to the CD95 death receptor. We aimed to determine the role of caspase-8 activation during radiation-induced apoptosis in human lymphoma cells.

Material and Methods: Activation of caspase-8, its substrate BID and apoptosis in response to CD95 stimulation or irradiation (XRT) was tested in Bcl-xl overexpressing Jurkat cells and the respective vector controls.

Results: In contrast to CD95 stimulation, apoptosis in response to XRT was abrogated completely in Bcl-xl expressing cells. CD95 induced apoptosis was delayed. In parallel, caspase-8 and BID activation by ionizing radiation was abrogated almost completely in Bcl-xl expressing cells. BID cleavage by XRT was still detectable in caspase-8 negative Jurkat cells, whereas no activation was visible after CD95 stimulation. Using the caspase-8 negative cells and a caspase8 dominant negative cell line we found that inhibition of caspase-8 activation interferes partially with radiation induced cell death.

Conclusion: Radiation induced activation of caspase-8 is secondary to a bcl-xl controlled process. BID can be activated independently of caspase-8 during radiation induced cell death. Caspase-8 is involved but not required for radiation induced cell death in human lymphoma cells.

704 POSTER

Ionizing radiation effect on transcription of estrogen receptor in human breast cancer cells

D. Devriendt[1], E. Kinnaert[3], M. Yan[2], P. Van Houtte[1], G. Leclercq[2].
[1]Service de radiothérapie, Institut J. Bordet, 1 rue Héger Bordet, 1000, Bruxelles; [2]Laboratoire de cancélogie maramaire JC. Heuson, ULB, Institut J. Bordet, 1 rue Héger Bordet, 1000, Bruxelles; [3]Fond National de la Recherche Scientifique (F. NRS. – Télévie) Belgique, Belgium

Purpose: Potential alteration of ionizing radiation on estrogen receptor (ER) transcriptional activity was assscsssed in vitro.

Method: Transcriptional activity of ER under estrogenic and antiestrogenic stimulation was assessed by spectrophotometric measurements of luciferase concentration in MVLN cells (i.e. MCF-7 cells stably transfected with a plasmid in which expression of lucifcrasc gene (LUC) is under the control of an estrogen-response element (ERE))

Results: Ionizing radiation (3 to 12 Cy) failed to suppress the transcriptional activity of ER. Thus, after irradiation luciferase activity or residual cells still increased with 10^{-10} M E_2 and decreased with both pure (RU58668) and partial (OHTain) antiestrogens (both at 10^{-7} M). Hence, no major loss of transcriptional activity was recorded. Interestingly RU 58668-induced inhibition of luciferase was not amplified by irradiation while the inhibition produced by OHTam significantly decreased.

Conclusion: ionizing radiations may select a receptor machineD, less sensitive to antiestrogen inhibition.

705 PUBLICATION

Different radiosensitizing effects of Gemcitabine in human squamous cell carcinoma cell lines

St. Mose, M. Karapetian, L. Jüling-Pohlit, B. Taborski, M. Damrau, U. Ramm, A.N. Rahn, H.D. Büttcher. *University Hospital Frankfurt, Frankfurt am Main, Germany*

Purpose: Gemcitabine (dFdC) has shown promising activity in different solid tumors in vivo and in vitro. Combined with irradiation a radiosensitizing effect is observed. We investigated the influence of dFdC on the radiosensitization of different human squamous cell carcinoma cells (#4197-oropharyngeal cancer cells, Hep2-larynx cancer cells, HeLa-cervical cancer cells).

Methods: Under standardized conditions monolayer cultures of each cell line were incubated in medium with dFdC for different times (4–24 h) and in non or slightly cytotoxic concentrations (0.01 + 0.03 μmol/l). After dFdC-exposure the cells were irradiated with 0–6 Gy. Cell survival was determined by colony forming assay. Using the linear-quadratic model survival curves were fit and the radiation enhancement ratio was calculated by the means of the mean inactivation dose.

Results: Depending on concentration (0.01 + 0.03 μmol/l) and time of exposure (4–24 h) the effect of dFdC on #4197-, HeLa-, and Hep2-cells decreases survival from 1–50%, 0–50%, and 4–18%, respectively. Combined with irradiation directly after 4-h- and 24-h-exposure the enhancement ratios are 1.03–1.05 (0.01 μmol/l) and 1.39–1.67 (0.03 μmol/l) in #4197-cells, 1.07–1.14 (0.01 μmol/l) and 1.49–2.48 (0.03 μmol/l) in HeLa-cells, and 1.04–1.14 (0.01 μmol/l) and 1.07–1.16 (0.03 μmol/l) in Hep2-cells, respectively.

