

Scientific and Technical Report

Analysis of the interactions between nanoparticles and biomolecules to understand the role of nano-bio-interface in predicting nanoparticle behavior and effects on biological systems

Project duration: 24 months

Execution phase nr. 1/2019

Project director,

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Objectives of this phase execution

Objective 2. Analysis of the evolution in time of the formation and dynamics of the protein corona of the nanoparticles - part II. Analysis of interactions between membrane models and nanoparticles with different characteristics. Investigating the interactions between nanoparticles and nucleic acids - part I. Data correlation according to the characteristics of nanoparticles - part II

Activity 2.1. Measurement of the kinetics of binding affinity and desorption of proteins on the nanoparticle surface over time

Activity 2.2. Establishing the composition of the protein corona on the nanoparticle surface

Activity 3.3. Measurement of the effects induced by nanoparticles on the organization of Langmuir-Blodgett films as a model of cell membrane

Activity 2.4. Determination of changes induced by nanoparticles on lipids

Activity 2.5. Evaluation of the effects induced by nanoparticles on DNA-protein complexes

Activity 2.6. Data analysis and correlation of experimental results obtained on nanoparticle-biomolecule interactions

Abstract of project phase

During this stage, the analysis of protein corona dynamics and of the interactions between membrane models and nanoparticles with different characteristics, as well as the investigation of the interactions between the nanoparticles and nucleic acids were performed. Measurement of the time kinetics of proteins binding affinity and desorption from the surface of silica, titanium dioxide and zinc oxide nanoparticles showed more significant changes after the incubation with bovine serum albumin (BSA) as compared to human serum albumin (HSA). The highest amount of protein adsorbed on the surface of iron oxide nanoparticles was revealed in the case of fibrinogen (FBN), followed by BSA and HSA. Characterization of the protein corona composition formed on the surface of Si quantum dots (Si QDs) showed that these rapidly developed a complex corona from bovine serum. Further, in order to understand the effect of nanoparticles on biological membranes, the interactions between these and the phospholipid monolayer were analyzed by measuring pressure isotherms using Langmuir-Blodgett trough. This analysis showed that the particles coated with the protein corona interacted strongly with phosphatidyl choline and were incorporated between the lipids, increasing the monolayer rigidity. Phase contrast images showed that the nanoparticles became an integral part of the monolayer, forming complex structures with serum proteins and phospholipids. QDs also exert a strong effect on the physical state of the phospholipid

monolayer leading to its expansion and fluidization, but the presence of serum proteins contributes to the formation of a protein corona responsible for attenuating the disruptive effect on this model system. In addition, only silicon QDs induced significant changes in the cholesterol structure over time, which may affect the lipid structure and cell membranes, and induce lipid peroxidation with malondialdehyde formation. Exposure to the tested nanoparticles (photocatalytic TiO₂, graphene or silicon QDs) did not induce genomic DNA fragmentation. Regarding the effect induced by the exposure to Si QDs, no significant changes in the length of telomeric terminal restriction fragments were observed throughout the study, the values obtained remaining close to the control. The obtained results were processed and disseminated by presenting at two specialized conferences, and publishing seven scientific articles. In conclusion, the activities associated with Stage 2 of the project activity plan were fully realized: A2.1, A2.2, A2.3, A2.4, A2.5 and A2.6.

The results were analyzed and correlated in order to conclude the main effects of the interactions between nanoparticles and biomolecules. These were disseminated as:

- oral presentations and posters at national and international conferences

- Stan M.S., Nica I.C., Miu B., Dinischiotu A. “*Are TiO₂ nanoparticles genotoxic? Their influence on the cell cycle of human pulmonary fibroblasts*”, Al XII-lea Congres National de Citometrie, 30-31 Mai, 2019, Bucuresti, Romania.
- Stan M.S., Mernea M., Cristian R.E., Mohammad I.J., Lambert C., Dinischiotu A. “*Evaluation of titanium dioxide nanoparticles effect on phagocytic activity of granulocytes*”, Al XII-lea Congres National de Citometrie, 30-31 Mai, 2019, Bucuresti, Romania.
- Stan M.S., Cristian R.E., Mohammad I.J., Mernea M., Sbarcea B.G., Trica B., Dinischiotu A. “*Analyzing the interaction between different types of nanoparticles and serum albumin*”, 21st Romanian International Conference on Chemistry and Chemical Engineering, September 4-7, 2019, Constanta-Mamaia, Romania.
- Nica I.C., Dinischiotu A. Stan M.S. “*Genotoxic potential of TiO₂ nanoparticles with enhanced photocatalytic properties investigated by Comet assay in human lung cells*”. 13th International Comet Assay Workshop, 24-27 June, Pushchino, Moscow, Russia, p. 65 (ICAW 2019).

- research articles published in ISI journals

- 1) Stan MS, Mernea M, Cristian RE, Mohammad IJ, Sbarcea BG, Trica B, Dinischiotu A. Correlating the serum albumin corona of zinc oxide nanoparticles with their physico-chemical properties. *Rom. Rep. Phys.* 2019, In press. Impact Factor: 1.940, RIS: 0.702.

- 2) Cristian RE, Mohammad IJ, Mernea M, Sbarcea BG, Trica B, Stan MS, Dinischiotu A. Analyzing the interaction between two different types of nanoparticles and serum albumin. *Materials* 2019, 12(19), 3183. Impact Factor: 2.972, RIS: 1.405.
- 3) Stan MS, Nica IC, Popa M, Chifiriuc MC, Iordache O, Dumitrescu I, Diamandescu L, Dinischiotu A. Reduced graphene oxide/TiO₂ nanocomposites coating of cotton fabrics with antibacterial and self-cleaning properties. *J. Ind. Text.* 2019, 49(3):277-293. Impact Factor: 1.884, RIS: 2.373.
- 4) Stan MS, Chirila L, Popescu A, Radulescu DM, Radulescu DE, Dinischiotu A. Essential oil microcapsules immobilized on textiles and certain induced effects. *Materials* 2019, 12(12), 2029. Impact Factor: 2.972, RIS: 1.405.
- 5) Voicu SN, Balas M, Stan MS, Trică B, Serban AI, Stanca L, Hermenean A, Dinischiotu A. Amorphous silica nanoparticles obtained by laser ablation induce inflammatory response in human lung fibroblasts. *Materials* 2019, 12, 1026. Impact Factor: 2.972, RIS: 1.405.
- 6) Strugari AFG, Stan MS, Gharbia S, Hermenean A, Dinischiotu A. Characterization of nanoparticle intestinal transport using an in vitro co-culture model. *Nanomaterials* 2019, 9(1), 5. Impact Factor: 4.034, RIS: 1.630.
- 7) Stan MS, Badea MA, Pircalabioru GG, Chifiriuc MC, Diamandescu L, Dumitrescu I, Trica B, Lambert C, Dinischiotu A. Designing cotton fibers impregnated with photocatalytic graphene oxide/Fe, N-doped TiO₂ particles as prospective industrial self-cleaning and biocompatible textiles. *Mat. Sci. Eng. C* 2019, 94:318-332. Impact Factor: 4.959, RIS: 1.231.

- review paper

- Stan MS., Badea MA., Strugari AFG. Carbon nanotubes: properties, applications and toxicity. *Rev. Biol. Biomed. Sci.* 2019; 2(1): 12-18. DOI: 10.31178/rbbs.2019.2.1.2.