# Short time of ZnO nanoparticles uptake induces DNA damage and specific mitochondrial degeneration in human colon carcinoma cells

**Abstract number:** 6707

**Session Code:** LS04-058

**DOI:** 10.1002/9783527808465.EMC2016.6707

**Meeting:** The 16th European Microscopy Congress 2016

**Session:** Life Sciences

**Topic:** Membrane Interaction

**Presentation Form:** Poster

**Corresponding Email:** stefania.meschini@iss.it

*Maria Condello (1), Stefania Meschini (1), Barbara De Berardis (1), Maria Grazia Ammendolia (1), Giancarlo Condello (2), Evelin Pellegrini (1)*

1. Dept. Technology and Health, National Institute of Health, Rome, Italie 2. Department of Movement, Human and Health Sciences, University of Rome Foro Italico, Rome, Italie

**Keywords:** genotoxicity, human colon carcinoma cells, nanoparticles uptake, oxidative stress, ZnO nanoparticles

Thanks to their unique physico-chemical properties, ZnO nanoparticles are widely used in consumer and industrial products, due to their higher chemical reactivity, stronger oxidation and corrosion resistance, antimicrobial properties, as compared with larger micro-sized counterparts (Madhumitha et al., 2016). Recent studies have shown that ZnO nanoparticles can be promising candidates for biomedical applications and therapeutic interventions, and also successful as drug carrier and in targeted gene delivery (Peng et al., 2015; Velmurugan et al.,2015). In our previous in vitro study, ZnO nanoparticles showed to induce oxidative stress in human colon carcinoma cells (LoVo), resulting in significant decrease of cell viability (De Berardis et al., 2010).

In order to gain insight into the mechanism of action at subcellular level, aim of the present investigation was to carry out an ultrastructural study by transmission electron microscopy (TEM) on the subcellular localization of ZnO nanoparticles and a semi-quantitative analysis of cellular uptake at multiple time points (from a few minutes up to 24 h of exposure). Electron microscopy observations of ZnO treated cells revealed two different mechanisms of cellular uptake, passive diffusion and endocytosis. Control cells show a mitochondria and nuclear normal shape (Fig. 1A). Small particles entry by passive diffusion crossing the plasma membrane without altering its structure (30 min of treatment, Fig. 1B; arrow indicates the nanoparticle in the cell membrane area). After 1h of treatment  ZnO nanoparticles are already visible in the mitochondria cristae (Fig. 1C). The induction of the apoptosis is clearly showed in Fig. 1D, after 24 h of treatment. Quantitative analysis of cell death has been performed by flow cytometry.

We also evaluated the intracellular ions release from ZnO nanoparticles, their genotoxic potential by determining 7,8-dihydro-8-oxo-deoxyguanosine (8-oxodG) levels, and the expression of phosphorylated histone H2AX (γ-H2AX). The simultaneous presence of ZnO nanoparticles and $Zn^{2+}$ ions in the LoVo cells determined the formation of reactive oxygen species at the mitochondrial and nuclear level, inducing severe DNA damage.

In conclusion, our observations showed that ZnO nanoparticles entered LoVo cells by either passive diffusion or endocytosis or both, depending on the agglomeration state of the nanomaterial. ZnO nanoparticles coming into contact with acid pH of lysosomes altered organelles structure, resulting in the release of $Zn^{2+}$ ions. Taken together, the results of this study provide the evidence that damage induced by ZnO nanoparticles in LoVo cells derives from a combined action between intact nanoparticles and $Zn^{2+}$ ions, leading new insights into their toxicity.

References

Madhumitha, G.,et al., 2016. Biotechnological aspects of ZnO nanoparticles: overview on synthesis and its applications. Appl. Microbiol. Biotechnol. 100, 571-581.

Peng, H., et al., 2015. ultifunctional β-CD-modified Fe3O4@ZnO:Er(3+),Yb(3+) nanocarrier for antitumor drug delivery and microwave-triggered drug release.Mater. Sci. Eng. C Mater. Biol. Appl. 46, 253-263.

Velmurugan, P., et al., 2015. Phytofabrication of bioinspired zinc oxide nanocrystals for biomedical application. Artif. Cells Nanomed. Biotechnol. 27, 1-8.

De Berardis, B., et al., 2010. Exposure to ZnO nanoparticles induces oxidative stress and cytotoxicity in human Ccolon carcinoma cells. Toxicol. Appl. Pharmacol. 246, 116-127.

