ROMANIAN ACADEMY
School of Advanced Studies of the Romanian Academy
Institute of Cell Biology and Patology „Nicolae Simionescu”

PhD THESIS SUMMARY

Innovative nanotherapeutic strategies for targeting vascular inflammation in atherosclerosis.

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SUMMARY

Keywords: atherosclerosis, vascular inflammation, resolution of inflammation, specialized pro-resolving mediators, nanotherapy, biomimetic nanoparticles, endothelial cells, vascular smooth muscle cells, macrophages.

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Published papers in ISI-indexed journals during PhD: 12 (5 as first author)

Abstracts in ISI-indexed journals: 4 (1 as first author)

Posters presented at international scientific events: 5 (first author)

Oral presentations at international scientific events: 3 (first author)

Patents: 1

Scholarships during PhD program: 2

Specializations and courses: 3

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A. Introduction and Objectives

Cardiovascular diseases (CVDs) are the leading cause of mortality in Romania, responsible for over 55% of annual deaths (National Institute of Public Health, 2024). In this context, atherosclerosis (AS), a chronic inflammatory condition of the vascular wall, plays a central role in the development of acute cardiovascular complications such as myocardial infarction or stroke. Although conventional therapies such as statins and antithrombotic agents reduce the incidence of cardiovascular events, they fail to effectively address persistent vascular inflammation, an essential component of atherosclerotic plaque progression (d'Aiello et al., 2024).

In particular, it has been shown that the failure of inflammation resolution, an active and coordinated physiological process, contributes significantly to plaque instability and disease progression (Fredman, 2019). In this context, specialized pro-resolving mediators (SPMs), such as resolvins or lipoxins, represent an emerging class of molecules capable of restoring vascular homeostasis by actively inducing inflammation resolution. However, the therapeutic use of SPMs is limited by their low stability in circulation and poor bioavailability at the site of the atherosclerotic lesion (Fredman & Serhan, 2024).

In parallel, natural compounds such as protocatechuic acid (PCA), with anti-inflammatory and antioxidant roles, have been proposed as adjuvants in combating endothelial and macrophage inflammation. Nevertheless, their therapeutic efficacy is limited by low bioavailability and nonspecific targeting (Cory et al., 2018). Nanotechnology offers an innovative solution to these challenges, facilitating targeted delivery and protection of compounds of interest in stable pharmaceutical forms (Ahmad et al., 2022).

Based on these premises, **the main objective of this doctoral thesis** was the development and characterization of **innovative nanotherapeutic platforms** for combating vascular inflammation in AS, with the following complementary mechanisms: (1) active induction of inflammation resolution by delivering SPMs or (2) inhibition of pro-atherogenic inflammatory pathways by delivering PCA.

The following specific **objectives** were proposed and achieved:

1. Characterization and testing of dextran-coated magnetic nanoparticles loaded with protocatechuic acid (MNP-Dex/PCA), aimed at inhibiting vascular inflammation by

reducing the expression of pro-inflammatory cytokines and monocyte adhesion to activated endothelial cells (ECs), in *in vitro* cellular models.

2. Development and characterization of biomimetic nanoparticles loaded with SPMs (Bio-LN/SPM) and testing their in vitro effects on the inflammatory phenotype of ECs, macrophages (Mφ), and smooth muscle cells (SMCs) involved in AS pathogenesis.

3. Evaluation of the biodistribution and acute effects of Bio-LN/SPM nanoparticles in a murine model of AS (hyperlipidemic ApoE$^{-/-}$ mice), by analyzing accumulation in the aorta, changes in the composition of circulating immune cells, and the inflammatory cytokine profile at 24 hours after administration.

4. Validation of the preclinical efficacy of the pro-resolving nanotherapeutic strategy in AS, in the ApoE$^{-/-}$ murine model, by demonstrating the therapeutic effect of Bio-LN/SPM nanoparticles on atherosclerotic lesions at two plaque progression stages, with emphasis on reducing vascular inflammation and lipid accumulation in the aorta and aortic root.

B. Structure of the thesis

The doctoral thesis is structured into two major parts:

Part I – Current state of the art includes an analysis of the literature regarding the role of inflammation in atherosclerosis (AS), the molecular mechanisms involved in its resolution, and emerging nanotherapeutic strategies that can positively influence disease progression. This part comprises six chapters that provide a solid theoretical basis for developing the two experimental directions.

Chapter 1 presents the structural and functional organization of the cardiovascular system, with emphasis on the architecture of the arterial wall and the critical role of ECs in maintaining vascular homeostasis. Imbalances that can disrupt endothelial function and contribute to the onset of vascular pathologies, such as AS, are discussed.

