The effect of combined heavy metal ions on copA, nikA and czcD genes expression of metal-resistant bacilli

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are blocked by ablation of miR210 expression during senescence by specific AntagomiRs.

Our data shed new light on the ability of senescent stroma to affect prostate cancer malignancy, sustaining the development of a favorable microenvironment for cancer progression, recruiting/organizing vessels and sustaining inflammation.

SW03.S13–72
The effect of combined heavy metal ions on *copA, nikA* and *czcD* genes expression of metal-resistant bacilli

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Heavy metal resistant microorganisms, thriving in environments with excessive concentrations of heavy metals, have evolved a variety of adaptation strategies. Reduced accumulation based on an active efflux of the bivalent cations is the primary resistance mechanism developed in prokaryotes. The goal of the present work was to investigate the expression of the *copA*, *nikA* and *czcD* genes of metal-resistant bacilli as a metal stress response to the presence of different concentrations of a combination of Cu (II), Ni(II), Cd(II) and Zn(II) metal ions. The test organisms were *Bacillus subtilis* AG4, *Bacillus megaterium* AA1, *Geobacillus pulidus* AA4 and *Clostridium saccharolyticum* LA5 strains isolated from different territories in Armenia with elevated levels of toxic metals. The resistance patterns, expressed as minimum inhibitory concentrations, were analyzed by using the agar dilution method. All isolates showed high resistance to Cu(II) and Ni(II) (up to 5 mM), but were more sensitive to Cd(II) and Zn(II) (up to 0.4 and 1 mM, respectively). PCR combined with DNA sequence analysis was used to investigate the presence of the *copA*, *nikA* and *czcD* genes, which are often responsible for resistance to mentioned ions. The presence of *copA* and *nikA* genes was confirmed in all the strains. *czcD* was confirmed only in *B. subtilis* AG4 and *C. saccharolyticum* LA5. Transcription analysis of selected genes in the presence of different concentrations of metal ions in the growth medium was performed by RT-qPCR. Expression of the *czcD* gene was not detected. Highest expression *copA* and *nikA* genes was observed in the presence of a combination of Cu(II), Ni(II), Cd(II) and Zn(II) in 0.016, 0.017, 0.01 and 0.015 mM concentrations, correspondingly, i.e. at very low metal concentrations. The absence or low expression of *copA* and *nikA* genes at high metal concentrations indicates that alternative resistance mechanisms might be present.

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Protective effect of natural polyphenol complex of red wine under radioinduced oxidative-nitrative stress

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Overproduction of reactive Oxygen (ROS) and Nitrogen (RNS) species play a key role in the development of pathological changes in the organism after exposure to low doses of ionizing radiation. Radioinduced changes in the prooxidant-antioxidant balance are caused by disorders in NO synthesis and metabolism and by the unbalanced function of antioxidant enzymes.

It is known, that polyphenolic compounds of red wine exhibit pronounced antioxidant properties under development of different diseases. Therefore studing their effect on the pathological changes in the organism under low doses of radiation presents a high interest. Under the X-ray exposure (30 cGy) was observed increasing in two times the content of thiobarbituric acid reactive substances (TBARS) and nitrotyrosine-modified (NT) proteins in the cortical layer of rat kidney. At the same time, the activities of superoxide dismutase (SOD) and NO-synthase (NOS) decreased on 72 h post-irradiation, while at the earlier time points (24 and 48 h after irradiation) the activities of SOD, catalase (CT) and glutathione peroxidase (GPO) increased when compared to control. Consumption of preparation of natural polyphenolic complex of wine (NPCW) for 10 days before and during 3 days after irradiation caused an increase in antioxidant capacity of the cortical layer of rat kidney. The polyphenols reduced the content of TBARS in rat kidney after irradiation by 1.4 times compared to irradiated rats without treatment, while the activity of antioxidant enzymes and NOS as well as the content of NO stable products did not differ from controls. The consumption of NPCW also decreased the content of NT proteins, a key marker of nitrative stress, in the cortical layer of rat kidney compared to irradiated nontreated rats.

Thereby, our results show that the preparation of NPCW diminishes oxidative-nitrative stress caused by the action of low doses of ionizing radiation. Red wine polyphenols implement their radioprotective function through ROS and RNS scavenging. In this way the activities of antioxidant defense system enzymes and L-arginine/NO system components were changed and corrected after irradiation.

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14-3-3 positively regulates murine protein serine-threonine kinase 38 in a phosphorylation-dependent manner

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Murine protein serine-threonine kinase 38 (MPK38)/maternal embryonic leucine zipper kinase (MELK) is a member of the family of AMP-activated protein kinase (AMPK) that respond to changes in cellular energy state. In this study, we demonstrate that 14-3-3 has a positive role in the regulation of MPK38 activity and function. The physical association of MPK38 and 14-3-3 is mediated through their C-terminal domains. MPK38 directly interacts with and phosphorylates 14-3-3 (Ser^{156} of 14-3-3 theta and Ser^{158} of 14-3-3 sigma). In addition, ectopic expression of wild-type 14-3-3, but not the 14-3-3 theta S156A (or 14-3-3 sigma S158A) mutant, dose-dependently enhances MPK38-dependent ASK1, TGF-beta, and p53 signaling by stabilizing the MPK38 protein, suggesting that 14-3-3 phosphorylation by MPK38 contributes to the stimulation of MPK38 activity and function. We also demonstrate an *in vivo* role of 14-3-3 in the regulation of MPK38 function using 14-3-3-null HCT116 cells. Together, our present results provide evidence that 14-3-3 functions as a physiological activator of MPK38 in cells.