The Toxicologist

Supplement to *Toxicological Sciences*

55th Annual Meeting and ToxExpo™

SOT

New Orleans, Louisiana

March 13–17, 2016

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The Official Journal of the Society of Toxicology

SOT | Society of Toxicology

Creating a Safer and Healthier World by Advancing the Science and Increasing the Impact of Toxicology

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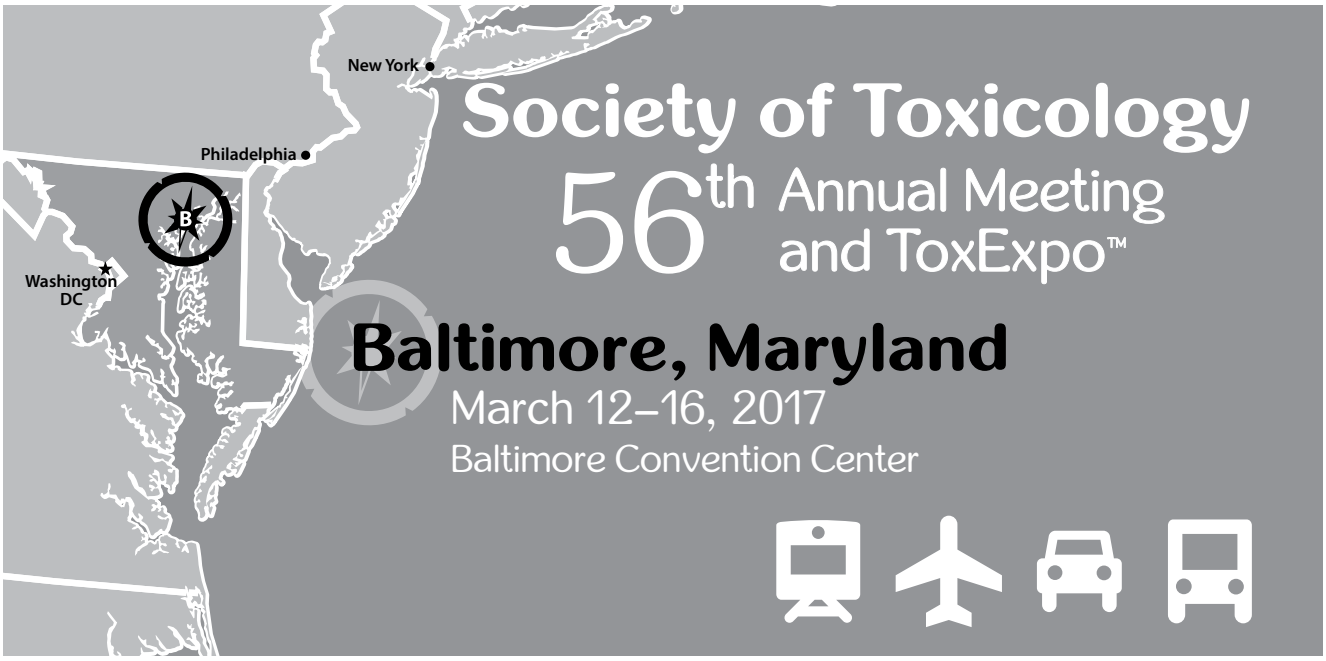

2017 Annual Meeting Session Proposal Deadline: April 30, 2016

Why Submit a Proposal?

1. To present new developments in toxicology
2. To provide attendees with an opportunity to learn about state-of-the-art technology and how it applies to toxicological research
3. To provide attendees with an opportunity to learn about the emerging fields and how they apply to toxicology

Session Types

Continuing Education—Emphasis on quality presentations of generally accepted, established knowledge in toxicology
Note: CE Courses will be held on Sunday.

Symposia—Cutting-edge science, new areas, concepts, or data

Workshops—State-of-the-art knowledge in toxicology

Roundtables—Controversial subjects

Historical Highlights—Review of a historical body of science that has impacted toxicology

Informational Sessions—Scientific planning or membership development

Education-Career Development Sessions—Sessions that provide the tools and resources to toxicologists that will enhance their professional and scientific development

Regional Interest—Central topics of relevance that describe public health and/or ecological problems of a particular region

