Therefore, the 2000 raw incidence rate of breast cancer is approximately 10.6 per 100,000 women in the north of Iran.

Conclusions: Cases in this cancer account for 10.7% of total malignant neoplasms. Also, breast cancer constitutes nearly a quarter of all female cancers in Mazandaran and Golestan provinces during the last 3 years. The available epidemiological data suggest that breast cancer is a common disease in the north of Iran, and this point to the increasing need of establishing a cancer registration center in the north of Iran.

448 POSTER

Induction of apoptosis in mouse mammary epithelial cells RIII/MG by epigallocatechin gallate (EGCG)

T. Koga[1], T. Fujii[2,3], H. Yanaga[2], E. Ogo[4], G. Yokoyama[2,3], M. Mishima[2,3], H. Yamana[5], K. Shirouzu[2]. [1]*Hirose Hospital, Surgery, Fukuoka, Japan;* [2]*Kurume University, Surgery, Kurume, Japan;* [3]*Kurume University, Research Center for Innovative Cancer Therapy, Kurume, Japan;* [4]*Kurume University, Radiology, Kurume, Japan;* [5]*Kurume University, Multidisciplinary Treatment Center, Kurume, Japan*

Green tea is a natural food ingested in daily life in Japan, and many studies regarding its preventive effect on carcinogenesis and anticancer effect have been performed. A major component of tea, epigallocatechin gallate (EGCG), has potent biological and pharmacological activity. EGCG has been reported to exert an antitumor effect on brain tumor, colon cancer, prostatic cancer, hepatoma, gastric cancer, lung cancer, Leukemia, oral cavity cancer, and a similar effect was shown for breast cancer. Although many studies of the antitumor effect of EGCG have been performed, there are few basic studies regarding how EGCG prevents carcinogenesis and the effect of EGCG on precancerous cells, and many points remain unclear. It is of interest to clarify how green tea ingested in daily life prevents cancers with few adverse effects. Thus, in this study, we investigated the effect of EGCG on precancerous mammary cells using the RIII/MG cell lines, which are mouse models of viral carcinogenesis in mammary epithelium, in vitro and in vivo to investigate whether green tea commonly ingested in Japan prevents carcinogenesis of precancerous cells. In the in vitro experiment, crude catechin (catechin) containing 50% or more EGCG significantly inhibited the growth of RIII/MG cells, which were precancerous cultured cells. Many cells died and a DNA ladder was observed. In the in vivo experiment, RIII/MG cells formed a tumor after 13 weeks in a group without catechin treatment and the tumor formation rate in the 20th week was 40%. In a group treated with 0.1% catechin, a tumor began to grow in the 13th week and the tumor formation rate in the 20th week was 20%. In a group treated with 1% catechin, no tumor was detected even in the 20th week. There was no significant difference in the change in body weight between the catechin treatment groups and the non-treatment group during the observation period. Tissue samples were stained by the nick end labeling method and apoptosis was observed in many cells. Based on the above findings, catechin inhibited growth in the mouse viral mammary epithelial carcinogenesis model, RIII/MG, and induced apoptosis, suggesting the usefulness of catechin as a chemopreventive substance.

449 POSTER

Familial risks of cancer as a guide to gene identification and mode of inheritance

X. Li[1], K. Czene[1], K. Hemminki[2]. [1]*Karolinska Institute, Biosciences, Huddinge, Sweden;* [2]*German Cancer Research Center (DKFZ), Heidelberg, Division of Molecular Genetic Epidemiology, Heidelberg, Germany*

Background: Familial clustering of a disease is caused by shared genes or shared environment. If the effect of environment can be quantified, the remaining familial clustering can be assigned to heritable causes. Occurrence of cancer in parents and offspring may be due to dominant causes, whereas cancer affecting only siblings may indicate a recessive causation. Systematic comparisons of mode of inheritance have not been available for most types of cancer.

Methods: We use the nationwide Swedish Family-Cancer Database, which includes the Swedish population in families, totaling over 10.2 million individuals and cancers from the Swedish Cancer Registry up to year 2000. Standardized incidence ratios (SIR) and 95% confidence limits (CI) were calculated for offspring whose parents or siblings were diagnosed with the same cancer.

Results: The degree of environmental causation was assessed by spouse correlation and by comparing risks among siblings of different ages. We identified reliable familial risks for all common neoplasms, SIRs ranging from 1.6 to 4.3 when only a parent was affected and up to 8.5 when only a sibling was affected. Risks between siblings were particularly high for renal cancer. Spouse correlation was found only for lung and stomach cancer but the analysis of sibling risks by their age difference suggested that even for some other cancers environmental effects in childhood may contribute to familial aggregation.

