cases and studying them, we are likely to notice a link between new mutations, polymorphisms and clinical features.

P17 - Oncology - Tumor marker 1

P17-01

New strategies to improve the quality and efficiency of health assistance to chronic cancer patients

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Background: Integral care to the cancer patient, has a relevant social impact while it requires a multidisciplinary vision of the different areas of medicine to the patient care. Patients in oncological units are the most common class of potentially difficult draws because they are subject to more frequent laboratory testing. It is necessary to evaluate how care is applied to cancer patients and to develop strategies for improvement oncological care process. The aim of the present work was to evaluate of the health care process of the cancer patient and to improve strategies aimed at incorporating the patients' prospects to the care provision measures.

Materials and methods: Development of two care models: 1º: High Resolution Model (MCAR) that include analytical process and the administration of the therapy at the hospital in the same morning; and 2º: Accessibility Analytics Patient Model (MAAP) improve the accessibility to the patients at the analytical tests, making possible the access to different flebotomy services points.

Results: The percentage of cancer patients who are in treatment has undergone a biannual 8.76% increase. MCAR are used by 58% oncology patients. In relation to MAAP model there was an increase in the use of this model up to 42% in the two years of its implementation.

Conclusion: The optimized and preferred care circuits implementation, in both models have proven to be safe, effective, improving the accessibility of patients to diagnostic testing.

P17-02

Usefulness of inflammatory markers in assessing the severity of colorectal cancer

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Background: Severe abdominal surgeries, including colorectal cancer (CRC) surgery lead to systemic inflammatory response, which is followed by the increase of inflammatory markers. Intensity of inflammatory response follows the severity of surgical injury and influences postoperative recovery. Considering that the duration of the surgery, as well as the time that the colon has been open during the surgery (open colon time, OCT) define the severity of CRC surgery, and consequently influence the postoperative recovery, we wanted to investigate if the inflammatory markers correlate with those two factors and thus provide useful information.

Materials and methods: The study included 20 patients who underwent CRC surgery. Duration of the surgery, and OCT were measured for the duration of the procedure. C-reactive protein (CRP), interleukine-6 (IL-6), ferritin and soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) were measured 24 hours after the surgery. CRP and ferritin were measured using immunoturbidimetric method (Beckman-Coulter, Tokyo, Japan), IL-6 and sTREM-1 using ELISA method (Quantikine, R&D Systems, Minneapolis, USA; IQ products BV, Groningen, The Netherlands).

Results: Statistical analysis showed no correlation between tested markers and the duration of the surgery. We found strong correlation for IL-6 ($r = 0.8147$, $P < 0.001$) with OCT. No correlation between CRP, ferritin and sTREM-1 and the OCT was found.

Conclusions: Our results showed that CRP, ferritin and sTREM-1 do not point to the injury and recovery after CRC surgery. We found strong positive correlation of IL-6 with the OCT during the surgery, so the rise of IL-6 could provide useful information in following CRC surgery severity and postoperative recovery.

P17-03

The phosphorescence as a predictive basis of early diagnosis of oncopathology

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Serum proteins phosphorescence state was studied and evaluated in 59 patients with stomach adenocarcinoma, aged from 35 to 68 years. Diagnosis was confirmed by clinical and histomorphological methods. Among patients with gastroadenocarcinoma phosphorescence was studied in 33 men and 26 women. I, II, III and IV stages of disease were detected in 8, 7, 9 and 9 men and 6, 7, 7, and 6 women, accordingly. The study of luminol-dependent serum films phosphorescence in patients with adenocarcinoma of the stomach revealed increasing in men at 94.5%, 41.9%; 44.5%, 73.95%, 286.8% and 217.9% at such activation spectral lines as 297, 313; 334, 365, 404 and 434 nm. In women, the intensity of phosphorescence in similar lines of activation with monochromatic light of 297, 313, 334, 365, 404 and 434 nm, rised up to 93.2%, 33.7%, 29.6%, 67.4%, 286.7% and 216.7%. The mostly significant indexes of phosphorescence were detected at activation with monochromatic light of 297 nm, 404 nm and 434 nm. Serum phosphorescence intensity in patients at activation with monochromatic light of 297 nm wavelength rised up by 1.94 and 1.93 times accordingly in men and women in comparison with a group of conditionally healthy people. At activation with wavelength of 404 nm serum phosphorescence in patients increased by 3.7 and 3.6 times, at 434 nm by 3.2 and 3.1 times in comparison with a group of conditionally healthy people.