Conclusion: Our results demonstrate that dFdC is a potent radiation sensitizer of HeLa- and #4197-cells. The only slight effect on Hep2-cells could be caused by a reduced or lacking activity of intracellular deoxycytidine kinase which is important for phosphorylation of inactive dFdC (pro-drug) into active dFdC-triphosphate.

706 PUBLICATION

Cytogenetic disorders and changes in peripheral blood in children living in the areas polluted after the accident at the Chernobyl AES

S. Loria, A. Rumiantsev, S. Chernysh, N. Triputen, E. Rogacheva, L. Derbeneva. *Institute of Pediatric Hematology, Moscow, Russian Federation*

Dynamic investigations carried out in the population of children living in the areas of Russia radionuclide polluted as a result of the accident at the Chernobyl AES, allowed to determine the correlation of specific changes in peripheral blood with cytogenetic status changes. It is indicated by the high frequency of different blood disorders (74.2%) in children with moderate and high extent of the cytogenetic disorders aggregate (75%). Increase in dicentric number and the stable-unstable aberration sum in 13.5% of all cases combined with erythrocytosis, in the same percent of cases – with two-blast cytosis, and in 10.8% of cases With trombocytosis. In all those children more than two chronic diseases and thyroid functional disorders were found. In the most polluted regions trombocytosis was found besides lymphocytopenia and anemia. The high sensitivity of erythrocytes and platelets is also confirmed by the variation size between lower and upper limits of the control indices in the total population of inspected individuals. Those indices dispersion values appeared to be the most unstable, deviations from the permissible range being 28–30%. The stability of the diagnostic index disorders in the blood counts of 85% of children is worth mentioning as an independent fact. It also concerns the most of sideropenic anemiae The immune diseases, such as neutropenia and trombocytopenia, obtain chronic and clinically marked nature. The problems also arise with functional disorders indicating of disorders of maturation, differentiation and active processes in the mature cell, directed towards its destabilization.

707 PUBLICATION

The effect of GM-CSF on wound healing in irradiated rats

A. Eroğlu[1], C. Kurtman[2], A. Ayhan[3], K. Karadayi[4], S. Demirci[1], G. Güler[3], H. Akgül[1]. *[1]Department of Surgical Oncology; [2]Department of Radiation Oncology; [4]Department of General Surgery, Ankara University Medical School; [3]Department of Pathology, Hacettepe University Medical School, Ankara, Turkey*

Purpose: Preoperative radiotherapy (RT) is frequently used as an adjuvant therapy to surgery for same solid turnouts, however irradiation can complicate surgical wound healing. Granulecyte macrophage-colony stimulating factor (GM-CSF) is one of the cytokins that have important roles in wound healing. We developed an animal model to investigate the effect of GM-CSF on wound healing in irradiated rats.

Methods: Thirty male adult wistam rats were divided into the following three groups: group 1 (n = 10), control (no irradiation, no GM-CSF); group 2 (n = 10), RT (irradiation, no GM-CSF); group 3 (n = 10), RT and GM-CSF (irradiation and GM-CSF). The irradiated groups received 30 Gy to their skin. The treatment schedule was 300 cGy/fraction, one fraction in a day, five fraction in one week. Three weeks after the final dose of radiation, all irradiated and normal rats received skin flaps. The wound healing was evaluated by histological, histochemical, and immunohistochemical studies. Biopsies taken on the postoperative day 3 and 10 were analyzed according to the following criteria: presence of crust, epidermal regeneration, presence of acute inflammatory elements (AIEs), collagenization of granulation tissue, collagen fibers, and neovascularization. Chi-square test was used to compare each criteria.

Results: On the postoperative day 3, there were statistically significant differences between the groups according to the present of crust, present of AIEs, and collagenization of granulation tissue. On the postoperative day 1 O, group 3 also displayed significant difference in epidermal regeneration, neovascularization, and collagen fibrils compared to the other groups.

Conclusion: Our experiments confirm that RT impairs wound healing and that GM-CSF therapy for radiation-damaged skin improves wound healing.