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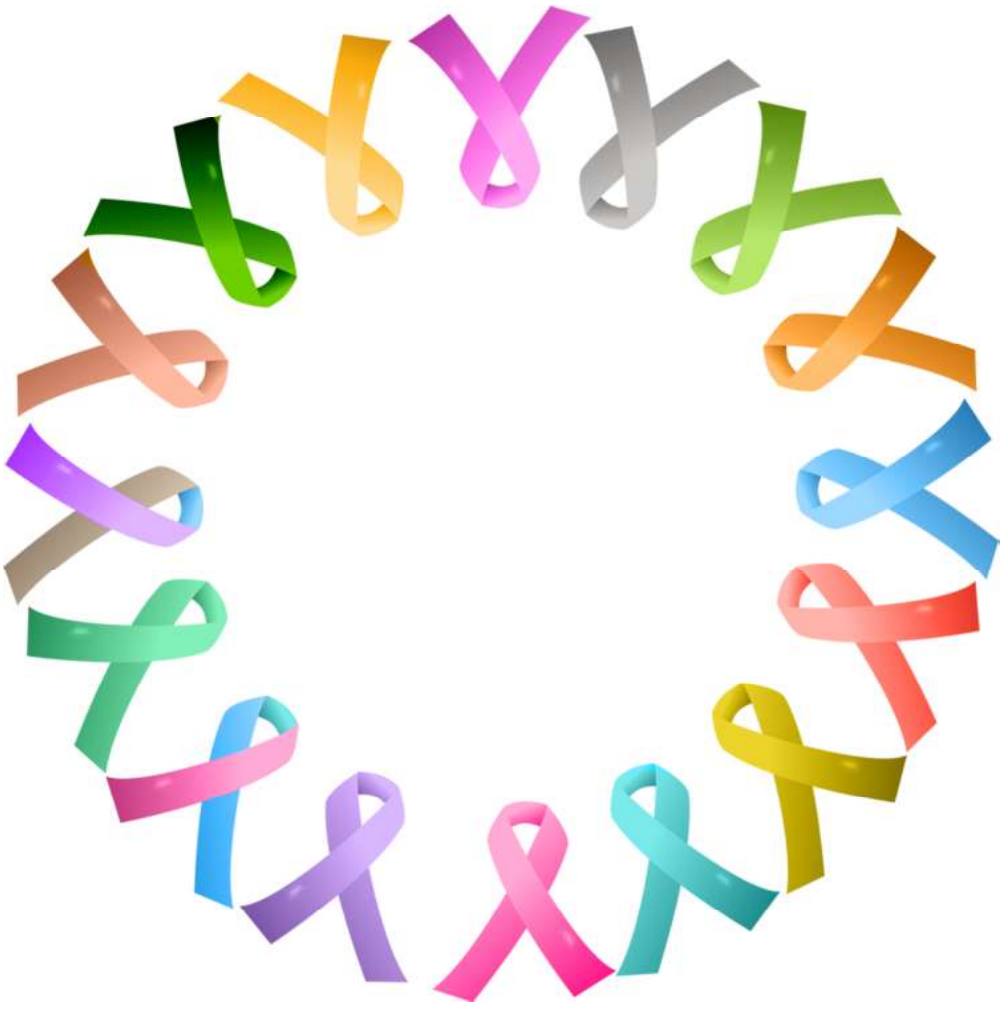

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gradual doxorubicin treatment were used. The functional properties were analyzed by studying the MAPK pathway, Dynamic Mass Redistribution (DMR) and the production of cAMP. Statistical significance was set at $p<0.05$. **Results:** No significant differences in expression of A2AR and D2R were detected between TC and AC at the genetic level. At the protein level, AC had statistically significant higher expression of A2AR than TC ($p= 0.0458$). No A2AR-D2R heteromers were detected in TC samples, while 80% of AC samples showed heteromerization. The existence of the A2AR-D2R heteromers was confirmed in both large cell NET cell lines, with 80% and 85% of cells containing heteromers, and a ratio of 13 and 16 heteromers per heteromer-containing cell, respectively. Co-stimulation with both agonists did not produce an additive effect (negative cross-talk). Antagonist binding to one of the receptors blocked signaling of the other receptor (bidirectional cross-antagonism) in both cell lines (MAPK and DMR results). By studying cAMP production, negative cross-talk was detected in both cell lines and cross-antagonism only in NCI-H460. **Conclusions:** Functional differences were observed in the expression and heteromerization of A2AR and D2R between typical and atypical neuroendocrine lung tumors and the sensitive and resistant neuroendocrine large cell tumor cells. This data will be validated in a prospective cohort of lung cancer patients.