Chapter 2, "Inflammation in Atherosclerosis," systematically details the stages of atherosclerotic lesion progression, from endothelial activation and LDL accumulation in the

subendothelial space to foam cell formation, necrotic core development, and plaque rupture. It highlights the inflammatory processes that increase plaque vulnerability and the involved cellular elements.

Chapter 3 is dedicated to the concept of "Resolution of inflammation" as an active process with complex regulatory mechanisms, distinct from classical inflammation inhibition. A complete conceptual framework of specialized pro-resolving mediators (SPMs) such as lipoxins, resolvins, maresins, and protectins is presented, emphasizing their role in restoring tissue homeostasis. An extensive synthesis of the classes, functions, mechanisms of action, and receptors of these mediators is detailed in this chapter, forming the theoretical foundation for the pro-resolving pharmacological strategies proposed later in the experimental part of the thesis.

Chapter 4 highlights the limitations of current conventional therapies, which mainly target lipid lowering or suppression of the inflammatory response. These strategies fail to prevent the progression of atherosclerotic lesions and do not address the cause of persistent inflammation. Thus, the need for innovative therapeutic interventions capable not only of inhibiting inflammation but also activating physiological resolution mechanisms is justified, promoting restoration of vascular homeostasis.

Chapter 5 introduces the field of nanomedicine, focusing on nanotherapy applied to CVDs. The types of nanoparticles used in this context are detailed, emphasizing targeted delivery advantages and functionalization strategies designed to increase therapeutic efficacy. The concept of biomimetic nanoparticles is also presented, highlighting their potential to mimic natural cellular components to facilitate specific recognition of inflamed tissues and improve targeted distribution of therapeutic agents.

Chapter 6 explores direct applications of SPMs and their synthetic analogues in chronic inflammation and AS. It describes preclinical studies and potential research directions in which SPMs are considered promising therapies with mechanisms complementary to traditional anti-inflammatory drugs.

Part II – Original contributions is dedicated to the experimental studies performed, divided into two distinct nanotherapeutic directions:

Chapter 1 describes the development, characterization, and *in vitro* evaluation of dextran-coated magnetic nanoparticles loaded with protocatechuic acid (MNP-Dex/PCA). The study demonstrates the effectiveness of these nanoparticles in reducing pro-inflammatory cytokine expression in ECs and M1-type macrophages. Additionally, MNP-Dex/PCA inhibit NF-κB and MAPK signaling pathways and reduce monocyte adhesion to activated endothelium, supporting their potential in vascular inflammation therapy.

Chapter 2 is dedicated to a comprehensive study comprising experimental sections that promote active resolution of inflammation using biomimetic nanoparticles loaded with specialized pro-resolving mediators (Bio-LN/SPM).

- Section 1 presents the biomimetic nanoparticle synthesis process and physicochemical characterization, including composition, size, and zeta potential evaluation.
- Section 2 analyzes the *in vitro* effects of these nanoparticles on AS-relevant cell lines (ECs, Mφ, and SMCs). A significant reduction in inflammatory marker expression and promotion of an anti-inflammatory phenotype were observed.
- Section 3 focuses on the *in vivo* testing of Bio-LN/SPM in the $ApoE^{-/-}$ murine model, 24 hours post-injection. Nanoparticle distribution and acute effects on the immune profile were evaluated.
- Section 4 investigates the therapeutic impact of Bio-LN/SPM on atherosclerotic lesions in $ApoE^{-/-}$ mice at two different progression stages (4 weeks and 8 weeks of high-fat diet), highlighting reductions in systemic and local inflammation and lipid accumulation, as well as induction of a pro-resolving phenotype in plaque-associated Mφ.

Thus, the structure of the thesis reflects an integrated and progressive approach, from a detailed understanding of AS pathology and molecular processes involved in inflammation and resolution, to the experimental development and validation of innovative therapeutic solutions. Each chapter logically and scientifically contributes to strengthening the research hypothesis and demonstrating the applicability of nanomedicine in personalized treatment of vascular inflammation associated with AS.

C. Main results and conclusions:

1. Development of MNP-Dex/PCA magnetic nanoparticles as theranostic vehicles combining diagnosis and therapy in a single platform

- Stable colloidal nanoparticles were obtained, in which PCA was efficiently adsorbed onto the nanoparticle surface and maintained in active form.
- MNP-Dex/PCA were efficiently taken up by endothelial cells and pro-inflammatory M1 macrophages, without cytotoxic effects at concentrations < 100 μg/mL.
- Treatment with MNP-Dex/PCA led to:
    - Inhibition of inflammatory signaling pathways NF-κB and MAPK with reduced expression of IL-1β, TNF-α, IL-6, MCP-1, p38, and ERK1/2.
    - Decreased monocyte adhesion to activated endothelium.

