

mined by EMSA and promoter assay by HSE-SEAP vector. High endogenous levels of Hsp 70 have been found to be a deterrent for sensitivity to chemotherapy. To confirm this we overexpressed Hsp70 in Hela cells and compared its reluctance to chemotherapeutic drug and UV induced apoptosis. Res has similar effects on CML patient samples without affecting the normal counterpart. We show here that Res could significantly enhance the apoptosis induction by 17-allylamino-17-demethoxygeldanamycin (17AAG), an anti-cancer agent. Furthermore the 17AAG-Akt-Hsp70 paradox was also revealed. We conclude that resveratrol possibly acts at one or more steps downstream from Bcr-Abl and blocks Akt phosphorylation and decreases expression of Hsp70 in K562 cells.

General and breast cancer prevention

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Anti-angiogenic activity of a novel class of chemopreventive compounds, oleanic acid terpenoids

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Angiogenesis is the base for solid tumor growth and dissemination, anti-angiogenic drugs demonstrated to be active in clinical trials. In addition, it has become increasingly clear that inflammation is a key component in tumor insurgence. Chemoprevention focuses on the primary or secondary prevention of cancer using natural or synthetic agents usually showing mild or no collateral effects. We noted that angiogenesis, particularly 'inflammatory angiogenesis', is a common target of many chemopreventive molecules where they most likely suppress the angiogenic switch in pre-malignant tumors, a concept we termed "Angioprevention". We have shown that various molecules, such as flavonoids, antioxidants and retinoids, act in the tumor micro-environment inhibiting the recruitment and/or activation of endothelial cells and phagocytes of the innate immunity. We have recently assessed the activity of novel compounds derived from the oleanolic acid triterpenoid, called CCDO-Me and CDDO-Imm. These compounds show a potent antiangiogenic activity at low dosages. In vivo they inhibit angiogenesis in the matrigel sponge assay and KS-Imm tumor growth. In vitro they are able to prevent endothelial cells tubulogenesis when cultured on matrigel. In HUVE cells these compounds can inhibit the activation of erk1/2 pathway after stimulation with VEGF. Moreover, from immunofluorescence experiments we observed that treatment with these triterpenoids prevents NF- κ B translocation into the nucleus and thereby the activation of downstream pathways. The particularly potent anti-angiogenic activity seen in vivo suggest that CDDO-Me may be interacting with an important network of molecular and cellular targets, on endothelial cells, and could be employed for 'angioprevention'. These substances are assessed in the US phase I trials in humans.

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Risk factors of the metabolic syndrome and cancer outcomes in a large primary prevention programme

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The metabolic syndrome was introduced in 1988 as a constellation of metabolic aberrations caused by overeating and sedentary lifestyle. The metabolic syndrome includes obesity, hyperglycaemia, high blood pressure, and dyslipidaemia and its presence has been consistently associated with an increased risk of cardiovascular disease, stroke and diabetes. Only a few studies of sufficient sample size have examined the link between risk factors of the metabolic syndrome and cancer. Since 1985, residents of Vorarlberg, the westernmost province in Austria, above 19 years of age, have been invited to yearly health check-ups for disease prevention. As of 2005, more than 180,000 individuals have participated in this so called Vorarlberg Health Monitoring and Promotion Programme (VHM&PP), with 1–21 examinations per individual resulting in a total of almost 700,000 examinations. The VHM&PP cohort has been linked to the regional Vorarlberg cancer registry for cancer incidence outcomes as well as to the Austrian National cause of death registry for mortality outcomes. Recent research of our group has shown associations of varying strengths of body mass index [1], fasting serum glucose [2], uric acid [3,4] and gamma-glutamyl transferase (unpublished) with cancer outcomes at different sites. Our results aid to the understanding of the role of these metabolic and lifestyle risk factors in cancer development supporting their use as valuable measures in not exclusively cardiovascular but also cancer prevention.

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First results of Breast Cancer Screening Program in Khanty-Mansiysk State region Ugra

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Introduction: Nowadays most developed countries in the world, including Russia, experience the increase of breast cancer rate. There has been a steady growth of breast cancer cases from 2002 to 2006 year both in Ugra and in Russia overall (cancer-register materials analysis of Khanty-Mansiysk State Clinical Hospital). At the present time, since February, 7th, 2007, there has been a Screening Program (SP) implemented on the territory of the region that is aimed at early breast cancer diagnostics. SP includes 3 consecutive stages. First stage particularity is based on northern regional aspects – town remoteness from each other and from big cities, absence of oncologists in each town. Gynecologists or medical assistants make a physical breast examination and order instrumental diagnostic. Second stage includes instrumental diagnostics measures. Third stage determines treatment-diagnostics measures performed by oncologists when second stage finds breast pathology.

