of resting energy expenditure (REE), increase of total daily physical activity, decrease of IL-6 and TNF-alpha and improvement of fatigue.
Methods: All patients were given as basic treatment: polyphenols + antioxidant agents alpha lipoic acid, carbocysteine, Vitamins E, A and C, all orally. Patients were then randomised to one of the following 5 arms: (1) Medroxyprogesterone Acetate (MPA)/Megestrole Acetate (MA); (2) Pharmaco-nutritional support containing 2 g EPA; (3) L-carnitine; (4) Thalidomide; (5) MPA/MA + Pharmaco-nutritional support + L-carnitine + Thalidomide. Treatment duration 4 months. The sample size was 475 patients. At May 2007, 160 patients, well balanced for all clinical characteristics, have been included. Body composition has been assessed by dual energy X-ray absorptiometry (DEXA) since January 2007.
Results: No severe side effects were observed. As for efficacy, an interim analysis on 145 patients showed an improvement of at least 1 primary endpoint in arm 3 (significant decrease of REE and fatigue), 4 (significant decrease of IL-6) and 5 (significant decrease of REE and fatigue), whilst arm 2 showed a significant worsening of LBM, REE and MFSI-SF. The t-test for changes demonstrated the worsening of LBM, REE and MFSI-SF in arm 2 versus arms 3, 4 and 5 and therefore it was withdrawn from the study. Arms 1, 3, 4 and 5 showed no statistical significant difference.
Conclusions: The interim results obtained so far seem to suggest that the most effective treatment for CACS/OS should be a combination regimen and L-carnitine alone. The study is still in progress up to completion of final accrual of 400 patients (sample size reduced because of withdrawal of arm 2 from the study).
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Study of ATP7B copper transporter mRNA levels as a prognostic factor in advanced colorectal cancer patients treated with 5-fluorouracil plus oxaliplatin

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Background: It has been demonstrated a correlation between ATP7B protein and/or mRNA levels and response to treatment in ovarian cancer patients treated with cisplatin based chemotherapy. The aim of our work was to determine ATP7B mRNA expression levels in colorectal cancer (CRC) tumor tissue of patients treated with oxaliplatin (OXA) and 5-fluorouracil (5FU) according Spanish TTD group schedule and to correlate with response to treatment.
Methods: mRNA levels were analyzed by using Real Time PCR (RT-QPCR). The housekeeping gene used was â-actin and as a reference sample we used commercial human mRNA from liver. Chi-square and Fisher test were used in order to value differences in response rate to treatment. Time to progression (TTP) was studied by using Kaplan Meyer curves and Log rank test.
Results: Fifty-three advanced CRC patients treated with 5FU plus OXA were analyzed. 62.15% of them were males; primary tumour was localized in colon in a 66.7% of cases. We did not observe any progression to treatment in the group of patients that had ATP7B expression levels under percentile 25 (group 1). In contrast, patients with expression levels upper (group 2) showed 13.2% of progressions. Group 1 patients also had a greater number of complete responses than group 2 (33.3% vs 15.8%). TTP median was 14.66 and 7.18 months for group 1 and 2 patients respectively (Log rank p = 0.035).
Conclusions: According our results, lower expression of ATP7B in tumor tissue of CRC patients treated with 5FU plus OXA correlates with a greater response rate and a better TTP. However, these results should be confirmed in a higher number of patients.

P12

SELDI-TOF MS serum protein profiling predicts poor prognosis renal cancer patients

