

respectively. Conclusions: 1- By IHC, non statistical differences among breast cancer, benign and normal samples were found although a different pattern of expression was observed; 2- Immunoprecipitation and WB indicated that MUC1 may behave as a possible carrier for Ley in breast cancer and 3- IgM/LeyCIC showed a significant statistical difference between breast cancer and normal and benign samples.

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Poster

Prognostic significance of tumor-infiltrating cytotoxic T-cells in colorectal cancer

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Purpose: Various immune/inflammatory cells can be found in colorectal cancer (CRC) tissue. Its potential influence on the prognosis of CRC is controversial. We have previously demonstrated that there is no prognostic significance of regulatory T-cells (TREG, CD4+ CD25+ FOXP3+) in patients (pts) with CRC. In this study, we focused on cytotoxic tumor-infiltrating T cells (CD8+) located in the tumor epithelium which are generally considered to be prognostically favorable. Moreover, pre-operative total white cell count and individual counts of eosinophiles, neutrophils, lymphocytes were evaluated from peripheral blood as well. Methods: Formalin-fixed, paraffin embedded tumor samples from 55 pts with CRC in clinical stage I-IV according to IUCC were evaluated by immunohistochemistry using commercially available anti-CD8 mouse monoclonal antibody. Intraepithelial CD8+ cells were enumerated in one high power magnification field in the area with the highest CD8+ cell infiltration, so called "hot spots". Its prognostic effect was evaluated using Kaplan-Meier method. Results: We did not prove any statistical significance between absolute number of CD8+ cells in "hot spots" and examined clinicopathologic parameters (clinical stage, overall survival, disease-free survival, left/right localization of tumor, "T" status, adjuvant chemotherapy, total white cell count and individual counts of eosinophiles, neutrophils, lymphocytes with overall survival or disease-free survival). Only between the pre-operative absolute number of peripheral eosinophiles and better survival we observed positive correlation and trend to statistical significance. The median follow-up was 50 months. Conclusion: We did not prove that infiltration of intraepithelial CD8+ T-cells correlates with overall survival of colorectal cancer patients and we conclude there is no prognostic significance of intraepithelial CD8+ cells in CRC. Supported by IGA MZ CR NR/9076-4.

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Poster

Leukocyte reprogramming mimics HIF-1α knock out

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Solid tumours as well as sites of bacterial inflammation recruit leukocytes to severely hypoxic areas. One of the key regulators during hypoxia and inflammation is the transcription factor complex hypoxia inducible factor-1 (HIF-1). It has already been shown that LPS as well as inflammatory cytokines induce the regulatory subunit HIF-1α in a non hypoxic manner.

In this work, we studied the consequences of a pre-treatment with low doses of LPS (reprogramming) for both HIF-1α protein and mRNA levels in different monocytic cell lines and animal models. Furthermore, we characterised the reprogrammed cells with regard to their viability under hypoxic conditions, phagocytic activity, and invasion into extracellular matrix.

Reprogrammed monocytes show diminished levels of HIF-1α protein after hypoxic stimulation and a significantly decreased LPS-induced HIF-1α gene expression. The expression of both HIF-1 target genes ADM and GLUT-1 are significantly reduced. The viability of reprogrammed cells exposed to hypoxia gets diminished, too.

From these results we conclude that prolonged exposure of leukocytes to low doses of LPS reduces the accumulation of HIF-1α and effects the induction of HIF-1 target genes. Thus, reprogrammed monocytes may fail to function properly under hypoxic conditions.

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Poster

Salivary cytokines profile and smoking in patients with oral cancer

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Background Cytokines play an important role in the pathology associated with chronic inflammatory diseases. Their role in cancer development is yet still underestimated. Interleukin 6 (IL-6) is the most studied mediator of the host response to tissue injury, infection and bone resorption. We also investigated several others cytokines saliva levels in our paper. Smoking is a well-documented risk factor for oral cancer, although the mechanisms of its negative influence are not yet fully understood.

