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GENITOURINÁRNE MALIGNITY

Timmerman DM, Gillis AJM, **Mego M**, Looijenga LHJ.

Comparative Analyses of Liquid-Biopsy MicroRNA371a-3p Isolation Protocols for Serum and Plasma

Cancers (Basel). 2021 Aug 24;13(17):4260.

MicroRNAs (miRNAs) are short, non-coding RNAs involved in translation regulation. Dysregulation has been identified in cancer cells. miRNAs can be secreted and detectable in body fluids; therefore, they are potential liquid-biopsy biomarkers. The miR-371a-3 cluster members are an example, monitoring the presence of malignant germ cell tumors based on patient serum/plasma analyses. However, a large variety of isolation techniques on sample types (serum vs. plasma) are reported, hampering interstudy comparisons. Therefore, we analyzed the impact of using the miRNeasy Serum/Plasma Kit (cell-free total RNA purification) Qiagen extraction kit and the TaqMan anti-miRNA bead-capture procedure of ThermoFisher for miRNA isolation. Ten normal male matched serum and plasma samples and seventeen testicular germ cell tumor patient serum samples were investigated. The Qiagen kit requires a higher input volume (200 µL vs. 50 µL), resulting in higher sensitivity. Serum and plasma comparison demonstrated high similarity in miRNA levels. Titration experiments showed that the bead-capture procedure is superior in cases of lower starting volumes (<100 µL). This study highlights the strengths and limitations of two different isolation protocols, relevant for in vivo analysis with small starting volumes. In summary, miRNA detection levels results varied little between plasma and serum, whereas for low volumes the bead capture isolation method is preferable.

Hadzega D, Minarik G, **Karaba M**, **Kalavska K**, **Benca J,** Ciernikova S, Sedlackova T, Nemcova P, **Bohac M, Pindak D**, Klucar L, **Mego M.**

Uncovering Microbial Composition in Human Breast Cancer Primary Tumour Tissue Using Transcriptomic RNA-seq

Int J Mol Sci. 2021 Aug 22;22(16):9058.

Recent research studies are showing breast tissues as a place where various species of microorganisms can thrive and cannot be considered sterile, as previously thought. We analysed the microbial composition of primary tumour tissue and normal breast tissue and found differences between them and between multiple breast cancer phenotypes. We sequenced the transcriptome of breast tumours and normal tissues (from cancer-free women) of 23 individuals from Slovakia and used bioinformatics tools to uncover differences in the microbial composition of tissues. To analyse our RNA-seq data (rRNA depleted), we used and tested Kraken2 and Metaphlan3 tools. Kraken2 has shown higher reliability for our data. Additionally, we analysed 91 samples obtained from SRA database, originated in China and submitted by Sichuan University. In breast tissue, the most enriched group were Proteobacteria, then Firmicutes and Actinobacteria for both datasets, in Slovak samples also Bacteroides, while in Chinese samples Cyanobacteria were more frequent. We have observed changes in the microbiome between cancerous and healthy tissues and also different phenotypes of diseases, based on the presence of circulating tumour cells and few other markers.

Kalavska K, Sestakova Z, Mlcakova A, Kozics K, Gronesova P, Hurbanova L, **Miskovska V, Rejlekova K, Svetlovska D, Sycova-Mila Z, Obertova J, Palacka P, Mardiak J, Chovanec M,** Chovanec M, **Mego M.**

Are Changes in the Percentage of Specific Leukocyte Subpopulations Associated with Endogenous DNA Damage Levels in Testicular Cancer Patients?

Int J Mol Sci. 2021 Jul 31;22(15):8281.

Chemoresistance of germ cell tumors (GCTs) represents an intensively studied property of GCTs that is the result of a complicated multifactorial process. One of the driving factors in this process is the tumor microenvironment (TME). Intensive crosstalk between the DNA damage/DNA repair pathways and the TME has already been reported. This study aimed at evaluating the interplay between the immune TME and endogenous DNA damage levels in GCT patients. A cocultivation system consisting of peripheral blood mononuclear cells (PBMCs) from healthy donors and GCT cell lines was used in an in vitro study. The patient cohort included 74 chemotherapy-naïve GCT patients. Endogenous DNA damage levels were measured by comet assay. Immunophenotyping of leukocyte subpopulations was performed using flow cytometry. Statistical analysis included data assessing immunophenotypes, DNA damage levels and clinicopathological characteristics of enrolled patients. The DNA damage level in PBMCs cocultivated with cisplatin (CDDP)-resistant GCT cell lines was significantly higher than in PBMCs cocultivated with their sensitive counterparts. In GCT patients, endogenous DNA damage levels above the cutoff value were independently associated with increased percentages of natural killer cells, CD16-positive dendritic cells and regulatory T cells. The crosstalk between the endogenous DNA damage level and specific changes in the immune TME reflected in the blood of GCT patients was revealed. The obtained data contribute to a deeper understanding of ongoing interactions in the TME of GCTs.