Goal: Define SP first results with diagnostics equipment performance evaluation in region municipal districts.

Results: The reports have been provided by 21 municipal districts from March till October 2007. 38360 women have been inspected with use of mammography and ultrasound for the period of 8 month, including 18123 within screening program. This number represents around 7% of female population of over-20-years age group. 20575 women, age group over 40 years, have been inspected using mammography, including 11630 within the SP – 56.5% of the total inspections. Ultrasound inspection has been performed on 17785 women, including 6493 within the SP – 36.5% of the total inspections.

Conclusions: Reports analysis in the region has demonstrated SP active implementation in majority of municipal districts. However, it has shown that some districts do not perform sufficient screening inspections even though there is all required equipment in place. Also it indicated 6 districts with no mammography set up or functioning for various reasons. The following measures are required to resolve the above problems: appointment of those responsible for SP implementation in each district; educational courses for medical specialists involved in first stage of SP; sufficient employment of specialists to maintain mammography equipment operations in all municipal districts; telemedicine use in the region for histologist and cytologist consultations when performing verification of breast biopsy results.

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Genetic counseling in breast cancer. The National Cancer Institute of Naples experience

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Genetic factors appear to contribute to at least a fraction of 5–10% of the women with breast cancer. Today the recent molecular biology acquisitions lead us to consider different clinical approaches in the treatment of women with higher risk to develop breast carcinoma. In 1994 our Institute started a perspective program (named "Family Project") for genetic counselling on families with higher incidence of breast cancer. 245 women distributed in 93 families have been entered into this study. The only criterion for admission was the presence of breast cancer in at least 3 components of the family. This

group was followed by a clinical-diagnostic protocol including anamnesis, genealogical tree reconstruction and clinical and instrumental examinations (ecography, mammography and FNAC where necessary). Peripheral blood samples were taken from each woman and genomic DNA was extracted to further evaluate putative genetic alterations after obtaining informed consent. This approach has permitted discovering pre-clinical lesions in 10 women enrolled belonging to family groups under study. From the first breast cancers analysis we found an hereditary component in 13% of all cases studied and these cases have peculiar characteristics: early age of diagnosis, frequent bilateral tumours, and the association with other tumours in the same person or in the same family group. The follow-up uses a protocol, which foresees the psychological approach, between the clinical team and the women in study, as a fundamental part of it.

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The patterns of BRCA1 and BRCA2 mutations in hereditary breast cancer in Ukrainian population

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Breast cancer (BC) is the most common malignancy in developed countries with lifetime risk about 70–90%. It is known, that specific inherited mutation in BRCA1 and BRCA2 (5–10% of overall BC incidence) associated with an extremely high risk of BC development. The most thoroughly studied manifestations of the founder effects are among Ashkenazi Jewish population where three common mutations in BRCA1 and BRCA2 are reported (185delAG, 5382insC in BRCA1 and 6174delT in BRCA2). The aim of the study: To estimate the patterns BRCA1 and BRCA2 mutations of Ukrainian population.

Material and Methods: We analyzed DNA samples of 20 patients with hereditary BC to determine the patterns of founder mutations and other mutations in BRCA1 and BRCA2 genes. We screened the genes BRCA1, BRCA2, and CHEK2 from 20 paraffin samples of Ukrainian patients with BC using gel electrophoresis and direct sequencing.

Results: 517delTG BRCA1 mutation has been found in 5 patients, T300G – in 3 patients, 5385insC – in 3 patients, 6174delT and 5909insA BRCA2 mutations has been found in 1 and 1 patient accordingly. IVS2+1G>A and I157T mutation CHEK2 where found in 4 patients and 3 patients accordingly. So the most frequent BRCA1 gene defects were detected 517delTG and 5382insC (founder mutations) in 5 and 3 patients accordingly. 617delT founder mutations in BRCA2 was identified in only one case.

Conclusion: Founder mutations in Ukrainian populations in our study make up only 15% for BRCA1 and 5% for BRCA2.

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The BRCA1 and BRCA2 mutation in Chinese breast cancer patients – a multi-center study of 489 cases

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