P17-04

Study of cytokines, as potential biomarkers in the diagnosis of oral squamous cell cancer

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Introduction: Oral cancer is one of the prevalent cancers of the body and is one of the 10 most common causes of death. Oral squamous cell carcinoma (OSCC) accounts for over 90% of these tumors. The aim of this study was designed to detect biochemical markers in serum and saliva of oral squamous cell carcinoma patients and to evaluate their validity in monitoring and diagnosis.

Materials and methods: The level of certain pro-inflammatory cytokines in the serum and saliva of (30) patients with OSCC and (20) healthy individuals as control group was measured. Levels of pro-inflammatory cytokines Interleukin 1" (IL-1"), Interleukin (IL-6), Interleukin (IL-8) and Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) was detected by enzyme linked immunosorbent assay (ELISA).

Results: Serum IL-6 and IL-8 level was detected at higher concentrations in patients with OSCC than the control group ($P < 0.001$). No significant differences in serum IL-1 alpha and GM-CSF of patients with OSCC as compared with control group.The levels of IL-1 alpha, IL-6, IL-8 and GM-CSF in saliva

showed significant increase in patients with OSCC when compared with control group.

Conclusion: Salivary IL-1 alpha and GM-CSF was useful in the diagnosis of OSCC patients. Serum IL-6 was useful in the diagnosis of OSCC patients than salivary IL-6. Serum and salivary IL-8 were very useful in the diagnosis of OSCC patients and separating between OSCC patients and control group. From the results of the presents study, it can be concluded that cytokines are important in proinflammatory and proangiogenic responses and are detectable in serum and saliva of patients with OSCC. These cytokines increase the pathogenicity of OSCC and prove useful as biomarkers for diagnosis.

P17-05

Germline polymorphisms in LRIG1 gene predict clinical outcome in metastatic colorectal cancer

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Background: Leucine-rich and immunoglobulin-like domains (LRIG) 1, 2, and 3 are integral membrane proteins. LRIG1 negatively regulates EGF signaling and increasing evidence indicates that LRIG1 is a tumor suppressor in certain cancer types. Lrig1 is expressed at low levels in several cancer types but is overexpressed in some colorectal tumors. We postulate that polymorphisms in the *LRIG1* gene could influence the EGFR signalling pathway and be related with the clinical outcome in metastatic colorectal cancer (mCRC).

Materials and methods: We studied 126 Spanish mCRC treated with a first-line oxaliplatin/5-fluorouracil regimen. Polymorphisms in the LRIG gene were selected using public literature resources and databases (NCBI, PubMed, db SNP, Ensembl and GeneCards Version 3). Two non-synonymous (c3158A>C and c1843A>G) and two synonymous (c2221T>C and c1317C>T) common and putatively functional polymorphisms were selected. These germline polymorphisms were analyzed using a Fluidigm equipment in DNA samples extracted from peripheral blood. Overall survival (OS) was evaluated according to each genotype.

Results and conclusions: There were significant associations between *LRIG1* c1317C>T and c3158A>C polymorphisms and clinical outcome. The analysis of the c1317C>T polymorphism revealed that OS was lower for patients harboring a T/T genotype than for patients with the C/C or C/T genotypes (P = 0.01). In the case of the c3158A>C polymorphism, patients harboring a C/C genotype had a lower OS than patients with a A/A or A/C genotypes (P = 0.047). We identified germline variants in LRIG1 gene predicting clinical outcome in patients with mCRC receiving first-line oxaliplatin/5-fluorouracil chemotherapy.

