Scientific and Technical Report

DYNAMICS OF NANOPARTICLES TRANSPORT THROUGH CELLULAR BARRIERS - RELEVANCE IN TOXICOLOGY AND DRUG DELIVERY SYSTEMS

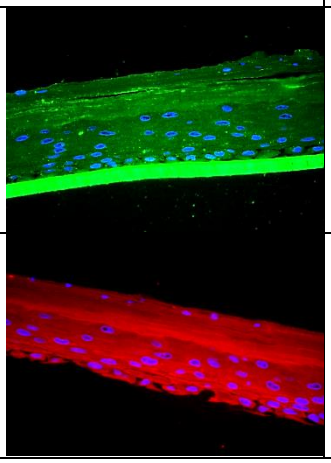
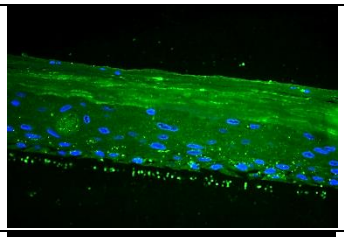
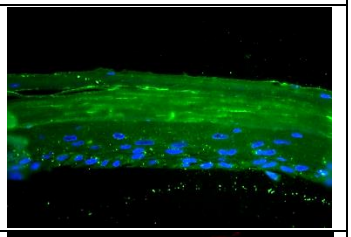
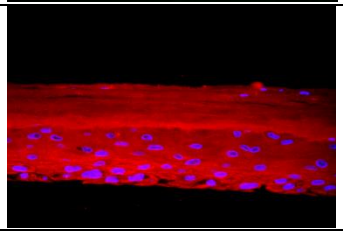
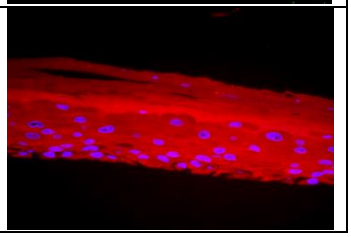
Project no. 81TE/2022

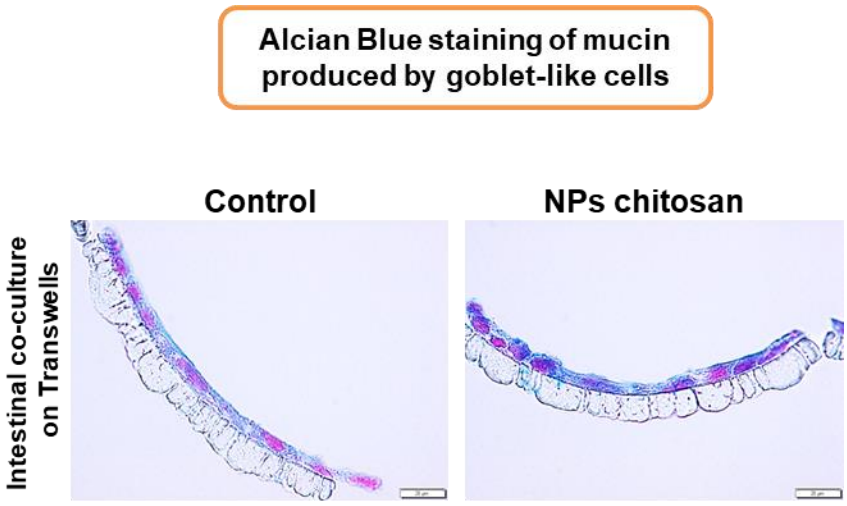
Execution phase nr. 2/2023

Project director,

Assoc. Prof. Miruna Stan

In the first stage of this Young Teams project "DYNAMICS OF NANOPARTICLES TRANSPORT THROUGH CELLULAR BARRIERS - RELEVANCE IN TOXICOLOGY AND DRUG DELIVERY SYSTEMS" all the proposed objectives were achieved. Several types of fluorescent nanoparticles with dimensions below 100 nm (e.g. TiO_2, PLGA, gold and iron nanoparticles) were purchased, as well as the cell lines necessary to obtain the four cell models of biological barriers (skin, pulmonary, intestinal and blood-brain barriers). All nanoparticles tested had very low toxicity at concentrations below 100 μg/mL, the cells preserving a morphology characteristic to the cellular type, comparable to that of the control. Inflammation was induced by magnetic nanoparticles in the intestinal model, as well as in the case of the blood-brain barrier model after the incubation with PLGA nanoparticles. The analysis of nanoparticles' transport through cellular models showed an increased permeability in the case of skin and blood-brain barriers for PLGA and gold nanoparticles, respectively. Also, P-glycoprotein expression increased in the case of titanium dioxide nanoparticles within the epidermal model. These results were correlated with the predictions of structure-activity relationship, building in silico models that highlighted nano-bio interactions during the transport of nanoparticles through biological barriers.