Amiri A, **Chovanec M**, Oliva V, Sedliak M, **Mego M,** Ukropec J, Ukropcová B.

Chemotherapy-induced toxicity in patients with testicular germ cell tumors: The impact of physical fitness and regular exercise

Andrology. 2021 Jul 10. doi: 10.1111/andr.13078. Epub ahead of print. PMID: 34245663.

Background: Testicular germ cell tumors (TGCTs) represent ~95% of testicular malignancies and are the most common type of malignancy in young male adults. While the incidence of TGCTs has increased during the last decades, the advances in treatment, namely introducing cisplatin into the chemotherapy regimen, have made TGCTs highly curable with the 10-year survival rate exceeding 95%. However, in parallel with increased cure rates, survivors may experience acute and late adverse effects of treatment, which increase morbidity, reduce the quality of life, and can be potentially life-threatening. Chemotherapy-related toxicities include cardiovascular and metabolic diseases, secondary cancer, avascular necrosis, cognitive impairment, cancer-related fatigue, poor mental health-related quality of life, nephrotoxicity, hypogonadism, neurotoxicity, pulmonary toxicity, anxiety, and depression. These treatment--related adverse effects have emerged as important survivorship dilemmas in TGCT cancer survivors. Recently, regular physical exercise has increasingly attracted research and clinical attention as an adjunct therapy for cancer patients.

Purpose: Herein, we review the most common chemotherapy-related adverse effects in TGCT survivors and clinical relevance of exercise and increased cardio-respiratory fitness in modulating chemotherapy-related toxicity and quality of life in this population.

Results and conclusion: Exercise has positive effects on a spectrum of physical and psychosocial outcomes during and after cancer treatment, and current guidelines on exercise prescription in chronic diseases define the recommended dose (volume and intensity) of regular exercise for cancer survivors, highlighting regular, sufficiently intensive physical activity as an essential part of patients› care.

HEMATOLOGICKÉ MALIGNITY

Oravcova I, Lukas J, Cingelova S, Demitrovicova L, Mikuskova E, Drgona L, Sopko L, Galffy B, Batorova A, Mistrik M.

Treatment of Adults and Young Adults with Acute Lymphoblastic Leukemia: Real Life Data from Two Centers in Slovakia

Clin Lymphoma Myeloma Leuk. 2021 Jun 20:S2152-2650(21)00236-6.

Introduction: The results of treatment of acute lymphoblastic leukemia (ALL) from the low population countries are missing in the literature.

Patients and methods: We retrospectively examined biological characteristics and survival of 90 patients with ALL.

Results: At median follow-up 17 months, 52 men and 38 women were eligible for the analysis with median age 43 years (18-74). As for the risk stratification, 25.6% of patients were in standard risk, 46.7% in high risk and 27.8% in very high-risk group. Complete remission achieved 88.9% of patients. We observed 5.6% of induction deaths and 4.5% of resistant disease. 47.8% of the patients underwent allogeneic stem cell transplantation (alloSCT), 59% in the young adults (YA; < 40 years) and 40% in adult group (≥ 40 years). We noticed 32.6% relapses overall with median survival of relapsed patients 3.9 months. YA patients had longer survival than adults: 3-year overall survival (OS) 65.0% vs 30.2%; (HR = 0.36; 95% CI 0.2-0.64; P = .001) and event free survival (EFS) 51.5% vs 21.9%; (HR = 0.45; 95% CI 0.26-0.78; P = .005). There was significant difference in 3-year EFS between risk groups in YA patients 90.9%, 48.0%, 11.4%; (P = .001). OS after alloSCT individually for the YA was 62.6% and for adults 39.1%, hazard ratio (HR) = 0.49 (95% CI 0.20-1.21); (P = .095). We observed 14% early deaths, 25.6% late deaths and 3 relapses (7%) after allogeneic stem cell transplantation.

Conclusions: Our data proved that even in a low population country similar result can be achieved as in larger ones while using well designed adapted protocols from leukemic study groups.

Abstrakty a príspevky z konferencií

A. Masarykova, D. Scepanovic, P. Povinec.

Prognostic role of [18F]FDG PET-CT after induction chemotherapy for locally advanced Non Small Lung Cancer.

ESTRO 2021, Madrid, Spain, 27 August – 31 August 2021