P17-06

Proantocyanidins in cytoprotection of antitumor drugs-treated cells

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Introduction: Antitumor drugs Doxorubicin (DOX) and Mitomycin C (MMC) are broadly used antitumor drugs, but their clinical use is significantly limited due to their systemic toxicity. The main cause of their toxic effects is the oxidative stress as a consequence of ROS (reactive oxygen species) gener-

ation during the DOX and MMC metabolism. The main aim of our study was to investigate the efficacy of different antioxidative agents in oxidative stress prevention and protection from DOX and MMC effects, in normal (CHO – Chinese hamster ovary) and malignant cells (K562 – human erythroleukemia cells).

Materials and methods: The antioxidative agents used in our study were the glutathione precursor N-acetylcystein (NAC) and proantocyanidins (PAC), natural antioxidative compounds derived from the plant polyphenols. According to the aim of this study, the parameters of oxidant status, activity of antioxidant enzymes glutathione-S-transferase and glutathione reductase were tested in human erythroleukemia (K562) and Chinese hamster ovary (CHO) cells lines. Both cell lines were pretreated with potentially protective agents (NAC and PAC) 30 minutes before DOX and MMC, as prooxidant agents. Cell supernatants were prepared after 24 hours and GST and GR were determined, as parameters of oxidant status.

Results and conclusions: Results of our study suggest that proantocyanidins and N-acetylcysteine exert the antioxidative activity and therefore also the potentially protective activity to the effects of DOX and MMC. Comparative analysis of activities of antioxidant enzymes GST and GR in healthy (CHO) and malignant (K562) cells lines shows that none of those antioxidant agents expresses selective activity to non-malignant, CHO cells.

P17-07

YKL-40, IL-1β and TNF-α in malignant glioma

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Background: Glioblastoma multiforme (GBM) is the most aggressive brain tumour. YKL-40 is a glycoprotein that has been associated with glioma grade and a poorer clinical outcome. The aim of the investigation was to analyze tissue and serum YKL-40 levels in glial tumours in comparison with pro-inflammatory cytokines.

Materials and methods: Serum YKL-40, IL-1β and TNF-α levels were measured in 7 patients with GBM, 14 patients with lower-grade glioma (grades II and III) and 40 healthy controls, by ELISA method. An immunohistochemical analysis of YKL-expression was performed.

Results and conclusions: Feeble reactivity was determined in single glial cells in the normal brain. In astrocytoma the glycoprotein was present in numerous malignant cells. The most intensive reactivity was detected in GBM. Our study revealed a significant difference in YKL-40 serum concentrations between healthy subjects and lower-grade glioma, as well as between astrocytoma and GBM. The level of the glycoprotein in tumors was twofold higher than in controls ($P < 0.01$). We found an association between serum YKL-40 values and tissue YKL-40 expression. Enhanced IL-1β concentrations in glioma patients were detected. The secretion of TNF-α showed a similar pattern, but the increase towards the controls was lower compared to IL-1β. In conclusion, YKL-40 correlates positively with pathological tumor grades and might serve as a novel biomarker in malignant glioma. We revealed IL-1β and TNF-α – dependent (Th1) immune response in these malignant tumors.

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P17-08

Tumour markers in fluid analysis in the differential diagnosis of cystic lesions of the pancreas

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Pancreatic cystic lesions include the most common pseudocysts and a variety of cystic tumours with different biologic and pathologic characteristics. With the increasing technological tools at our disposal, cystic neoplasm became more visible. Preoperative differential diagnosis of cystic lesions of the pancreas may be difficult because decision making through reliable clinical and, or imageological criteria is uncertain. In the last decade, the cystic fluid analysis using a panel of tumours markers and in some studies, serum pancreatic enzymes like amylase and lipase, combined with endoscopic ultrasonography fine needle aspiration, became an important tool in the pancreatic lesions workup and even in follow up. The authors propose to make the evaluation of the assay of tumour markers, CEA, CA 19.9, CA 125 in net drainage of cystic lesions and their application in the differential diagnosis of cystic pancreatic lesions. Drainage fluids were obtained in 195 patients with pancreatic cysts for a period of 6 years (2006 to 2012) with variable histological diagnoses: pseudocysts, mucinous cystic carcinomas, ductal carcinomas and cystadenomas. The aims of this study are to establish the cut off levels for our laboratory in the light of the study population as well as verify the correlation between the determinations of these biological markers and severity of histological lesions.

