

curd may be included to complex treatment of cancer patients but only if it would be dosed correct. At the same time, FS curd is contradicted for cancer patients.

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#### P9

##### **The effect of cabbage juice and its components on the expression and activity of phase 1 and 2 enzymes in rats**

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Cruciferous vegetables (Brassica) are rich in glucosinolates which undergo hydrolysis to form isothiocyanates (ITCs), thought to be responsible for the chemopreventive properties of this food group. One of the Brassica representative common in Central and Eastern European diet is raw, or cooked cabbage and sauerkraut. The aim on this study was to search the possible mechanism of anticarcinogenic activity of cabbage juice and its components by evaluating their effect on phase 1 and phase 2 enzymes expression and activities in rats. Male Wistar rats were treated by gavage with cabbage juice (1.25 mL), indole-3-carbinol (I3C) (100 mg/kg b.w.) or phenethyl isothiocyanate (PEITC) (100 mg/kg b.w.) for 4, 10 and 30 days. The administration of cabbage juice resulted either in increase or decrease in CYP450 content and activity depending on the tissue and treatment period. In rat liver the significant increase of EROD (the marker of CYP1A1) and MROD (the marker of CYP1A2) activities were observed after 30 days of treatment with cabbage juice in comparison with the control group of animals receiving only water. I3C and PEITC enhanced the activities of all CYP450 markers at all time points, with most significant increase after 30 days of treatment. Administration of cabbage juice increased also the activities of GST and NQO1 in rat liver at all point time. In kidney the increase of these enzymes activities was observed only after 4 days of cabbage juice administration. The similar effects were observed as result of I3C and PEITC treatment. Western blot analysis showed significant enhancement of hepatic GST alpha and mu protein levels after treatment with cabbage juice, I3C and PEITC in comparison with control. Among tested CYP450 isoforms significant increase in the level of hepatic CYP1A1 in cabbage juice and indole-3-carbinol treated animals was found. PEITC treatment changed the expression of CYP2B only. This compound increased the level of CYP2B in liver and to lesser extend in kidney. The translocation of Nrf2 from cytosol to nucleus in liver was observed after treatment with PEITC. The results of this study indicate that cabbage may exert its chemopreventive activity by modulation the expression and activity of CYP1A P450 isozymes and induction of phase 2 enzymes. Since similar results were observed after treatment with I3C and PEITC, it suggests that these compounds may be responsible for the observed effects.

#### P10

##### **The exploitation of anticarcinogenic potential of white cabbage to improve nutritional value of meat products**

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Two recent decades marked the rise of new approach to cancer control emphasizing rather prophylaxis including

the one involving dietary means (chemoprevention) as opposed to treatment (chemotherapy). A number of groups of phytochemicals present in food were identified displaying various activities protecting against malignant transformation or slowing down cancer development. Accordingly, vitamin (mainly antioxidant) supplements were suggested as possible anticarcinogenic agents and consumption of fruits and vegetables recommended as anticarcinogenic diet. However, recent statistical analyses of large epidemiological studies gave not very optimistic results as the association between plant food consumption and decrease of cancer risk turned out hardly convincing. The question arises why the approach successfully employed in the development of new pharmaceuticals (from mechanistic through in vivo to human studies) did not seem to work in the case of dietary chemoprevention? What bits in the puzzle are missing? One of the reasons might be that in our assessments we kept forgetting about a very important factor, i.e. quality of fruits and vegetables that depends on both agricultural practices and processing. The majority of human studies took into account only amounts consumed ignoring the actual content of health promoting vs. unhealthy substances present in food. And food industry used the raw materials with high content of e.g. antioxidants seldom following their fate upon processing. In the light of current knowledge, it appears necessary to undertake efforts to use chemopreventive potential of fruits and vegetables for designing foods with carefully planned composition and verified biological potential of final products. With this in mind, we exploited the benefits offered by white cabbage components to elaborate the technology of meat processing to obtain meat products enriched with cabbage anticarcinogenic components hence with improved nutritional value. The choice of vegetable stemmed from both traditional usage of cabbage in Central Europe and our studies demonstrating its technological and nutritional advantages. The scientific base and probable health benefits of these products to be introduced into Polish market next year (2008) will be presented.

#### P11

##### **Polyphenolic compound resveratrol targets heat shock protein 70 in chronic myeloid leukemia to induce apoptosis**

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Chronic myelogenous leukemia (CML) is a myeloproliferative disease associated with a characteristic chromosomal translocation called the Philadelphia chromosome resulting in BCR-ABL fusion protein. Though there are a few treatment options but drug resistance is often encountered. Resveratrol (Res) is a phytoalexin produced by several plants. We studied the chemotherapeutic effects and mode of action of Res on K562 (CML) cells. Res induces apoptosis in K562 cells in a time and dose dependent manner. This was established by cell cycle analysis by flow cytometry, caspase-3 activity measurement, nuclear fragmentation and AnnexinV binding. The pro-survival protein PKB/Akt and was identified as the molecular targets of Res. The activation of this protein was impeded by Res, as confirmed by western blot analysis. For the first time we elucidate that Res treatment also caused suppression of Hsp 70 both in the mRNA and protein level. The downregulation of Hsp70 in presence of Res was correlated with Akt by using Akt siRNA and PI3K inhibitor LY294002. The down regulation of transcriptional activity of HSE was deter-

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

### P12

#### 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- $\kappa$ 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.

### P13

#### 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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### P14

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

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