Silver nanoparticles downregulate p53 activation and induce desacetylation of histone 3 in human lung cancer epithelial cells

Jordi Blanco, Daisy Lafuente, Domènec Sánchez, José Luis Domingo, Mercedes Gómez

Laboratory of Toxicology and Environmental Health, School of Medicine, IISPV, Universitat Rovira i Virgili, 43201 Reus, Spain.
jordi.blanco@urv.cat

Abstract

Nanomaterials have been widely used in recent years in aerospace engineering, nanoelectronics, environmental remediation, medical health care, and consumer products. Silver nanoparticles (AgNPs) are one of the most commonly used nanomaterials, because possess potent antibacterial and antifungal characteristics. AgNPs have been used extensively as an antimicrobial agent in cosmetics, textiles and the food industry, as well as a disinfectant for medical devices and for coating home appliance [1]. The emerging number of consumer products containing AgNPs and increasing enviromental concentration, have led to concerns, because nanoparticles may pose a risk for humans and the environment. The main ways by which people may be exposed to AgNP are by inhalation, dermal contact, and oral ingestion. The absorbed AgNPs can pass through the respiratory or gastrointestinal tracts and stored in many organs such as lung, liver, spleen, kidney and the central nervous system. There is growing evidence that AgNPs are highly toxic in terms of cytotoxicity, genotoxicity, and oxidative stress [3].

The present study evaluated the cytotoxic effects of AgNPs (20 nm of diameter coated with 0.3% of PVP) in A549 cells. A549 cells were exposed to 0, 25, 50, 100 and 200 µg/mL of AgNPs along 72 hours. AgNPs caused cell death in a dose- and time- dependent manner (Figure 1). Cell death induced at high doses was positively correlated with a down regulation of the expression and phosphorylation of p53 protein and acetylation of histone 3 (H3, Figure 2). Contrarily, the expression of total H3 protein was overexpressed at high doses.

The desacetylation of H3 at high doses of AgNPs suggests that epigenetic changes could be happening into the chromatin. These sugestion are reinforced by the morphologic changes observed in A549 at high doses. In the same way, downregulation of the expression of p53 could be also due to a desacetylation of lysine residues which lead to its proteosomal degradation. The down regulation of p53 could lead to a deregulation of cell cycle and could induce arrest in S phase and thereby increase of the expression of histones proteins. The knowledge of the mechanisms by which AgNPs induce these changes could help to better understanding how nanoparticles could induce cancer cells death.

References

[1] Navarro E, Baun A, Behra R, Hartmann NB, Filser J, Miao AJ, Quigg A, Santschi PH, Sigg L: Environmental behavior and ecotoxicity of engineered nanoparticles to algae, plants, and fungi. Ecotoxicology 2008, 17:372-386.

[2] Chen X, Schluesener HJ: Nanosilver: a nanoproduct in medical application. ToxicolLett 2008, 176:1-12.

[3] Kim S, Choi JE, Choi J, Chung KH, Park K, Yi J, Ryu DY: Oxidative stressdependent toxicity of silver nanoparticles in human hepatoma cells. Toxicol In Vitro 2009, 23:1076-1084.

Figures

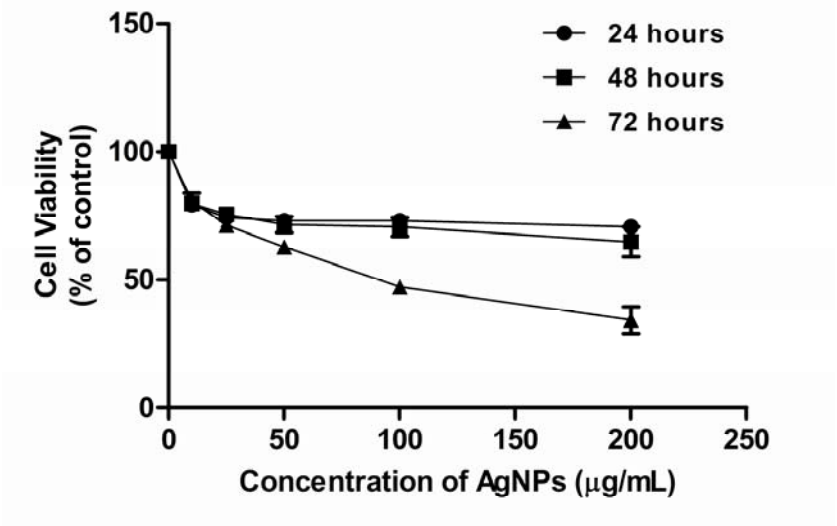

Figure 1.

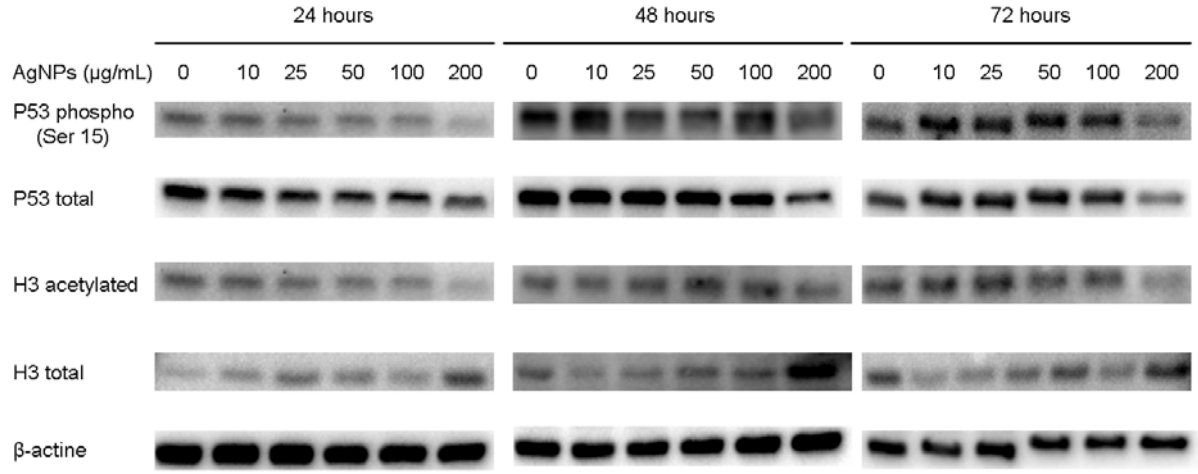

Figure2.