**Figures:**

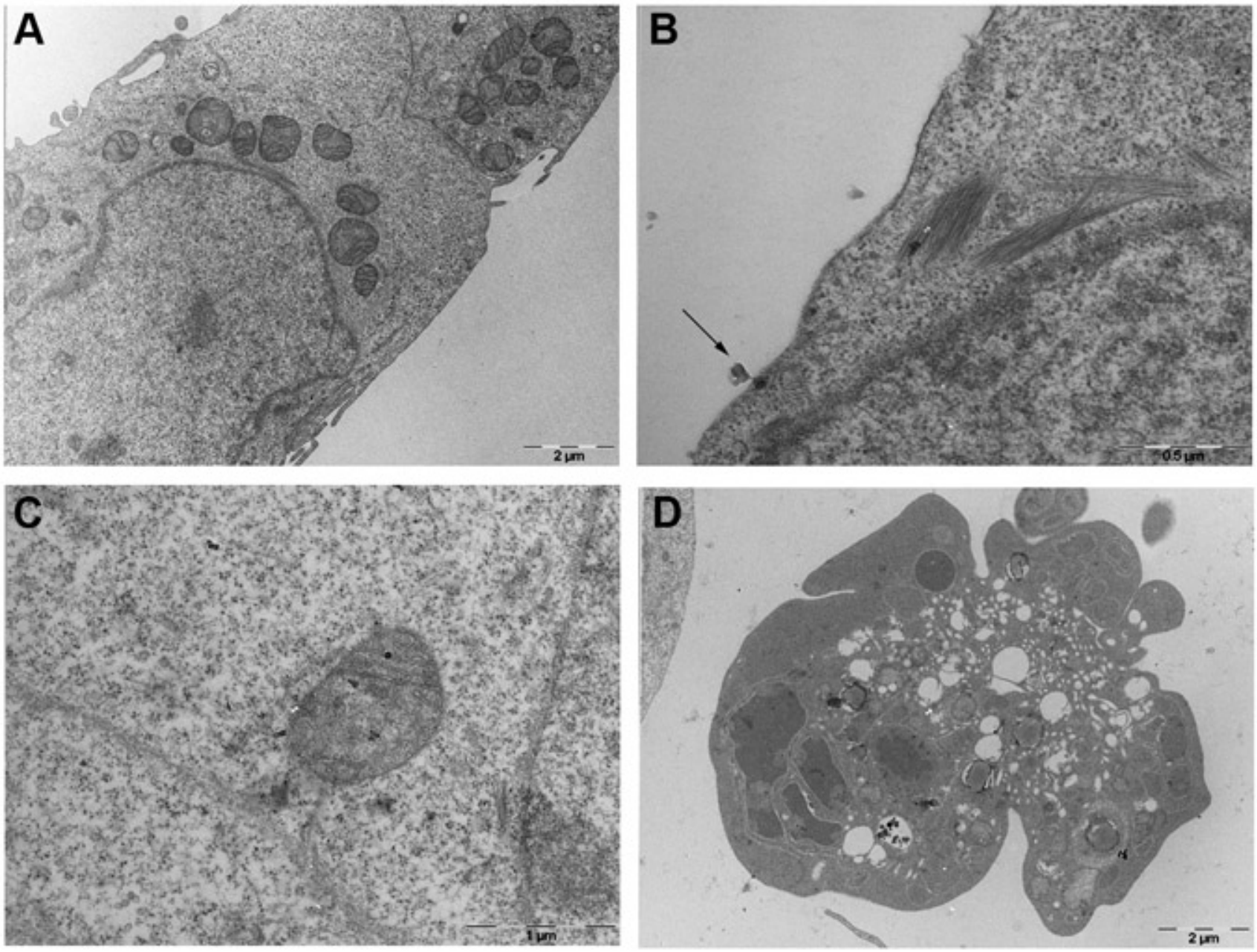


Figure 1: ZnO NPs cellular uptake followed by TEM analysis. Control cells (A); ZnO NPs enter the cell by passive diffusion (B); NPs crossed the plasma membrane and were transported through filamentous structures to the mitochondrion (C); apoptotic cells (D).

**To cite this abstract:**

Maria Condello, Stefania Meschini, Barbara De Berardis, Maria Grazia Ammendolia, Giancarlo Condello, Evelin Pellegrini; Short time of ZnO nanoparticles uptake induces DNA damage and specific mitochondrial degeneration in human colon carcinoma cells. The 16th European Microscopy Congress, Lyon, France. http://emc-proceedings.com/abstract/short-time-of-zno-nanoparticles-uptake-induces-dna-damage-and-specific-mitochondrial-degeneration-in-human-colon-carcinoma-cells/. Accessed: January 9, 2017

---