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Background: Approximately 30% of patients with renal cancer (RCC) present with metastasized disease and only 15−25% of patients respond to anti-tumor treatment. Although treatment outcome is improving due to the development of various targeted therapies, adequate selection of patients for these treatment approaches is important. Profiling of proteins in body fluids to predict patient outcome would be an attractive and non-invasive approach for utilization in the clinic. Surface-enhanced laser desorption/ionization-time of flight mass spectrometry (SELDI-TOF MS) was used to identify protein signatures in the serum proteome of RCC patients that discriminate between patients with poor or good outcome.
Methods: In this pilot study we analyzed protein profiles in the serum of 57 renal cancer patients (2% stage I, 12% stage II, 7% stage III and 79% stage IV patients according to the American Joint Committee on Cancer) and 59 healthy controls. Denatured serum samples were incubated on CM10 ProteinChip arrays and analyzed using the PBS-IIC ProteinChip Reader. Clinical data was collected and the extended Memorial Sloan-Kettering Prognostic Factors Model for survival was calculated. Ratios discriminating between RCC cases and controls were selected to generate a predictive multi-protein model. Univariate and multivariate Cox Proportional Hazard analyses were performed. Protein masses included in the predictive model were identified.
Results: In RCC serum samples we identified ion masses predictive for patient survival, and built a protein-model consisting of five signature peaks with m/z ratios of 2944, 3331, 6457, 6654, and 9201 Da, that could correctly identify poor prognosis patients with sensitivity and specificity of 80% and 76% for 1-year survival. Cumulative 1-year survival was 93% for low-risk patients, compared to 48% for high-risk patients (P = 0.0001, Log-rank test). Multivariate analysis indicated that our model was an independent predictor of survival when compared to the Memorial Sloan-Kettering Prognostic Factors Model. The tentative protein identities were apolipoprotein C-I (doubly and singly charged, and a singly charged fragment), a haptoglobin-alfa1 fragment and a yet unidentified 2.9 kDa protein fragment.
Conclusions: SELDI-TOF MS can be used to assess the prognosis of RCC patients independent of present prognostic factor models.

P23

Novel computational paradigms in breast cancer familiarity profiling

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Background: Genomic DNA copy number aberrations are frequent in solid tumours although their underlying causes of chromosomal instability in tumours remain obscure. The aim of our work was to individualize a genomic profile characterizing familial breast cancer.
Methods: For this purpose, a series of 124 consecutive breast cancer patients analyzed for aCGH entered the study. The results have been elaborated by an Artificial Immune System paradigm that we hypothesized could be successfully employed in the elucidation of biological dynamics of cancerous processes using a novel fuzzy rule induction system for data mining (IFRAIS) of aCGH data.
The most important characteristic of IFRAIS is that it discovers fuzzy classification rules, naturally comprehensible. It is obvious, of course, that comprehensible knowledge is essential in real-world data mining problems (e.g. in bioinformatics). The accuracy of results are expressed in terms of medians of the extracted values. The selected strategy for training and validation was the KFold cross-validation with K = 5. The global level of accuracy reached by the system nears the 97%; a quite competitive result indeed, even if we consider that algorithms like J48 (C4.5 evolution) is not able to go beyond the 94.34% of accuracy.
Results: We evidenced 3 rules to define familial and 5 rules to define sporadic breast cancer. In particular, rule 1 for familial cases involved genes linked to neurodegenerative pathway and comprised genes involved in important step of cell cycle, including apoptosis and signalling transduction in processes activating NFKB (locus 20p13, locus 11q22.3), or with growth factor activity (locus Xq26.2). Rule 2 of sporadic cases included genes involved in cell metabolism and differentiation (TGIF, CYP2R1, PUM1), while rule 4 involved genes of apoptosis pathway and a gene encoding a protein highly conserved among species, SCOC, probably involved in regulation of important cell cycle processes.
Conclusions: In this work we present the study of a novel rule induction system. We can conclude that novel biologically-inspired data mining techniques seem to be competitive interesting tools in cancer research. However, the full understating of the underlying dynamics in cancer settlement and progression still remains a primary objective.

P82

18F-fluorothymidine(FLT)-PET as a biomarker of the antineoplastic effects of radiation therapy combined to the anti-angiogenic agent Enzastaurin in lung cancer model

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Background: Positron emission tomography (PET) with 15F-fluorodeoxy-glucose is an established tool in diagnosis, staging, and surveillance of cancer. A limitation of this imaging modality, however, is its nonspecificity