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Oxidative stress induced NRF2 regulation in BxPC-3 cells and identification of targets for therapeutic intervention

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Pancreatic cancer is one of the most aggressive human malignancies and ninth leading cause of cancer death in the world. Estimated new cases and deaths from pancreatic cancer in 2013 in the United States would be 45,220 and deaths 38,460. Most patients diagnosed with pancreatic cancer die within 6 months, and only 4% survive 5 years after diagnosis. Pancreatic cancer is characterized by colossal local invasion and early metastatic growth to the liver and regional lymph nodes. Expression of Nrf2 was up-regulated in oxidatively stressed BxPC-3 cell line and ductal adenocarcinomas. Furthermore the BxPC-3 cell line responds to stress signals and resist chemotherapeutic interventions and have shown drug resistance. The Nrf2 has also been implicated in proliferation in certain pancreatic adenocarinomas. Normally, ROS levels are tightly controlled by an inducible antioxidant program that responds to cellular stressors and is predominantly regulated by the transcription factor Nrf2. It was also identified the presence of a number of gene products involved in integrin signaling pathways. The comparative proteomic analysis using Protein Center and Ingenuity Pathway Analysis have shown the activation of DNA repair pathway genes like RAD50, ApeX, damage-specific DNA binding protein which have the capability to repair DNA damage. The activation of NRF2 transcriptional factor in BxPC-3 treated cells shows that it may bind to the DNA at the location of the Antioxidant Response Element (ARE) or also called hARE (Human Antioxidant Response Element) which is the master regulator of the total antioxidant system. These results may have some promise in therapeutic intervention in the treatment of pancreatic cancer adenocarcinoma.

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Heavy metal-induced up regulation of anti-oxidative enzymes and hemo-lymph biochemical compositions in *Oxya hyla hyla*

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Present study was conducted to determine toxic effects of heavy metals (Cd, Pb and Hg) on antioxidant enzymes of a grasshopper species i.e., *Oxya hyla hyla* (Serville). Changes in the activities of antioxidant enzymes, Superoxide Dismutase (SOD), Catalase (CAT), Peroxidase (POD), Lipid Peroxidation (LPO)] and biochemical composition of hemolymph were measured by exposing trailed insect to Cd^{+2}, Pb^{+2} and Hg^{+2} at different concentrations (0, 0.50×10^{-4}, 1.10×10^{-4}, 1.55×10^{-4} gg^{-1}) of $CdCl_2$, $PbCl_2$ and $HgCl_2$ for variable exposure time (24 h, 50 h and 75 h). The insect showed significant accumulation of metals with the increase in exposure of dose and time. The SOD activity was lowered at 1.10×10^{-4} to $1.55 \times 10^{-4}gg^{-1}$ than at $0.50 \times 10^{-4}gg^{-1}$ Cd^{+2}, Pb^{+2} and Hg^{+2} levels. Detoxification effect was expressed by SOD at low metal concentrations, and this effect disappeared at high concentrations. Assayed activities of CAT, POD and LPO level were significantly accelerated and correlated positively as metal exposure time increased showing species dependency. A significant decrease in total soluble protein, sugar, lipids and glycogen contents was observed due to metal exposure throughout the entire tested period except after the first 24 h of exposure at the lower concentrations. Thus CAT had a strong detoxification effect as compared to SOD whereas POD had a weak detoxification effect. The study thus concludes that O. *hyla hyla* (Orthoptera: *Acrididdae*) and its antioxidant enzyme level can be used as bio indicator and bio marker of biotic and abiotic stresses.

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