Keywords: Adenosine, dopamine, GPCR, heteromerization, lung cancer, neuroendocrine tumors

P09

Detection of viral proteins in locally advanced rectal cancer patient samples by mass spectrometry – predictive potential for response to neoadjuvant chemoradiotherapy

Aleksandra Stanojević[1], Martina Samiotaki,[2] Vasiliki Lygirou[3], Mladen Marinković[4], Vladimir Nikolić[5], Suzana Stojanović-Rundić[4,6], Radmila Janković[1], Ana Banko[7], Danijela Miljanović[7], Antonia Vlahou[3], George Panayotou[2], Remond J.A. Fijneman[8], Sergi Castellvi-Bel[9], Jerome Zoidakis[3,10], Milena Čavić[1]

[1]*Department of Experimental Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*
[2]*Institute for Bioinnovation, Biomedical Sciences Research Center "Alexander Fleming", Vari, Attica, Greece*
[3]*Department of Biotechnology, Biomedical Research Foundation, Academy of Athens, Athens, Greece*
[4]*Clinic for Radiation Oncology and Diagnostics, Department of Radiation Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*
[5]*Clinic for Medical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia*
[6]*Faculty of Medicine, University of Belgrade, Serbia*
[7]*Institute of Microbiology and Immunology, Faculty of Medicine, University of Belgrade, Serbia*
[8]*Department of Pathology, The Netherlands Cancer Institute, Amsterdam, the Netherlands*
[9]*Gastroenterology Department, FundacióClínic per la RecercaBiomèdica-Institutd'InvestigacionsBiomèdiques August Pi iSunyer, Centro de InvestigaciónBiomédicaen Red de EnfermedadesHepáticas y Digestivas, Hospital Clínic, University of Barcelona, Barcelona, Spain*
[10]*Department of Biology, National and Kapodistrian University of Athens, Greece*

Background: Phenotypic profile of patients with locally advanced rectal cancer (LARC) is still unexplored and represents a field of great potential. Standard treatment for LARC involves neoadjuvant chemoradiotherapy (nCRT) followed by total mesorectal excision. Response to therapy varies and there is an unmet clinical need for new predictive markers. The aim of this study was to detect viral proteins in locally advanced rectal cancer patient biopsies by mass spectrometry and to examine their predictive potential for response to nCRT. **Materials and methods:** Data-independent acquisition mass spectrometry (DIA-MS) was performed on a carefully selected LARC patient cohort treated with nCRT. Patients were assessed for tumor response in week 8 post-nCRT (pelvic MRI scan and rigid proctoscopy). No immediate surgery was suggested for patients with clinical complete response (cCR) and initially distant-located tumors ("watch and wait" approach). Response after surgery was assessed using histopathological tumor regression grading(TRG) categories from postoperative specimens using the Mandard scale. Responders(R) were defined as patients with cCR without operative treatment and TRG 1/2. Non-responders(NR) were patients classified as TRG 3-5. Twenty patient samples with the most distinctly different responses to therapy were chosen for comparison – 11 NR and 9 R. DIA-NN was used for the deconvolution of the mass spectra and the Perseus software was used for the statistical analysis of data. **Results:** In total 12 non-human proteins were identified in 20 rectal cancer FFPE samples. After initial processing 7 proteins originating from viral particles were detected, including proteins encoded by the following genes: L4 from Human adenovirus 2,5 and 12, U17/U16 from Human herpesvirus 6A, U44 from Human herpesvirus 7, UL26 from Human herpesvirus 1, UL47 and UL82 from Human cytomegalovirus and L1 from HPV28, HPV30 and HPV53. Differential expression analysis suggested that protein encoded by L4 gene was differentially over-expressed in R/NR ($p= 0.046$). **Conclusion:** Locally advanced rectal cancer (LARC) patient samples contain proteins derived from viral genomes. The detection of these viral proteins suggests the significance of infections in the development of rectal cancer and its response to therapy.

