Aim: This study aims to investigate the signaling pathway AMP-activated protein kinase (AMPK)-Peroxisome proliferator-activated receptor-gamma coactivator (PGC)1α-sirtuin (SIRT3) in the human corpus cavernosum (HCC) between healthy individuals and those with cardiovascular disease risk factors (CVDRF).

Introduction: SIRT3 is a mitochondrial NAD+-dependent protein-deacetylase involved in the regulation of cellular metabolism. As a key factor in AMPK and PGC1α activation in stress, the decrease in SIRT3 expression or activity is associated with diverse pathologies and aging. Actually, SIRT3 expression was found decreased in HCC of aged individuals with CVDRF. CVDRF such as diabetes mellitus (DM), dyslipidemia, hypertension and obesity strongly associate to endothelial dysfunction, which early manifests as erectile dysfunction (ED).

Methods: HCC’s samples from individuals aged 40-60 years, submitted to programmed urological surgeries at Hospital São João-Porto, were divided in three groups (n = 4): (1)-controls without ED or CVDRF; (2)-DM patients; and (3)-patients with three or more CVDRF including DM. Dual immunolabelling of SIRT3 and superoxide dismutase (SOD)2 with alpha-actin was carried out. As well, levels of SIRT1, SIRT3, SOD2, PGC1α, NADPH oxidase (Nox)1, phospho-AMPK and AMPK were assessed by Western-blotting (WB).

Results: We observed SIRT3 and SOD2 expression in α-actin-labelled fusiform muscle cells in all groups. The semi-quantification by WB demonstrated a significant decrease in SOD2 expression in group 3 relatively to controls, as well as, an increased tendency of Nox1 and PGC1α and a decreasing trend in phospho-AMPK in groups 2 and 3. No differences in SIRT1 and SIRT3 were observed among groups.

Conclusion: This study suggests that CVRF including DM increase oxidative stress in HCC owning to a decrease in SOD2 expression and concomitant increment in Nox1. Further studies with an increased number of HCC samples will be necessary to elucidate the role of the AMPK-PGC1α-SIRT3 signaling pathway in the response to oxidative damage.

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References
Introduction: Prostate cancer is the second most diagnosed cancer, and the second most common cancer-cause of deaths in men worldwide. The apparent diffusion coefficient (ADC) derived from DWI has been shown to improve the detection of prostate cancer and is the primary imaging method for the differentiation between low to high grade cancers. ADC values show reduction with increasing Gleason's score.

Methods: Prospective study included 60 subjects. Male patients were divided into the groups with pathohistology verified benign and malignant lesions (aged, 46–81; average age, 67.7 years) with abnormal PSA values (>4 ng/ml), and into control group (aged, 44–81; average age 65.3) with normal PSA values (0–4 ng/ml). Prostates were first examined on MRI, determining the diffusion values on ADC map, by placing the region of interest (ROI), through the middle of lesions. Later, the TRUS-guided biopsies were performed. Three intersections of the prostate (apex, middle, and base) were observed, and at total of 12 places (4 places per section) the mentioned methods were indicated.

Results: Statistically significant difference (p < 0.05) between the groups of patients with malignant and benign lesions in relation to the ADC values of the apex, base and middle of prostate. ADC values of malignant lesions at apex were in range 952–1030, at base 859–977 × 10⁻⁶ mm²/s, while in benign lesions value at apex where in range 1234–1336, and at base 1096–1183 × 10⁻⁶ mm²/s.

Conclusion: Determination of the numerical value of ADC map represents a significant additional diagnostic parameter for prostate cancer. All values in the range of 1179–1229 for base, 1063–1139 for middle, and 1199–1379 × 10⁻⁶ mm²/s for apex were considered normal. Values between the range of 857–1030 × 10⁻⁶ mm²/s have been suspected for possible presence of the prostate cancer.

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PS101
Deoxycytidine kinase expression in AML blasts and its relationship to leukemia-free and overall survival

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Aim: Study the correlation of expression of genes involved in cytarabine metabolism to leukemia-free (LFS) and overall survival (OS) in AML.

Introduction: Cytarabine is the backbone of AML therapy. Understanding the roles and polymorphisms of genes involved in cytarabine metabolism and resistance in AML will facilitate development of novel therapeutics.

Methods: Adults less than 60 years with non M3 AML were included. Archived diagnostic marrow samples were studied for expression of 10 genes involved in cytarabine metabolism by RT-qPCR; gene expression normalized to GAPDH was compared using the unpaired t-test with Welch correction. SNP rs4694362 in deoxycytidine kinase (DCK) gene was tested using Taqman assay. Median time to relapse and survival was calculated by Kaplan Meier method.

Results: 21 Han Chinese patients (median age: 50) were identified; 15 were male; 16 had intermediate risk cytogenetics; 5 had a blast count of over 100 × 10⁶/L at diagnosis. 17 patients achieved CR; 12 after first induction. No difference in gene expression was seen between CR (n = 12) versus non CR (n = 9) with first induction. 17 CR patients were followed for a median duration of 67.5 months; median time to relapse was 15 months. 1 patient who underwent allogeneic transplant in CR1 was excluded. Higher mean DCK expression was seen in patients with LFS longer than (n = 7) versus less than 2 years (n = 9) (1.91 ± 0.67, p = 0.01) and in those with OS longer than (n = 8) versus less than 3 years (n = 8) (2.02 ± 0.69, p = 0.01). DCK rs4694362 TT genotype was less prevalent than CT in patients with >2 year LFS; but not statistically significant. (49% vs 60%, p = 0.6).

Conclusion: DCK phosphorylates cytarabine to its active metabolite. Our work shows that higher DCK expression is correlated to LFS and OS in AML. The role of DCK SNP rs4694362 should be explored further in the Chinese.

References

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PS108
Analysis of MTHFR C677T polymorphism significance in patient preparation for the in vitro fertilization procedure

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Aim: The aim of this study is to determine if in relation to general population, there is a statistically significant difference in the frequency of alleles and genotypes of the C677T polymorphism of MTHFR gene, amongst women with unknown cause of infertility, who are undergoing in vitro fertilization preparation.

Introduction: Methylene tetrahydrofolate reductase (MTHFR) is an enzyme coded by MTHFR gene. Polymorphism of MTHFR gene C677T leads to decreased function of MTHFR enzyme, which is associated with high level of homocysteine and low concentration of folate, which can undermine female reproductive function and affect the outcome of in vitro fertilization.

Methods: The study included the experimental group consisted of 31 women and the control group consisted of 100 women. C677T polymorphism was detected via PCR/RFLPS method. The statistical difference in genotype and allele frequencies was conducted using the Chi-square test.

Results: The comparison of genotypes amongst the experimental and control group has not shown a statistically significant difference (p > 0.05). Frequency of the MTHFR677 TT genotype was 22.6% in the experimental group, and 12.0% in the control group, while the allele T frequency amongst the experimental group was 0.01). DCK rs4694362 TT genotype was less prevalent than CT in patients with >2 year LFS; but not statistically significant. (49% vs 60%, p = 0.6).