Submit your proposal online at www.toxicology.org

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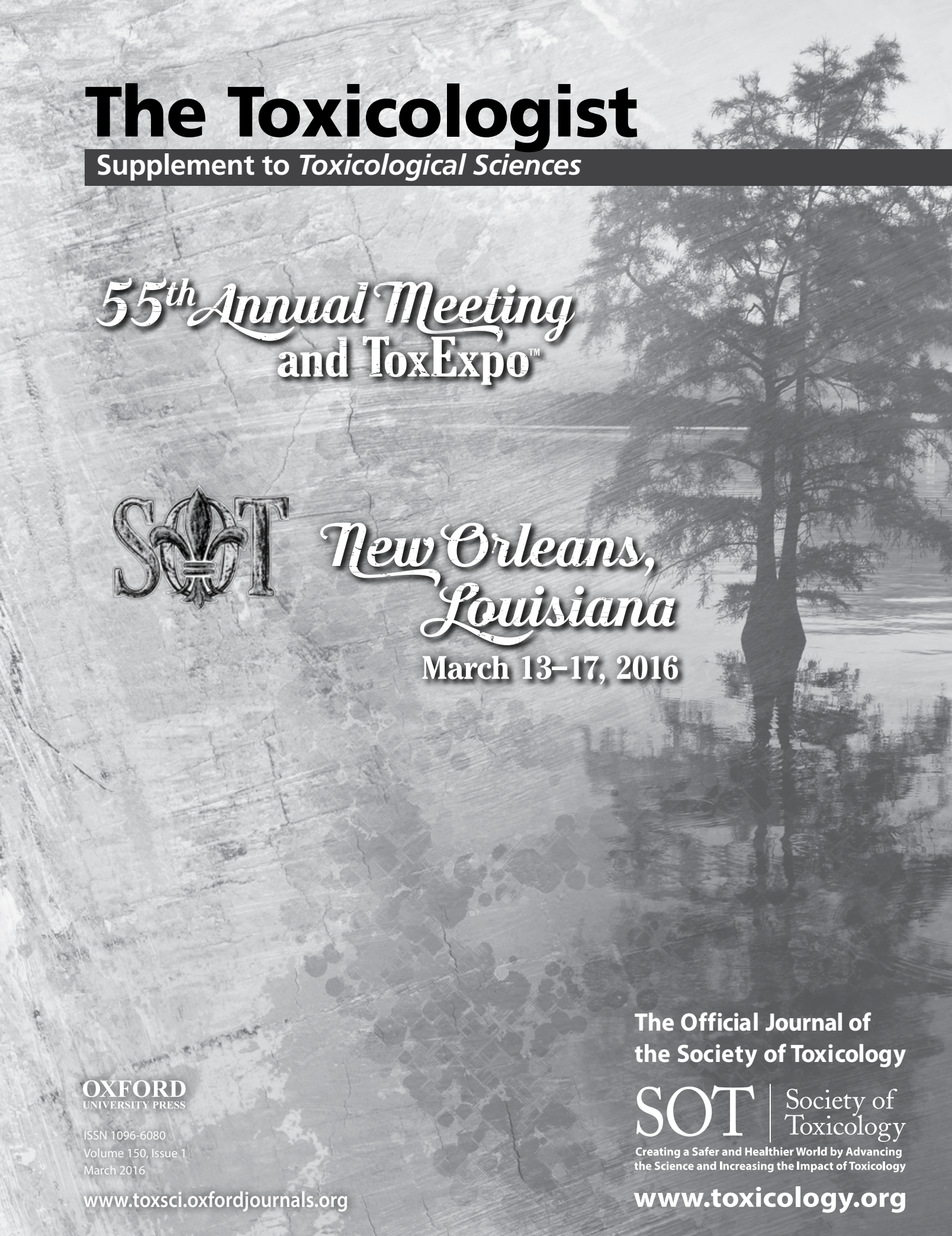

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Preface

This issue is devoted to the abstracts of the presentations for the Continuing Education courses and scientific sessions of the 55th Annual Meeting of the Society of Toxicology, held at the New Orleans Ernest N. Morial Convention Center, March 13–17, 2016.

An alphabetical Author Index, cross referencing the corresponding abstract number(s), begins on page 603.

The issue also contains a Keyword Index (by subject or chemical) of all the presentations, beginning on page 629.

The abstracts are reproduced as accepted by the Scientific Program Committee of the Society of Toxicology and appear in numerical sequence. Author names which are underlined in the author block indicate the author is a member of the Society of Toxicology. For example, J. Smith.

Scientific Session Types:

- CE Continuing Education Courses
- EC Education-Career Development Sessions
- FS Featured Sessions
- HH Historical Highlights Sessions
- IS Informational Sessions
- PL Platform Sessions
- PS Poster Sessions
- RI Regional Interest Sessions
- R Roundtable Sessions
- S Symposium Sessions
- W Workshop Sessions

The 2016 SOT Mobile Event App and Online Planner

The Mobile Event App and Online Planner are available via the SOT website and app marketplaces. These mobile tools enable you, the attendee, to engage with organizers, exhibitors, and each other, and to manage your time and maximize your experience during the Annual Meeting. You also can access some ePosters electronically via the Mobile Event App until May 11, 2016.

To cite a 2016 SOT Annual Meeting Abstract, please format as follows: *The Toxicologist*, Supplement to *Toxicological Sciences*, 150 (1), Abstract #__, 2016, Title, First Author.