Many of these viruses have been associated with the development of other types of cancer, indicating a promising avenue for further validation and research in this area.

Keywords: data-independent acquisition mass spectrometry, neoadjuvant chemoradiotherapy, proteomics, rectal cancer, viral infection, viral proteins

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P10

Prognostic value of combined hematological/biochemical indexes and tumor clinicopathologic features in colorectal cancer patients — a pilot single center study

Vladica Ćuk[1,2], Aleksandar Karamarković[1,2], Jovan Juloski[1,2], Radosav Radulović[1], Ljiljana Milić[1,2], Bojan Kovačević[1,3], Silvio De Luka[4] and Jelena Grahovac[5]

[1]Zvezdara University Clinical Center, "Nikola Spasi´c" Surgical Clinic, Faculty of Medicine, University of Belgrade, DimitrijaTucovica 161, 11000 Belgrade, Serbia

[2]Faculty of Medicine, University of Belgrade, Dr Subotica 1, 11000 Belgrade, Serbia

[3]Faculty of Dental Medicine, University of Belgrade, Dr Subotica 1, 11000 Belgrade, Serbia

[4]Department of Pathological Physiology, Faculty of Medicine, University of Belgrade, Dr Subotica 1, 11000 Belgrade, Serbia

[5]Department of Experimental Oncology, Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Serbia

Background: Colorectal cancer (CRC) is a significant public health problem. There is increasing evidence that the host's immune response and nutritional status play a role in the development and progression of cancer. The aim of our study was to examine the prognostic value of clinical markers/indexes of inflammation, nutritional and pathohistological status in relation to overall survival and disease free survival in CRC. **Patients and Methods:** The total number of CRC patients included in the study was 111 and they underwent laboratory analyses within a week before surgery. Detailed pathohistological analysis and laboratory parameters were part of the standard hospital pre-operative procedure. Medical data were collected from archived hospital data. Data on the exact date of death were obtained by inspecting the death registers for the territory of the Republic of Serbia. All parameters were analyzed in relation to the overall survival and survival period without disease relapse. **Results:** The follow-up median was 42 (24–48) months. The patients with the III, IV and V degrees of the Clavien–Dindo classification had 2.609 (HR: 2.609; 95% CI: 1.437–4.737; p = 0.002) times higher risk of death. The modified Glasgow prognostic score (mGPS) 2 and higher lymph node ratio carried a 2.188 (HR: 2.188; 95% CI: 1.413–3.387; p < 0.001) and 6.862 (HR: 6.862; 95% CI: 1.635–28.808; p = 0.009) times higher risk of death in the postoperative period, respectively; the risk was 3.089 times higher (HR: 3.089; 95% CI: 1.447–6.593; p = 0.004) in patients with verified tumor deposits. The patients with stage III/IV and tumor deposits tumor deposits had 1.888 (HR: 1.888; 95% CI: 1024–3481; p = 0.042) and 3.049 (HR: 3.049; 95% CI: 1.206–7.706; p = 0.018) times higher risk of disease recurrence, respectively. The emphasized peritumoral lymphocyte response reduced the risk of recurrence by 61% (HR: 0.391; 95% CI: 0.196–0.780; p = 0.005). **Conclusions:** Our study presents evidence that standard laboratory parameters, which do not present any additional cost for the health system, may provide additional information on the CRC patient outcome and lay the groundwork for a larger prospective examination. In our patient cohort, Clavien–Dindo classification of postoperative complications, modified Glasgow prognostic score, lymph node ratio, tumor deposits and peritumoral lymphocyte response were factors that were significantly associated with survival of operated patients.

Keywords: biochemical indexes, colorectal cancer, prognostic value, tumor clinicopathologic features