Episkin™ model	*Control*	*TiO_2 NPs*	*Chitosan NPs*
P-gp expression			
Actin cytosckeleton			



Dissemination and performance indicators:

one WEB page with the project' s description

https://unibuc.ro/cercetare/promovarea-rezultatelor-cercetarii/proiecte-de-cercetare/proiecte-cu-finantare-nationala/trans-nano-bio/?lang=en

6 abstracts presented at international conferences

1. Voicu S., Voinea I.C., Niculescu A., Mihaescu D., Grumezescu A., Stan M. "*Characterizing the biological behavior of Fe_3O_4 nanoparticles conjugated with acridine orange using in vitro co-culture systems relevant to skin, lung and gut barrier models*", in Proceedings of the 4th International Electronic Conference on Applied Sciences, 27 October–10 November 2023, MDPI: Basel, Switzerland, Online. https://sciforum.net/paper/view/15411
2. Adeniyi, B., Pieraccini, L., Cirstea, G., Vilcoci, S., Mernea, M., Stan M. "*Evaluation of the anti-cancer activity of Goji leaves extracts against HT-29-MTX colon cancer cell line*", in Proceedings of the 4th International Electronic Conference on Foods, 15–30 October 2023, MDPI: Basel, Switzerland, Online. https://sciforum.net/paper/view/15016
3. Dula A.G., Stan M.S. "*Fluorescent PLGA nanoparticles: in vitro toxicity study using a co-culture of human keratinocytes and dermal fibroblasts*", NanoInnovation2023, 18-22 September 2023, Rome, Italy.
4. Voicu S.N., Voinea I.C., Gosee C., Carteret C., Callewaert M., Moreau J., Chuburu F., Stan M.S. "*Biocompatibility evaluation of chitosan fluorescent nanohydrogels using human*

EpiDerm™ 3D model". Toxicology Letters 384S1 (2023) S73-S300, p. S120-121. The 57th Congress of the European Societies of Toxicology (EUROTOX 2023), Ljubljana, Slovenia, 10 –13 September 2023.

5. Voinea I.C., Voicu S.N., Mernea M., Miu B.A., Serban M.V., Stan M.S. "*Prediction of respiratory toxicity induced by P25 Degussa nanoparticles using human EpiAirway™ 3D model*". Toxicology Letters 384S1 (2023) S73-S300, p. S172. The 57th Congress of the European Societies of Toxicology (EUROTOX 2023), Ljubljana, Slovenia, 10 –13 September 2023.
6. Voinea I.C., Voicu S., Mernea M., Miu B., Serban M., Stan M. "*Using EpiDermTM to evaluate the toxic effects of P25 Degussa nanoparticles on skin barrier*", in Proceedings of the 4th International Online Conference on Nanomaterials, 5–19 May 2023, MDPI: Basel, Switzerland, Online. https://sciforum.net/paper/view/14460

3 articles published in ISI journals

1. Burdusel A-C, Neacsu IA, Birca AC, Chircov C, Grumezescu A-M, Holban AM, Curutiu C, Ditu LM, Stan M, Andronescu E. Microwave-assisted hydrothermal treatment of multifunctional substituted hydroxyapatite with prospective applications in bone regeneration. *J. Funct. Biomater.* 2023, 14(7), 378. Impact Factor: 4,8; Q2. https://doi.org/10.3390/jfb14070378

2. Marinescu G, Culita DC, Mocanu T, Mitran R-A, Petrescu S, Stan MS, Chifiriuc MC, Popa M. New nanostructured materials based on mesoporous silica loaded with Ru(II)/Ru(III) complexes with anticancer and antimicrobial properties. *Pharmaceutics* 2023, 15(5),1458. Impact Factor: 5,4; Q2. https://doi.org/10.3390/pharmaceutics15051458

3. Miu BA, Voinea IC, Diamandescu L, Dinischiotu A. MRC-5 human lung fibroblasts alleviate the genotoxic effect of Fe-N co-doped titanium dioxide nanoparticles through an OGG1/2-dependent reparatory mechanism. *International Journal of Molecular Sciences* 2023, 24(7), 6401. Impact Factor: 5.6. Q2. https://doi.org/10.3390/ijms24076401