Virchows Archiv

European Journal of Pathology

Volume 481 · Supplement 1 · September 2022

Springer
428 • 481(S1) S1-S364 (2022)
ISSN: 0945-6317 (print)
ISSN: 1432-2307 (electronic)

European Society of Pathology

concentrations. The obtained results did not show a significant difference between C/P alone and C/P in combination with low doses of mitochondrial energy metabolism modulators. In contrast, at higher concentrations, UK-5099, DNP, and DCA potentiated the cytotoxicity of C/P. When combined with a high glucose concentration, lower concentrations of DNP and DCA potentiated the cytotoxic effect of C/P and at higher concentrations this effect was annulled.
Conclusion: The presented results showed that all three tested mitochondrial energy metabolism modulators, UK-5099, DNP and DCA, when used in higher concentrations, have a similar pattern of action; potentiating the cytotoxic effect of cisplatin and pemetrexed. This suggests a synergistic effect of antineoplastic agents and mitochondrial metabolism modulators on reducing mesothelioma cell proliferation. Mitochondrial metabolism modulators have potential for mesothelioma treatment. However, further studies are needed to examine their precise mechanisms of action.
Funding: These findings are a part of the research project Reprogramming cytoprotective pathways in malignant mesothelioma (IP-2014-09-4173), funded by the Croatian Science Foundation.

PS-15-016
The clinical significance of epigenetic and RNAPII variabilities occurring in clear cell renal cell carcinoma as a potential prognostic marker
N. Ördög, B.N. Borsos, H. Majoros, Z. Ujfaludi, L. Kuthi, G. Pankotai-Bodo, S. Bankó, F. Sükösd, T. Pankotai*
*University of Szeged, Faculty of Medicine, Institute of Pathology, Hungary

Background & objectives: Patients diagnosed with clear cell renal cell carcinoma (ccRCC) have poor prognosis. For this reason, the more detailed molecular characterisation of the primary tumour, and metastasis, are crucial to select the proper adjuvant therapy.
Methods: As a potential molecular biomarker, to follow the transcriptional kinetics in 30 ccRCC patients, we analysed γH2A.X, H3K4me3, and H3K9me3 and the alterations of RNAPII by immunohistochemical staining. The variabilities between the tumorous and non-tumorous parts of the tissue were detected using quantitative image analysis by monitoring 100 cells either the tumorous or the control part of the tissue sections.
Results: We detected a synergistic elevation both in H3K4me3 and RNAPII level which confirms the reliability of our data. The present study also establishes a strong correlation between H3K4me3 and RNAPII marks. We also found that the alteration in the global level of H3K9me3 corresponding with changes in the level of H3K4me3 and RNAPII was correlated with the presence of ccRCC. Finally, in ccRCC tumour-derived specimens, we observed increased γH2A.X level, which is the hallmark of persistence DNA damage. In correlation with the perpetual presence of γH2A.X, in ccRCC patients considerable number of DNA damage or insufficient DNA repair takes place.
Conclusion: Data obtained from the analyses were used to identify potential prognostic features and to associate them with the progression. These markers might have a value to predict patient outcomes based on their individual cellular background. These results also support that detection of any alteration in the level of H3K4me3, H3K9me3, and γH2A.X can account for valuable information for presuming the progression of ccRCC and the clinical benefits to select the most efficient personalised therapy.
Funding: This research was funded by the National Research, Development and Innovation Office grant GINOP-2.2.1-15-2017-00052 and NKFI-FK 132080. T.P. was funded by National Research, Development and Innovation Office grant GINOP-2.2.1-15-2017-00052, the János Bolyai Research Scholarship of the Hungarian Academy of Sciences BO/27/20, UNKP-20-5-SZTE-265, by NKFI-FK 132080, UNKP-21-5-SZTE-563 and EMBO short-term fellowship 8513. L.K. was funded by the University of Szeged, Faculty of Medicine Research Fund-Hetényi Géza Grant (Grant No. 5S 340 A202) and the New National Excellence Programme (Grant No. UNKP-21-4-SZTE-131).

PS-15-017
Long non-coding RNA H19 expression in rectal cancer and therapy response
K. Eric*, M. Miladinov, S. Dragicevic, J. Rosic, Z. Krivokapic, K. Zeljic
*Department of Patohistology, University Clinical Centar of Serbia, Belgrade, Serbia

Background & objectives: Long non coding RNA, H19 is an imprinted, maternally expressed gene, usually deregulated in different cancer types, including rectal cancer. This study aimed to investigate H19 role as a potential biomarker to predict therapy response in rectal cancer patients.
Methods: The study included 14 patients diagnosed with rectal cancer, treated with neoadjuvant chemoradio therapy (nCRT). RNA was isolated by TRIzol reagent from samples of rectal cancer tissue before and after nCRT. Relative expression of H19 was normalized to housekeeping GAPDH gene, and expression was analysed by quantitative real-time PCR. Relative expression of H19 was calculated by 2-ΔCt method.
Results: Relative expression of H19 was significantly increased in rectal cancer tissue after nCRT (0.244±0.408) compared to the tissue before nCRT (0.043±0.055), p=0.004, Wilcoxon test. According to tumour regression grade (TRG), 85.71% (12/14) of patients did not respond, while 14.28% (2/14) responded to preoperative CRT. Responders (TRG1, TRG2) and non-responders (TRG3, TRG4) did not differ in H19 expression in tumour tissue before (p=0.659, Mann-Whitney U test) as well as after nCRT (p=0.999, Mann-Whitney U test). Receiver operating curve analysis indicates that H19 expression in colorectal tissue before nCRT can not be used as a biomarker for distinguishing responders from non-responders (AUC=0.625, 95%CI=0.257-0.992, p=0.583).
Conclusion: Our study suggests H19 upregulation upon neoadjuvant chemoradiotherapy in rectal cancer. The potential predictive value of H19 as a biomarker of therapy response should be studied in a larger group of patients.

PS-15-019
BRG1-deficient non-small cell lung carcinomas. Clinicopathologic characteristics and correlation with SMARCA4 mutations
V. Pedrero Castillo*, V. Cristóbal Redondo, A. Francia García-Calvo, C. Alenda González, F.I. Aranda López
*HGU Dr. Balmis (Alicante), Spain

Background & objectives: SMARCA genes are responsible for chromatin remodelling. Inactivating mutations in SMARCA4 induce BRG1 deficiency and thus a set of malignancies, mostly undifferentiated carcinomas. To facilitate translation of preclinical findings into clinical studies, we assessed clinicopathological features of BRG1-deficient tumours.
Methods: Data sets from our department were reviewed to determine the prevalence of SMARCA4-mutant non-small cell lung carcinomas (NSCLC) and describe their clinicopathologic characteristics. Genetic alterations were identified