inhibits monocyte chemotactic protein-1 (MCP-1) in the human mast cell line HMC-1, decreasing its abiliy of monocyte recruitment, but the effects of EGCG directly on monocytes has not yet been explored. This work shows that EGCG decreases monocyte migration ability in response to MCP-1 and inhibits MCP-1 secretion and CCR2 expression, the specific receptor for MCP-1, using the human monocyte cell line THP-1. Moreover, EGCG has been described to inhibit the expression of some integrins. Our work demonstrates that EGCG decreases the levels of integrin beta1 activated, one of the primary integrins that can assembly monocytes to extracellular matrix under normal conditions, and THP-1 adhesion to fibronectin. We conclude that this study support the effects of EGCG as an anti-inflammatory compound.

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High excretion of etheno adducts in liver fluke-infected patients: protection by praziquantel against DNA damage

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Background: Chronic infection by liver fluke (Opisthorchis viverrini, OV), is a strong risk factor for developing cholangiocarcinoma (CCA). To clarify the involvement of oxidative stress and lipid peroxidation (LPO)–derived DNA damage, the excretion of LPO-derived etheno DNA adducts was measured in urine samples collected from healthy volunteers and OV-infected Thai subjects.

Materials and Methods: The study was performed in healthy volunteers (n=20, 9 males and 11 females) and OV-infected subjects (n=50, 26 males and 24 females). Urinary 1,N^6-etheno-2'-deoxyadenosine (εdA)- and 3,N^4-etheno-2'-deoxycytidine (εdC)-levels were quantified by immunoprecipitation-HPLC-fluorescence detection and ^{32}P-postlabeling thin-layer chromatography. Urinary malondialdehyde (MDA) was measured by the thiobarbituric acid-based method. Urinary nitrate/nitrite was measured by a simple Griess-based method. Plasma alkaline phosphatase (ALP) activity, a marker of hepatobiliary tract damage, was analyzed by a standard automated spectrophotometer using a commercial kit.

Results: Excreted etheno adduct levels were related to indicators of inflammatory conditions, MDA-, nitrate/nitrite-levels in urine and plasma ALP activity. Mean εdA- and εdC-levels were 3-4 times higher in urine of OV-infected patients; MDA, nitrate/nitrite and ALP were also increased up to 2-fold. MDA and ALP were positively related to εdA excretion. Two months after a single dose of the anti-parasitic drug praziquantel, εdA and εdC concentrations in urine of OV-infected subjects were decreased; MDA, nitrate/nitrite and ALP were concomitantly lowered.

Conclusions: We conclude: chronic OV-infection through oxidative/nitrative stress leads to massive urinary excretion of the etheno-bridged deoxy-ribonucleosides, reflecting high LPO-derived DNA damage in vivo. These promutagenic DNA etheno-adducts in bile duct epithelial cells may increase the risk of OV-infected patients to later develop CCA. Urinary εdA and εdC levels should be explored (i) as non-invasive risk markers for developing opisthorchiasis-related CCA and (ii) as promising biomarkers to assess the efficacy of preventive and therapeutic interventions.

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Tumor associated antigens identify a high risk benign disease group

