Revealing Melanoma Cell Proteome Transformations with Silver Nanoparticles: An Innovative Comparative Study

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Malignant melanoma represents the most lethal form of skin cancer, also due to its resistance to drug-induced apoptosis. Here, we present a comprehensive analysis of global proteomic changes induced in the human melanoma cell line (A375) upon exposure to AgNPs synthesized through two different routes, at two time points (24 and 48 hours). The traditional method of AgNPs colloidal synthesis is compared with a "green" method that uses polyphenols present in the *Laurus nobilis* extract as reducing and stabilizing agents. After a careful physico - chemical characterization of AgNPs with different techniques, the cellular response, observed through proteomic changes, offers valuable insights into the affected cellular functions and pathways. The results show that green AgNPs are less toxic to normal cells compared to colloidal AgNPs, showing a selective impact on oncoproteins and reducing the viability of cancer cells. After 24 hours of exposure to green AgNPs, a downregulation of proteins crucial for cell proliferation, survival and differentiation is observed, highlighting a cellular response to DNA damage, programmed cell death and autophagy. All the treatments with green AgNPs led to a decrease in a series of oncogenes, demonstrating a cancer cell growth inhibition that is even higher over time.

Furthermore, prolonged exposure (48 hours) leads to an increase in the metabolism of carboxylic acids, related to an improved carbohydrate metabolism via aerobic glycolysis rather than anaerobic glycolysis, thus indicating a prominent feature of cancer state. Lastly, the study highlights the reaction of melanoma cells to AgNPs in the context of dysregulated copper homeostasis, a key process in the angiogenesis of solid tumors. To the best of our knowledge, this is the first study to report the effects of differently synthesized AgNPs on melanoma cells using an integrated proteomic approach.