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NDMW at 2.4 and 24 µg/cm2. By contrast, number and size of colonies was increased by 0.024 and 0.24 µg/cm2 HTMW and NDMW and 2.4 µg/cm2 HTMW. Significant increases in mitotic aberrations, predominantly monopolar, were observed by exposure to all MW for 24 hours. All MW were found to penetrate the nucleus and associate with the DNA, mitotic spindle and centrosomes. Nuclear penetrations were greatest for the PMW followed by HTMW and NDMW, respectively. Significantly increased fragmentation of the centrosome and centromere were found in response to all MW exposure at all doses indicating a possible mechanism of genotoxicity, however a lower limit was not apparent. A dose-dependent increase in aneuploidy was observed from exposure to all MWs. These data indicate that altering the physiochemical properties of MWs may not reduce their genotoxic effect.

2774 Size and Crystal Structure Dependent Inhibition of Human Mesenchymal Stem Cell Adipogenic Differentiation by Nanoscale Titanium Dioxide

J. Yao[1,3], Y. Jones[3], W. Monroe[3], J. Collins[3], P. Howard[3], A. K. Patri[3] and Y. Zhang[3]. *[1]US FDA Commissioner's Fellowship Program, Jefferson, AR; [2]NCTR/ORA Nanotechnology Core Facility, Jefferson, AR and [3]Office of Scientific Coordination, National Center for Toxicological Research, NCTR/ORA Nanotechnology Core Facility, Jefferson, AR.*

Titanium dioxide (TiO2) has been used in a broad spectrum of consumer products, including food, cosmetics and various medical products. Increased use of nano-scale TiO2 in recent years has raised concern regarding their safety. In the current study, we characterized TiO2 nanoparticles with different crystal structures and particle sizes through electro microscopy, diffraction and scattering techniques. . Subsequently, we determined the impact of TiO2 nanoparticles on cell viability using LDH, ATP assays, and the adipogenic differentiation capacity using Oil red O Staining assay in human mesenchymal stem cells (hMSCs). We further investigated whether the impact of TiO2 nanoparticles was associated with specific particle size and/or crystal structure. Data revealed that TiO2 nanoparticles exhibited minimal acute (up to 72 hours exposure) cytotoxicity in hMSCs. There was a size- and crystal structure- dependent inhibition of hMSC adipogenic differentiation (21 days) by TiO2 nanoparticles. Cellular uptake and media "stripping" studies indicated that the inhibition of hMSC adipogenesis was likely due to direct cellular response to TiO2 nanoparticles instead of a "charcoal-stripping" effect of TiO2 leading to depleted growth factors in the culture media. Additional exploratory gene expression array analyses suggested that TiO2 nanoparticles inhibit hMSC adipogenesis by down-regulating key genes involved in adipogenesis promotion, including FGF2, IRS1, CEBPA, CEBPB, and ACACB, etc. Findings from this study indicate that TiO2 nanoparticles, while exhibiting minimal acute cytotoxicity, may impost long-term impact on hMSC adipogenic differentiation. Future planned studies will reveal the mechanism of TiO2 nanoparticle interaction in stem cell models. Disclaimer: The views presented in this article do not necessarily reflect those of the Food and Drug Administration.

2775 *In Vitro* Toxicity of Tio2 Nanoparticles Immobilized on Clay to Human Hepatic Cells

M. J. Bessa[4], J. J. Reinosa[2], J. F. Fernández[2], M. Bañares[1], J. P. Teixeira[3,4] and C. Costa[3,4]. *[1]Catalytic Spectroscopy Laboratory, Instituto de Catálisis y Petroleoquímica, CSIC, Madrid, Spain; [2]Electroceramic Department, Instituto de Cerámica y Vidrio, CSIC, Madrid, Spain; [3]EPIUnit-Institute of Public Health, University of Porto, Porto, Portugal and [4]Portuguese National Institute of Health, Porto, Portugal.* Sponsor: E. Coskun.