P17-09

Multiplex biochip arrays allow simultaneous assessment of serum markers for colon cancer screening

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Background: Colorectal cancer is the third most commonly diagnosed cancer in males and the second in females. Despite the implementation of screening programs such as colonoscopy, approximately 50% of patients are diagnosed at advanced tumor stages resulting in poor prognosis. Innovative, patient-friendly screening tools could aid in the early detection and allow curative treatment interventions.

Materials and methods: A nine target multiplex protein biochip was generated based on a thorough literature review. Diagnostic performance was evaluated using a training- and validation-set of a highly standardized, liquid nitrogen preserved serum collection of 317 samples comprising controls, adenomas, and colon cancers.

Results: Serum levels of CEA, IL-8, VEGF, S100A11, C3adesArg, CD26, MCSF and CRP showed significant differences between colon cancer cases and controls ($P < 0.05$). The largest areas under the receiver operating characteristics curve were observed for CEA(0.69), IL-8(0.68), and CRP(0.64). At threshold levels yielding specificities of 90%, the sensitivities for CEA, IL-8 and CRP were 26%, 22%, and 17%, respectively. Testing all possible combinations of these markers at the predefined threshold levels, CEA + IL-8 reached a sensitivity of 37%

at 83% specificity and CEA + CRP obtained a sensitivity of 35% at 81% specificity for detecting colon carcinomas.

Conclusions: Multiplex biochip array technology offers an innovative and patient-friendly approach to colorectal cancer screening. The diagnostic value of identifying further serum biomarkers and the potential advantage of combining biochip analysis with fecal occult blood has the potential to improve the performance of colorectal cancer screening and warrants further investigation.

P17-10

Identification of novel cancer biomarkers using the Randox-QuantiPlasm69 monoclonal antibody chip

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Background: Recently a novel monoclonal antibody based protein chip – QuantiPlasm69 (QP69) – has been introduced by Randox Laboratories. This system uses 69 monoclonal antibodies (mAbs) – developed by BioSystems International – that are immobilized on 9x9 mm ceramic chips. The QP69 assay can recognize concentration changes of several human plasma proteins simultaneously and in this way can identify novel plasma markers in a wide variety of diseases.

Materials and methods: Plasma samples and clinical data of 150-150 patients with prostate and lung cancer and 300 healthy controls were collected. Individual and pooled samples of the patients and controls were evaluated by the QP69 system. The plasma pools were created from the individual samples based on clinical, histopathological and laboratory data. Other biochemical parameters and the classical tumormarkers were also measured. To find the most predictive parameters principal component, binary logistic regression and ROC analysis was performed beside the classical statistics.

Results: A set of mAbs (three antibodies) present on the QP69 chip were able to discriminate between healthy controls and lung cancer patients, and a different set of mAbs (three antibodies) were able to distinguish samples of healthy controls from those of prostate cancer patients. These differences were independent of age and smoking habits. Combination of these antibodies in themselves or with classical tumormarkers could further improve their efficacy.

Conclusions: The QP69 kit can be an effective tool in biomarkers' search and discovery. This work was supported by the National Office for Research and Technology of Hungary (TECH-09-A1-2009-0113; mAB-CHIC).

P18 - Oncology - Tumor marker 2

P18-01

Evaluation of tumor marker HE4 assay on the Elecsys 2010 analyzer

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Background: Whey-acidic protein human epididymis protein4 (HE4), a new promising biomarker for epithelial ovarian cancer (EOC). The measured HE4 value of patients sample can depending on the testing procedure use.

Methods: We evaluated a HE4 method on Elecsys 2010 analyzer. The method for quantitative determination of HE4 is direct, competitive electrochemiluminescence immunoassay. For quality control we use Elecsys PreciControl HE4 1 and 2. HE 4 was measure on sera obtained from 96 women (40 healthy and 56 with epithelial ovarian cancer).