

(OR 0.71; 95%CI 0.27–1.87), and no significant interactions between the COX-2 genotype and NSAID use were found.

Conclusions: In this exploratory study, NSAID use was associated with a reduced risk for BE, a premalignant lesion associated with progression to esophageal adenocarcinoma. This protective effect was not modulated by the common COX-2 T8473C polymorphism, suggesting further studies to define underlying biologic mechanisms of NSAID chemoprevention.

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Cancer chemopreventive potential of apple juice – Results of a short-term human intervention study with ileostomy patients

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Apples are widely consumed and a rich source of phytochemicals. Regular consumption of one or more apples/day was linked to reduced risk for lung- and colon cancer in various epidemiological studies. In addition, dietary intervention with turbid apple juice reduced adenoma formation in ApcMin/+ mice (Pan et al., in preparation), and DNA-damage, hyperproliferation, and aberrant crypt foci in the dimethylhydrazine-induced rat colon model (Barth et al., 2005). In the present study we determine whether apple juice polyphenols may reach the colon after oral intake of cloudy apple juice and retain chemopreventive properties after passage through the gastrointestinal tract. Eleven ileostomy volunteers consumed 1 l of cloudy apple juice after overnight fast. Ileostomy effluents were collected after 0 to 8 h and freeze-dried. A maximum of 33% of the ingested low molecular weight polyphenols were detected 1, 2, and 4 h after ingestion, in addition to 80% of the ingested oligomeric procyanidins (Kahle et al., 2005, 2007). Based on dried weights, polyphenol concentrations up to 10.2±1.6 mg/g bag contents (average ± standard error, n=11) were recovered with a maximum after 4 h. We detected a transient increase in radical scavenging activity with a maximum at 4 h after apple juice consumption. Half maximum inhibitory concentrations for DPPH scavenging were significantly reduced by 65% from 0 h to 4 h (ANOVA with Student-Newman-Keuls Test for multiple comparison, $p < 0.05$). Concomitantly, potential to scavenge peroxyl radicals significantly increased from 2.9±0.3 to 4.5±0.5 ORAC units after 4 h (measured at 25 µg/ml). In contrast, potential to modulate carcinogen metabolism by inhibition of Cyp1A enzymatic activity and by induction of detoxifying mechanisms (measured as NAD(P)H:quinone reductase (QR) activity in Hepa1c1c7 cells) was highest at time point 0 h. After apple juice consumption, activities initially declined, and maximum preventive effects were then observed after 6 to 8 h. A similar trend was detected for the inhibition of aromatase (Cyp19) activity with strongest inhibitory effects at time 0 h, whereas Cox-1 activity was not affected. From these results we conclude that selected apple juice polyphenols, especially oligomeric procyanidins, may reach the colon and exert a local antioxidant effect. Modulation of additional chemopreventive mechanisms is likely.

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Endogenous IFN alpha during liver transition from quiescence to proliferation

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Background: Interferon alpha (IFN α) is used as main or adjuvant treatment in the therapy of viral infections and several types of cancer. This cytokine is a common therapy for chronic viral hepatitis and contributes to hepatocarcinogenesis prevention. However, the mechanism of IFN α antiproliferative activity in vivo is still obscure. The situation in the liver is complicated by the various types of cells revealing cell-specific response to IFN α , the expression of endogenous cytokine and specific intercellular communication during the transition of liver cells from quiescence to proliferation at preneoplasia. The aim of the study was to evaluate the production of endogenous IFN α during liver transition from quiescence to proliferation induced by partial hepatectomy at the rats.

Materials and Methods: The rats after 2/3 partial hepatectomy (PHE) and laparotomy (LAP) were used in 1, 3, 6 and 12 h post-surgery to model correspondingly G0–S transition and acute phase response, the latter being a constituent part of the former. The genes expression was assessed in liver samples, isolated Kupffer cells (KC) and hepatocytes by quantitative real-time RT-PCR and antiviral test.

Results: PHE induces 2-fold transient increase of IFN α mRNA content and liver antiviral activity at 1–3 h post surgery with subsequent normalization of the indices during 6–12 h period. LAP induces down regulation of IFN α mRNA content in comparison with intact animals. The antiviral activity after LAP was less than the detection limit. KCs and not hepatocytes in both models are responsible for IFN α expression.

Conclusions: The changes in IFN α expression may be essential for liver G0–S transition and acute phase response.

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Prevention of gynecological cancers

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Expression of proliferation biomarkers in female reproductive system malignancies

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Proliferative potential is known to be the integral characteristic enabling impartial estimation of tumor processes peculiarities and their prognosis. The realization of proliferative signals is provided by a complex mechanism through the interaction of several oncogenes and tumor suppressor genes controlling cell cycle checkpoints and whose expression changes is a key event in cell malignant transformation.

Aim: To investigate the role of cooperative interactions between p53, p21WAF/CIP1 and p16INK4a in determination of proliferative activity in endometrial and ovarian tumors.

Materials and Methods: Operative material of 56 patients with endometrial adenocarcinoma (EC) and 41 patients with serous ovarian cancer (OC) aged 41–76 years. The