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Benign breast diseases appear in more than half of all women after 20. Although a history of benign breast disease (BBD) indicates some increase in breast cancer, only a fraction develops malignant disease. The relationship between benign breast diseases and cancer development remains a subject of controversy. The aim of the present report is to detect associated tumor antigens in 80 tissue samples belonging to BBD. Samples were classified in three risk groups depending on proliferation: without or minimal proliferation: no risk benign disease (NRBD); increased proliferation: low risk (LRBD) and atypical epithelial hyperplasia: high risk (HRBD). An immunohistochemical study was performed employing the following antibodies: anti-MUC1 protein core (C595, HMFG2 and SM3 monoclonal antibodies, MAbs), anti-MUC1-cytoplasmic tail (MUC1-CT) polyclonal antibody (Ab) (CT33), anti-MUC4 Ab, anti-MUC2 MAb (PMH1) and anti-carbohydrate associated antigens MAbs: sialyl Lewis x (KM93), Lewis x (KM380), Lewis y (Lewis y) and Tn antigen. Statistical analysis: Frequencies Analysis and Multiple correlation including principal components analysis (PCA) were performed. Results: In NRBD: MUC1 was detected in 62,9% with C595, 27,4% with HMFG2 and 17,2% with SM3. In LRBD, the percentages were: 53,3%, 50% and 31,3%, respectively while in HRBD: 50%, 50% and 16,7%, respectively. MUC1-CT percentages were: 80%, 93,8% and 50%, respectively. Lewis x was the carbohydrate antigen more frequently found in the three groups while sialyl Lewis x were less found (0% in HRBD); on the contrary, Lewis y was more expressed in HRBD than in the other risk groups. MUC2 was also mainly detected in HRBD while MUC4 in LRBD. A statistical significant ($p<0.05$) correlation between anti-MUC1 protein core MAbs and anti MUC1-CT Ab was found ($r=0,7373$). PCA explained 86% of data variability (risk groups and tumor antigenic expression); PCA first two components grouped all HRBD patients while LRBD and NRBD remained spread. Conclusions: 1- HRBD express a determine pattern of tumor associated antigens employed in this study and 2- In BBD, anti-MUC1 CT was the more useful MAb to detect MUC1 showing a high correlation with anti-MUC1 protein core MAbs.

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The immunoproteome of pancreatic cancer

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The purpose of our study is to identify novel tumour antigens by characterising a panel of proteins related to pancreatic cancer. These antigens may be used as tools for early diagnosis, prognosis and some may be good targets for cancer vaccine development.

In developed countries, pancreatic cancer is the fifth leading cause of cancer death. This cancer form is difficult to diagnose even at more advanced stages of the disease with prognosis very poor due to limited treatments offered. Thus, tools for early diagnosis and prognosis as well as new therapeutic agents are essential. Patients diagnosed with pancreatic cancer develop antibody responses against pancreatic tumour related proteins, also called tumour antigens, during the course of the disease. We utilised this and conducted an autologous SEREX analysis involving phage display and automated high-throughput screening of a cDNA tumour library made from a pancreatic cancer patient.

We identified cDNAs encoding 11 different identities. The dominating cDNAs encoded insulin, a hypothetical protein and NADH dehydrogenase (ubiquinone) flavoprotein 1. Other identities were the chromosome 19 open reading frame 60, keratin 19, calcineurin binding protein 1, coiled-coil domain containing 85B, heterogeneous nuclear ribonucleoprotein, TIMP metallopeptidase inhibitor 1, interferon alpha-inducible protein 27 and ADP-ribosylation-like factor 6 interacting protein 4. Furthermore, we found that of 37 pancreatic cancer patients examined 33% had autoantibodies against insulin whereas the percentage was 16% for healthy donors.

The antigens identified from the pancreatic cancer patient reflect a well known relationship between pancreatic cancer and diabetes since some of the antigens are related to the cancer development such as interferon alpha-inducible protein 27 and TIMP metallopeptidase inhibitor 1 and some e.g. insulin are related to diabetes. Due to the broad expression of the majority of the identified antigens they may not be targets for immunotherapy but further evaluation of the antigens will determine their diagnostic value.

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Development of monoclonal antibodies for the identification of novel invasion associated targets in human cancer

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Monoclonal antibodies (MAb's) have emerged as an ever increasingly important tool in cancer therapy. They have yielded promising results when used alone or in combination with current therapies. The development of MAb's also allows for the discovery of novel cancer associated antigens. In this study, monoclonal antibodies were generated by immunising Balb/c mice with the invasive melanoma cell line MDA-MB-435S/F and an invasive variant of the MiaPaCa pancreatic cell line. Following fusion, all resultant hybridomas were screened against their respective target immunogens using newly developed screening systems based on live cell immunofluorescence and a 96 well based invasion assay (Boyden chamber) system. MAb 7B7 has been shown to inhibit invasion (up to 50% of control level), and motility (up to 70% of control level). MAb 9E1 inhibits invasion (up to 70% of control level), but not motility. A dose response inhibitory effect on invasion has also been observed with MAb 7B7.