Proffered Papers

vitro treatment with or without TNF-alpha in presence anti-CD45 and CD95 MoAb, FLT3, IL-3 and GM-CSF.

Cell viability were analyzed by cell enumeration; intracellular metabolic activity by determination of total LDH activity after sonification, cell proliferation by 3H thymidine incorporation into DNA, cell membrane molecule expression, apoptosis and necrosis using flow cytometry (Becton Dickinson) on gated cell population. Analyses were performed 2, 6, 8 and 24 h after treatment under some experimental conditions.

Our results showed that in comparison with untreated cells, TNF-alpha induced significantly increase in apoptosis and necrosis, in PC cells, which expressed high level of CD95 and TNF alpha receptors. Pretreatment of PC cell with anti-CD45 and anti CD95 monoclonal antibodies modulated cell death induced by TNF. In addition, presence of TNF in cell culture medium induced significantly decrease in cell proliferation, stimulated by IL-3, FLT3, GM-CSF, TNF-alpha, or its combination. However, no changes in CD13 and CD33 antigen expression following cell proliferation, determined after 4 days stimulation with cytokine combination in comparison to percentage expression before treatment. No changes in intracellular LDH activity before and after cell proliferation induced with different cytokines.

We conclude that sensitivity to apoptosis limited cell proliferation estimated on this cell line.

546 PUBLICATION

The immunoreactivity of serum immunoglobulins with gliadin in patients with myeloma multiplex and non-Hodgkin's lymphoma

A. Konic-Ristic<sup>1</sup>, Z. Juranic<sup>2</sup>, I. Besu<sup>2</sup>, S. Jelic<sup>2</sup>, N. Milanovic<sup>2</sup>, M. Marinkovic<sup>2</sup>, D. Milosevic<sup>2</sup>, I. Stankovic<sup>1</sup>, N. Stanojevic-Bakic<sup>2</sup>.

<sup>1</sup>Faculty of Pharmacy, Institute of Bromatology, Belgrade, Serbia and Montenegro; <sup>2</sup>Institute for Oncology and Radiology of Serbia, Belgrade, Serbia and Montenegro

Background: Gluten intolerance is system immunological disorder which is characterized in part by the presence of antigliadin antibodies, which sometimes are also directed to calreticulin. The results from previous work showed high intensity of the interaction of serum IgA with gliadin in two patients with IgA plasmacytoma (only in patients with IgA, M component in the serum). Antigliadin IgA immunoreactivity was also found in 1 out of 4 patients with IgG plasmacytoma and in 1 patient with non-Hodgkin's lymphoma. Patient with two M components, showed IgA immunoreactivity with the blocker, bovine albumin, but not with gliadin.

Therefore, the aim of this work was to determine is there any immunoreactivity of serum immunoglobulins with gliadin, in group of patients with myeloma multiplex, non-Hodgkin's lymphoma and in healthy controls

Patients, material and methods: Six patients with IgA plasmacytoma, 10 patients with IgG plasmacytoma, 8 patients with non-Hodgkin's lymphoma and 16 healthy people were included in the study. For determination of the level of the immunoreactivity of antigliadin IgA or IgG antibodies two ELISA tests were used: a home made ELISA test with 5 micrograms of crude gliadin (SIGMA) as the antigen, while 1% bovine serum albumin was used as blocker, and commercial ELISA test (Binding Site). The absorbance of sample was divided by absorbance of positive control serum and multiplied by 100, providing arbitrary units, in the aim of standardization of the results. The cut off values, calculated as Xav+2SD of arbitrary units for healthy controls were 14.31 for IgA reactivity and 18.88 for IgG reactivity.

Results: The antigliadin IgA immunoreactivity was higher then cut off value for 3 of 6 patients with IgA plasmacytoma (27.4, 63.6, 72.5), 2 of 8 patients with non-Hodgkin's lymphoma (16.4, 20.9) and less then cut off for all patients with IgG plasmacytoma. Antigliadin IgG immunoreactivity was higher then cut off for 2 of 6 patients with IgA plasmacytoma (26.4, 19.4), for 2 of 10 patients with IgG plasmacytoma (26.4, 22) and 4 of 8 patients with non-Hodgkin's lymphoma (22.3, 21.2, 92.5, 23.9). Two patients with IgA plasmacytoma showed high IgA reactivity to BSA.

Conclusion: These preliminary results are the first showing antigliadin IgA and IgG immunoreactivity in patients with IgA and IgG plasmacytoma and non-Hodgkin's lymphoma; they set up a question on the importance of gluten intolerance in the emergence and development of myeloma multiplex.