Conclusions: The results from these analysis suggest that familial cluster of cancer at most sites is heritable, caused by dominant effects; for renal cancer recessive effects may be most important.

450 POSTER

Set-up of a population-based familial breast cancer registry in Geneva Switzerland: Validation of first results

H. Verkooijen[1], G. Fioretta[1], P. Chappuis[2,3], G. Vlastos[4], P. Sappino[2], S. Benhamou[5], C. Bouchardy[1]. [1]*Geneva Cancer Regisry, Institute for Social and Preventive Medicine, Geneva, Switzerland;* [2]*Geneva University Hospitals, Division of Oncology, Geneva, Switzerland;* [3]*Geneva University Hospitals, Division of Medical Genetics, Geneva, Switzerland;* [4]*Geneva University Hospitals, Department of Obstetrics and Gynecology, Geneva, Switzerland;* [5]*Evry University, INSERM, Evry, France*

Background: This study evaluates the accuracy of family history (FH) of breast and ovarian cancer among first-degree relatives (FDRs) of breast cancer patients, retrospectively collected during the set-up of a population-based family breast cancer registry.

Methods: FHs of cancer of all women with breast cancer recorded at the Geneva cancer registry between 1990–1999 were retrospectively extracted from medical files. The accuracy of these FHs was validated among Swiss women born in Geneva: all 119 with a FH of breast cancer (n=110) or ovarian (n=9) cancer and a representative sample of 100 women with no FH of breast or ovarian cancer. We identified the FDRs of these women with information of the Cantonal Populational Office. All FDRs, resident in Geneva between 1970–1999, were linked to the cancer registry database for breast and ovarian cancer occurrence. Sensitivity, specificity, and level of overall agreement (kappa) were calculated.

Results: Among 310 FDRs identified, 61 had breast cancer and 6 had ovarian cancer recorded at the Geneva cancer registry. The sensitivity, specificity and kappa of the reported FHs of breast cancer were respectively 98%, 97% and 0.97. For ovarian cancer, the sensitivity, specificity and kappa were respectively 67%, 99%, and 0.66.

Conclusion: This study indicates that retrospectively obtained FHs are very accurate for breast cancer. For ovarian cancer, FHs are less precise and may need additional verification.

451 POSTER

Increased rates of chromosome breakage in BRCA1 carriers are reduced by oral selenium supplementation

E. Kowalska[1], S.A. Narod[2], T. Huzarski[1], S. Zajaczek[1], J. Huzarska[1], B. Gorski[1], J. Lubinski[1]. [1]*Pomeranian Medical University, International Hereditary Cancer Center, Szczecin, Poland;* [2]*Sunnybrook and Women's College Health Sciences Centre, Centre for Research on Women's Health, Toronto, Canada*

Women who are born with constitutional heterozygous mutations of the BRCA1 gene face greatly increased risks of both breast and ovarian cancer. The product of the BRCA1 gene is involved in the repair of double-stranded DNA breaks and it is believed that increased susceptibility to DNA breakage contributes to the cancer phenotype. We measured the frequency of chromosome breaks in BRCA1 carriers and in non-carrier relatives in cultured blood lymphocytes following in vitro exposure to bleomycin. Carriers of BRCA1 mutations demonstrated significantly greater mean frequencies of induced chromosome breaks per cell than the control relatives (0.58 versus 0.39; $p<10^{-4}$). We then supplemented 35 BRCA1 carriers with oral selenium for a period of one to three months. In all 35 carriers studied, the frequency of chromosome breaks was reduced, from a mean of 0.63 breaks per cell to 0.40 breaks per cell ($p<10^{-10}$) and the frequency was then similar to that of the non-carrier controls (0.39 breaks per cell). Oral selenium is a good candidate for chemoprevention in women who carry a mutation in the BRCA1 gene.

452 POSTER

Identification of women at high risk of hereditary breast cancer

G.M. Baratelli[1], P. Valsecchi[1], R. Necchi[1], C. Capici[1], M. Grazioli[2]. [1]*Centro di Senologia, Delegazione Alto Lario della Lega Italiana per la Lotta contro i Tumori, Gravedona, Italy;* [2]*Centro di Senologia, Sezione Provinciale di Sondrio della Lega Italiana per la Lotta contro i Tumori, Sondrio, Italy*

Objective: To identify women with moderate to high risk of hereditary breast cancer in order to offer them specific management strategies for cancer prevention and early detection.

Setting: Centro di Senologia della Delegazione Alto Lario della Lega Italiana per la Lotta contro i Tumori at Gravedona (Italy) and Centro di Senologia della Sezione Provinciale di Sondrio della Lega Italiana per la Lotta contro i Tumori at Sondrio (Italy).

Methods: 234 women with family histories of breast cancer completed, by themselves, simple questionnaires prior to undergoing a breast cancer