Introduction: Nanotechnology is growing in rapid pace, discovering innovative and attractive nanomaterials for several applications. The fact that nanoparticles induce more damage and are more biologically active when compared to larger micro-sized particles encouraged the emergence of nanoarchitectonics. The immobilization of nanoparticles on the surface of inorganic or organic supports results in the creation of nanocomposites that combine the best properties of both components. Although it has been stated that micro-sized particles induce less toxicity than the nano-size ones, few studies have been made regarding the *in vitro* characterization of cellular responses to this type of materials. Objective: Evaluate *in vitro* toxicity of TiO2 nanoparticles immobilized on clay (C-TiO2) in a hepatocellular carcinoma human cell line (HepG2) as well as of its single elements. Materials and Methods: Materials were supplied by the Ceramic for Smart System Group of the Electroceramic Department, Instituto de Ceramica y Vidrio, Madrid, Spain and characterized by scanning electron microscopy for particle morphology and dynamic light scattering for average hydrodynamic size and potential zeta. After characterization, different concentrations and time periods were tested in regards of HepG2 viability, by employing MTT and Alamar Blue assays, and DNA integrity, by using comet assay. Results and Discussion: Results showed that all studied materials were capable to induce hepatocyte cell death in a dose dependent way and for the majority of the studied periods of exposure. Besides that, the HepG2 DNA was also affected after longer periods of exposure to TiO2 NPs, kaolinite and C-TiO2 nanocomposites. Conclusions: Nanocomposites are promising materials for different nanotechnological applications. Notwithstanding, it is of paramount importance to evaluate their potential toxicity. Data obtained suggests that other subtracts must be tested to immobilize TiO2 NPs as kaolinite mineral was found to be both cytotoxic and genotoxic for the studied cell line. Acknowledgements: Financial support from TD1204 MODENA COST Action.

2776 Effects of Zinc Oxide Nanomaterials on the Cellular Responses in THP-1 Cells

A. Miyajima-Tabata, T. Kawakami, K. Komoriya, R. Kato, S. Niimi and K. Isama. *National Institute of Health Sciences, Tokyo, Japan.* Sponsor: A. Hirose.

Purpose: The biological effects of nanomaterials are related to the physicochemical properties such as composition, shape, particle size, aggregation state, surface area and surface charge. An *in vitro* cellular toxicological study using well-characterized nanomaterials is conducted for evaluation of the biological effects of nanomaterials. In this study, we examined the effects of zinc oxide (ZnO) nanomaterials on the cytotoxicity of THP-1 cells and the expression of CD54 and CD86. Methods: The size distribution and the zeta potential of ZnO nanomaterials were measured by dynamic light scattering. The cellular cytotoxicity and the expression of CD54 and CD86, skin sensitization marker, were measured by cellular ATP method and flow cytometry, respectively. Results and Discussion: The primary particle size and hydrodynamic diameter of ZnO nanomaterials in distilled water suspension were <35 nm and 66 nm (Sigma-Aldrich), and 40 nm and 165 nm (NanoTeK Alfa Aesar). The zeta potentials of ZnO nanomaterials in distilled water suspension were positive (44.9 mV, Sigma) and negative (-7.5 mV, Alfa). The cytotoxicity by ZnO (Sigma) was stronger than that by ZnO (Alfa). ZnO nanomaterials increased the CD54 in a dose-dependent manner, but did not affect the expression of CD86. The CD54 relative fluorescence intensity (RFI) after treatment with 50 µg/mL of ZnO for 24h were 2007 % (Sigma) and 1207 % (Alfa). In conclusion, ZnO nanomaterials showed the cellular cytotoxicity and increased the expression of CD54. The extent of these effects caused by ZnO (Sigma) was higher than that by ZnO (Alfa). The differences of the cellular responses may due to the differences of physicochemical properties between ZnO (Sigma) and ZnO (Alfa). Further analysis at the molecular-level would help the better understanding of the relation between biological effects and the physicochemical properties of nanomaterials.

2777 Induction of the Epithelial-Mesenchymal Transition by Zinc Oxide Nanoparticles

J. J. Kim. *Sungkyunkwan University, Seoul, Korea, Democratic People's Republic of.* Sponsor: D. Y. Shin.

Zinc oxide (ZnO) nanoparticles are one of the promising materials applied in the various kinds of the commercial products such as sunscreens. At the same time, there are growing concerns about unintended toxic effects of ZnO. Many researches on the toxicity of ZnO have been studied, except for the epithelial-to-mesenchymal transition (EMT). EMT is one of the significant multistep processes. Epithelial cells reduce intercellular adhesion and increase cell mobility which is crucial for the cancer metastasis. The aim of our study is to investigate the ZnO-induced EMT in the human alveolar epithelial A549 cells. At first, size distribution of ZnO nanoparticles was observed by dynamic light scattering (DLS). The cytotoxicity test was performed to find the appropriate exposure concentration. Real-time PCR was used for the mRNA expression, related with EMT. In addition, the EMT-associated protein level was measured by western blot. The morphology changes were obtained by the microscopy. The average size of ZnO showed 208 ± 16.10 nm measured by DLS. Cell viability as the cytotoxic effects was decreased in a dose-dependent manner. When A549 cells are exposed to ZnO nanoparticles, mRNA level of EMT-related transcription factor was increased including Snail. Furthermore, the protein levels related with EMT markers were found. In microscopy, ZnO induced morphology changes of A549 to spindle-like elongated shapes. Our data demonstrated that ZnO nanoparticles induced the EMT in A549 cells.