Aim The current results in patients with different stages oral malignant tumors may indicate different mediator functions of salivary cytokines in response to smoking, thus leading to a milder or a more aggressive cancer phenotype.

Methods The influence of smoking on the gingival crevicular fluid (GCF) content of the pro-inflammatory cytokines was investigated in patients with oral malignant tumors and healthy controls by use of XMAP Array technology (Luminex 200). TNM classification, histopathological data, as well as tumor localization and size were also recorded. Results The expression of salivary cytokines was higher in subjects with oral tumors. The correlation with smoking was also noted, based on the differences between the results from the two groups.

Conclusion It is possible that monitoring cytokine production or its profile may allow us to early diagnose an oral malignant tumor also taking into account the smoking habits.

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Poster

Preliminary results of a six months toxicity study in rats of the CIMAvax-EGF vaccine

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The CIMAvax-EGF vaccine consists of human recombinant EGF, coupled to a recombinant carrier protein, P64k from the meningitis B bacteria, and Montanide as adjuvant. The vaccine immunization induces the production of specific antibodies inhibiting the EGF/EGF-R interaction through EGF deprivation. The objective of the present study was to determine the toxicity of the CIMAvax-EGF vaccine obtained by ultra-filtration in Sprague Dawley rats after intramuscular administration of repeated doses (6 months). Rats were randomly distributed into four experimental groups: Control, Control plus adjuvant, Treated with the human total dose, and Treated with fifteen times the human total dose. The frequency of immunization was one weekly immunization for 9 weeks, plus 9 immunizations every 14 days. All rats were inspected daily for clinical signs. Body weight, food and water consumption, and rectal temperature were measured during the administration of test substances. Blood samples were collected for hematological and serum biochemical determinations at the beginning, three months later, and at the end of the study. Gross necropsy and histological examination of tissues was performed on all animals at the end of the assay. The study concluded with a survival of 95%, dying 4 animals of the Group Control + Adjuvant. The vaccine and the vehicle produced clinical signs of toxicity in the administration site, where macroscopic lesions was observed. The behaviour of the body weight gain and food and water consumption was normal for the used specie. There were not statistical differences of the behaviour of rectal temperature between groups. It could be preliminarily concluded that the intramuscular injection of CIMAvax-EGF vaccine produces only alterations limited to the administration site.

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Poster

Comparative study of the molecular profile of the inflammatory and non-inflammatory breast cancer in Tunisia

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Introduction: Breast cancer is the most common type of cancer affecting women in the western world and represents approximately 13 % to 30% of new diagnosed malignancies in women in North Africa. Inflammatory cancer (IBD) is a clinical form of breast cancer characterised by a peculiar geographic distribution in incidence, particularly common in Tunisia. The aim of this study was to compare expression of two genes RhoCguanosine triphosphate and WNT-1(induced secreted protein WISP3) in IBD and non IBD tumors. Predicated on the high rate of concordance of WISP3 and RhoC changes in IBD, it has been proposed that these two genes cooperate in the development of the disease.

Methods: Our investigation is based on 45 tumors from breast cancer patients aged between 23 and 52 years diagnosed at service of Salah Azaiez Institute in Tunis: 17 tumors from patients with IBD and 28 tumors

from non IBD patients. We studied expression of the Wisp3 and RhoC by RT-PCR and immunohistochemical tests.

Results: Considering both methods, we showed that the Wisp3 protein was decreased in about 80% of the cases of mammary carcinoma studied while RhoC is accumulated. Positive immunohistochemical test and high RhoC expression shown by RT-PCR analysis correlate with the high histological grade of the tumor corresponding to IBD.

Conclusion: Our work focused on determining the gene expression alterations that is associated with this aggressive breast cancer phenotype. RhoC functions as an oncogene, and WISP3 as a tumor suppressor gene. In IBD tumors we confirmed over expression of RhoC and loss of expression of WISP3