF might be more active in evoking synergism between humoral and cellular immune system at the neutrophil level in cancer patients.

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Intraperitoneal hrec TNF α (Tumor Necrosis Factor α) administration in patients with hydroperotoneum in the course of an advanced neoplastic disease.

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There were presented the several data about the trial of clinical administration of TNF α in advanced cancer, in the last few years. The reports about the general administration of that cytokine are not very encouriging and it is because of seroius side effects connected with TNF α administration.
And that is why we have decided to present our own results of the treatment with hrec TNF α given intraperitoneally in patients with hydroperitoneum due to advance neoplastic disease.
14 patients with terminal phase of the disease were treated with intraperitoneal infusion of hrec TNF α in the dose of 150 μg/day and futherly the dose was gradually increased in the case of seroius side effects absence. Maximum 8 infusion were administrated to the maximum dose of 225 μg/day; repeated every one week. Summarizing, the efficacy of the treatment (total or partial remission) were odserved in 7 patients, the hrec TNF α administration significantly decrease the hydroperitoneum and through that action improve patients' quality of life. Finally, that kind of therapy does not prolong the patients' survival time.

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ENHANCEMENT OF RADIOSENSITIVITY BY BETA-INTERFERON IN CELL CULTURE MCF 7 AND ZMK 1

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Clinically and in studies, β-Interferon is used intratumorous and intravenous parallel with radiotherapyin different squamuous cell carcinomas of the ENT tract and the lung with promising results. Therefore it is of interest to what extent beta - Interferon influences radiosensibility of the tumour cells.
Methods: Human mammary carcinoma cell line MCF-7 (obtained from DKFZ) and the new cell line ZMK 1 (undifferentiated cell line of the buccal mucosa, biopsied and cultivated by the authors) were cultivated using standard conditions. β-Interferon (Rentschler) was added using different concentrations and incubation times. Celle were irradiated with 200 kV - x-rays (single doses 2 - 10 Gy). Standard colony forming test was performed.
Results: β-Interferon acts as an antiproliferative substance on MCF-7 and ZMK 1 cells. If the cells are cultivated as a suspension, the additional irradiation has no further effect on the cells. If on the other hand cells are cultivated in the flasks (adherent), short time preirradiation (4 hous) incubation with β-Interferon induces a pronounced enhancement of radiosensibility (Faktor 1,13 in MCF 7 - cells, faktor 1,5 in ZMK 1 - cells).
Conclusion: These results suggest that an enhancement of radiosensibility in breast cancer cells and ENT-tumours can be possible in vivo. This should be proven in a clinical study.

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TGF - β is an inhibitory cytokine for normal and leukemic B - cell precursors

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The identification of inhibitory cytokines is of decisive importance for the understanding of the pathogenesis of B - cell precursor (BCP) - ALL and may help in the development of innovative therapeutic strategies. Aim of our study was to assess the effect of TGF - β on normal and leukemic B - cell precursor (BCP) cells. Normal CD10+/CD19+ pre - B cells of 6 healthy donors and CD 10+/CD19+ leukemic pre - B cells of 26 cALL patients were isolated from bone marrow aspirate by FACS with a purity > 98% from bone marrow samples. 1 x 10^5 normal pre - B cells/ml or 5 x 10^5cells/ml of highly purified leukemic pre - B cells were cultured on murine feeder cells with TGF - β (10ng/ml) or in medium alone (control). Cell viability was assessed by trypan - blue exclusion, S - phase and apoptosis by propidium iodide staining. Specifity of TGF - β activity was assessed by α - TGF - β mAK. TGF - β induced apoptosis of normal pre - B cells in 4 of 6 samples tested with a relative increase of 76 % (19 - 129 %). In BCP - ALL TGF - beta lead to a loss of cell viability in 22 of 26 samples with a mean reduction of 53 % (17 - 100). The cytokine increased programmed cell death in 9 of 12 samples by a mean of 68 % (-8 - 276). In five samples tested the effect of TGF - β was efficiently blocked by α - TGF-β mAK. In the leukemic pre - B cell line BLIN - 1 TGF - beta specifically suppressed S - phase and induced G0/G1 arrest. BCL - 2 expression was moderately elevated by the cytokine and expression of the FAS ligand CD95 reduced. TGF - beta did not modulate the costimulatory antigen profile with the exception of reduction of CD18 antigen expression. The cell line was negative for transcription of TGF - beta as assessed by RT - PCR. However, RT - PCR was positive for transcripts of the TGF - beta receptor I and II and for the receptor modulating proteins betaglycan and endoglin. Our data show that TGF - β is a potent growth - inhibitory cytokine of normal and leukemic BCP - ALL.