## Epidemiology, Prevention and Public Health

Oral presentations (Wed, 2 Nov, 9.15–11.15) **Epidemiology** 

547 ORAL

Long-term risk of non-germ cell malignancies in 5-year survivors of testicular cancer

F.E. Van Leeuwen<sup>1</sup>, A.W. Van den Belt-Dusebout<sup>1</sup>, G.M. Ouwens<sup>1</sup>, R. De Wit<sup>2</sup>, J.A. Gietema<sup>3</sup>, S. Horenblas<sup>4</sup>, J.G. Ribot<sup>5</sup>, W.J. Louwman<sup>6</sup>, B.M.P. Aleman<sup>7</sup>. <sup>1</sup> The Netherlands Cancer Institute, Department of Epidemiology, Amsterdam, The Netherlands; <sup>2</sup> Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam, Department of Medical Oncology, Rotterdam, The Netherlands; <sup>3</sup> University Medical Center Groningen, Department of Medical Oncology, Groningen, The Netherlands; <sup>4</sup> The Netherlands Cancer Institute, Department of Urology, Amsterdam, The Netherlands; <sup>5</sup> Catharina Hospital, Eindhoven, Department of Radiotherapy, Eindhoven, The Netherlands; <sup>6</sup> Eindhoven Cancer Registry, Comprehensive Cancer Center South, Cancer Registry, Eindhoven, The Netherlands; <sup>7</sup> The Netherlands Cancer Institute, Department of Radiotherapy, Amsterdam, The Netherlands

**Background:** To assess long-term risk of non-germ cell malignancies (NGCMs) in 5-year survivors of testicular cancer.

Patients and methods: We conducted a nation-wide cohort study comprising 2707 5-year survivors treated for testicular cancer between 1965 and 1995. Complete medical follow-up information until at least January 1, 2000 was available for 90% of all patients. The number of non germ-cell malignancies was compared with general population rates to assess relative risk (RR) and absolute excess risk (AER) of non-germ cell tumors

Results: After a median follow-up of 16.3 years, 255 NGCMs were observed. The risk of NGCM overall was 1.7-fold (95%CI: 1.5-1.9) increased compared to the general population. Among survivors treated before age 30 the risk of any NGCM was even 3.9-fold (95%CI: 2.9-5.3) increased compared to the general population. When survivors grew older, the RR for NGCM overall decreased from 3.2 (95%CI: 2.4-4.1) for patients with attained age 50 or younger to 1.3 (95%CI: 1.0-1.7) for patients with attained age of 70 or older. There was an increase of RRs with longer follow-up time for all gastro-intestinal cancers combined, stomach cancer, urinary bladder cancer and especially prostate cancer, consistent with a radiation effect, whereas this time-trend was not found for all NGCMs combined. However, due to a rising background incidence of cancer with increasing age, the AERs for NGCM overall increased strongly with followup time till 25 years after testicular cancer diagnosis, with 86 excess cases per 10,000 person-years in the 20-25 year follow-up interval, and slightly decreased thereafter. NGCM risk overall was rather constant over treatment periods, whereas RRs of stomach, bladder and kidney cancer decreased with more recent treatment eras. Patients treated with chemotherapy alone had increased risks of urinary bladder cancer and melanoma (RRs of 5.0 (95%CI: 0.9-14.8) and 6.2 (95%CI: 2.0-14.7), respectively). Patients who received combined modality treatment had a 2.7-fold (95%CI: 1.9-3.9) increased risk of NGCM overall compared to the general population.

Conclusion: Survivors of testicular cancer, especially of nonseminomatous testicular cancer, were still at significantly elevated risk of developing NGCMs more than 20 years after testicular cancer diagnosis. Excess risks of NGCMs were mainly attributable to radiotherapy, but to a lesser extent also to chemotherapy.

548 ORAL Second non-breast malignancies following breast cancer

Y. Kirova<sup>1</sup>, L. Gambotti<sup>2</sup>, J.R. Vilcoq<sup>1</sup>, B. Asselain<sup>2</sup>, F. Campana<sup>1</sup>, R. Dendale<sup>1</sup>, M. Bollet<sup>1</sup>, A. Fourquet<sup>1</sup>. <sup>1</sup>Institut Curie, Radiation Oncology, Paris, France; <sup>2</sup>Institut Curie, Biostatistics, Paris, France

**Background:** The place of the adjuvant radiotherapy (RT) for breast cancer (BC) in the increasing the incidence of second primary cancers is debatable.

**Purpose:** To estimate the risk of second non-breast malignancies (SNBM) following radiotherapy (RT) for breast cancer in one institutional homogeneous cohort of patients.

Patients and methods: We reviewed the records of 16 705 patients (pts) with non-metastatic breast cancers treated at the Institut Curie between 1981 and 1997. Of them, 13 471 (81%) received radiotherapy and 3 234 (19%) did not. SNBM included all first cancers occurring after treatment of the primary breast cancer, except contalateral breast