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

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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 1out 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

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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 follow-up 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

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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

cancer. Cumulative risks for each group were calculated using Kaplan-Meier estimates, censoring for contralateral cancer or death. Adjustment for other factors such as adjuvant treatments or individual risk factors for some cancer locations was not performed in this study. The risk of occurrence of SNBM was calculated using: [1-S(t)] where S(t) formula is the survival, using Kaplan-Meyer method. These cumulative risks were stratified by RT and groups were compared by the log-rank test.
Results: At 10.5 years median follow-up [0.2–24 yrs], there was a significant difference in the incidence of sarcomas and lung cancers between the group who received RT and the group who did not. The cumulative risks of different cancers in no RT group vs. RT group were as follows:

Cumulative risks of second malignancies at 10 years of follow-up

SNBM	No radiotherapy (No. pts = 3,234) 230	Radiotherapy (No. pts = 16,705) 1113	p*
Head and neck	0.03%±0.03	0.12%±0.03	0.15
Lung	0.18%±0.09	0.41%±0.07	0.02
Gastro-Intestinal (GI)	1.53%±0.26	1.06%±0.11	0.12
Ovarian	0.26%±0.11	0.56%±0.08	0.08
Gynaecological	0.71%±0.19	0.89%±0.09	0.28
Genito-Urinary (GU)	0.25%±0.10	0.21%±0.05	0.87
Others	0.13%±0.07	0.17%±0.04	0.87
Sarcoma	0.00%±0.00	0.26%±0.05	0.02
Malignant melanoma	0.20%±0.09	0.29%±0.06	0.41
Lymphomas	0.26%±0.11	0.26%±0.05	0.78
Leukaemia	0.29%±0.11	0.34%±0.06	0.95
Thyroid	0.16%±0.09	0.14%±0.04	0.65
All	4.00%±0.41	4.60%±0.22	0.06

*log-rank test

Conclusion: This study showed that adjuvant radiotherapy increased the rate of sarcomas and lung cancers, whereas it did not increase the rate of other malignancies. At a median follow-up of ten years, this study showed that radiotherapy did not increase the risk of other types of cancers, as for example thyroid cancer, malignant melanoma, GI or GU cancers. The risk of hematological malignancies was not increased either. Long-term follow-up is needed for this population of patients to exclude other late complications.

549 ORAL

Familial risk of colon and rectal cancer in Iceland. Different etiologic factors for colon cancer and rectal cancer

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Aim: The aim of the present study was to characterise the familial risk of colon or rectal cancer in Iceland.
Method: The standardized incidence ratio (SIR) was used to estimate the risk among relatives of colorectal cancer index cases diagnosed in Iceland over a 46 year period (1955–2000). All data was retrieved from population based registries (The Icelandic Cancer Registry and a Genealogic database from The Genetical Commity of the University of Iceland).
Result: In all 2770 colorectal cancer patients had 23,272 first degree relatives. Among the first degree relatives there was an increased risk of colon cancer (SIR 1.47, 95% confidence interval [CI]: 1.34–1.62) and rectal cancer (SIR 1.24, 95%CI: 1.04–1.47). Among the 17119 first degree relatives of colon cancer patients there was an increased risk among siblings of both colon cancer (SIR 2.03, 95%CI: 1.76–2.33) and rectal cancer (SIR 1.56, 95%CI: 1.19–2.02). If the colon cancer patients were 60 years or younger the risk of colon cancer in first degree relatives was: SIR 3.14, 95%CI: 2.27–4.23. The risk of colon cancer and rectal cancer was not increased among parents and offspring. The risk was equally distributed among men and women. Among the 6767 first degree relatives to rectal cancer patients there was an increased risk among siblings of colon cancer (SIR 1.61, 95%CI: 1.23–2.06) and of rectal cancer (SIR 1.75, 95%CI: 1.13–2.58). If the rectal cancer patients were 60 years or younger the risk of rectal cancer in first degree relatives was: SIR 2.43, 95%CI: 0.89–5.29. The risk of colon cancer was increased for brothers to rectal cancer patients (SIR 1.79, 95%CI: 1.22–2.53) and for sisters (SIR 1.45, 95%CI: 0.98–2.07) however, the risk of rectal cancer was only increased among brothers (SIR 2.46, 95%CI: 1.46–3.89) to rectal cancer patients but not among the sisters (SIR 1.0 95%CI: 0.40–2.06).
Conclusion: Family history of colon cancer is supported as a risk factor for the disease. Family history has different association with colon cancer and rectal cancer giving evidence to different etiologic factors for colon cancer and for rectal cancer. Siblings to colorectal cancer patients diagnosed in Iceland when 60 years or younger should be offered screening for colorectal cancer.

550 ORAL

Population based mammography screening results in substantial savings in treatment costs by reducing the number of breast cancer deaths

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Background: The aim of the study was to assess the effect of population based mammography on treatment costs for fatal breast cancer.
Material and methods: Population based mammography screening for women aged 40–74 years in the city of Turku, Finland was launched in 1987. The current study included 556 invasive breast cancers diagnosed among women aged 40–74 years between 1987 and 1993: 427 in the screening group (which included screen-detected and interval cancers) and 129 in the non-screening group (which included breast cancers detected before initial screening and those detected in patients who chose not to undergo screening). The treatment costs due to breast cancer for each patient at the different hospitals, in a hospice, and at a cancer clinic of the Cancer Society were followed up for eight years from diagnosis or until death, whichever occurred first.
Results: During the 8-year follow-up, 82% of patients survived in the screening group and 66% in the non-screening group, while 12% versus 25% died of breast cancer and 6% versus 9% died of other causes, respectively. In the screening group, the mean treatment costs were Euros 27,803 (95%CI: 23,175–32,431) for patients with fatal breast cancer versus Euros 8,915 (CI: 8,350–9,480) for the survivors ($p < 0.001$). In the non-screening group, they were Euros 23,800 (CI: 19,033–28,566) versus Euros 11,583 (CI: 10,258–12,909) ($p < 0.001$), respectively. Among the 81 patients who died of breast cancer there was no statistically significant difference in the mean costs per patient between screened and unscreened women ($p = 0.245$). As a result of fatal breast cancer occurring more often among unscreened than screened women, 29% of the total treatment costs in the screening group were used for the treatment of fatal breast cancer, compared to 41% in the non-screening group. On the basis of breast cancer death rates and mean costs per patient, it was estimated that without a screening programme the treatment costs of 2.1 million Euros for fatal breast cancer would have been 0.9–1.1 million Euros higher during the study period. Thus, approximately 29–33% of these costs were saved through mammography screening.
Conclusions: The treatment costs associated with fatal breast cancer are high. Early detection of breast cancer by population based mammography screening results in substantial savings in treatment costs by reducing the number of breast cancer deaths.

551 ORAL

Prevalence of abnormal Pap smears among young adult women participating in human papillomavirus (HPV) L1 virus-like particle (VLP)-vaccine clinical trials

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Background: HPV infection by oncogenic types is a necessary cause of cervical cancer and infection by non-oncogenic types causes anogenital warts and some low-grade cervical lesions. A quadrivalent vaccine against HPV types 6, 11, 16, and 18 (GARDASIL™) is currently in development. The baseline characteristics of this large Phase III study population are described here.
Methods: Two parallel pivotal clinical trials of GARDASIL™ enrolled women from Europe (50.6%), Latin America (30.6%), North America (14.7%) and the Asia-Pacific region (4.2%). Participants were to be either