These data confirm the potential of these nanoparticles to inhibit the vascular inflammatory response, opening the possibility of their use in preventing the progression of atherosclerotic plaque.

2. Development and preclinical validation of biomimetic nanoparticles loaded with specialized pro-resolving mediators in a murine model of atherosclerosis

- Nanoemulsions coated with cellular membranes were obtained to mimic the structure of circulating monocytes, with SPMs as active cargo (Bio-LN/SPM).
- *In vitro*, Bio-LN/SPM:
    - Reduced inflammatory marker expression (VCAM-1, MCP-1, NLRP3, IL-1β),
    - Promoted a pro-resolving M2 phenotype in macrophages (decreased iNOS and increased phagocytic capacity),
    - Decreased monocyte adhesion and transmigration through activated endothelium.
- *In vivo* (ApoE$^{-/-}$ mice fed a high-fat diet):
    - Intravenous administration of Bio-LN/SPM led, after 24 hours, to:
        - Reduction of circulating monocytes and neutrophils,
        - Decreased plasma levels of cytokines (IFN-γ, CXCL10, IL-16, TIMP-1, and TNF-α) and chemokines (MCP-1 and C5a),
        - Selective accumulation in the aorta

- Repeated administration at two different stages of plaque progression demonstrated:
  - Reduced systemic inflammation and modulation of circulating immune populations,
  - Decreased local inflammation and induction of a pro-resolving M2 phenotype in aortic macrophages, shown by increased expression of CD206 and MerTK markers, along with decreased iNOS levels,
  - Reduced lipid accumulation in lesions

These results confirm that Bio-LN/SPM not only inhibit inflammation but also promote its resolution, reprogramming the immune phenotype and the aortic microenvironment.

D. Original contributions of the thesis

1. Development of two nanotherapeutic platforms with complementary mechanisms, validated in vitro or in vivo, for combating vascular inflammation:

a) MNP-Dex/PCA – anti-inflammatory effect via inhibition of NF-κB and MAPK (Figure 1).

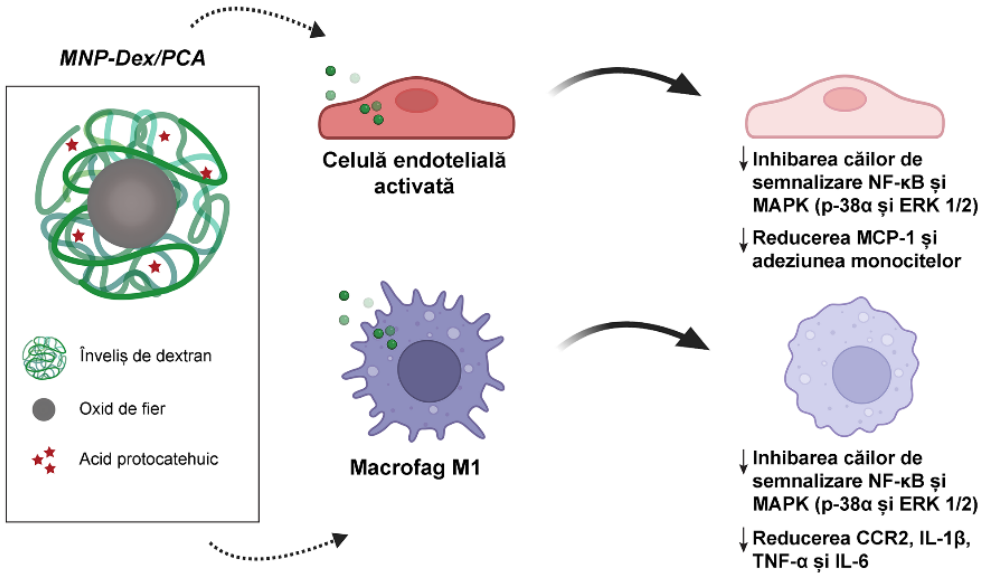

Figure 1. Nanotherapeutic strategy developed in the first study for combating vascular inflammation associated with AS. The scheme illustrates the mechanism of action of dextran-coated magnetic nanoparticles loaded with protocatechuic acid (MNP-Dex/PCA), which are internalized by ECs and M1-type MΦ, leading to inhibition of inflammatory signaling pathways (NF-κB and MAPK p38α and ERK1/2) and reduced monocyte adhesion.

b) Bio-LN/SPM – pro-resolving effect, via induction of an M2 phenotype in macrophages, decreased inflammatory markers, and reduced lipid deposits in the atherosclerotic plaque (Figure 2).

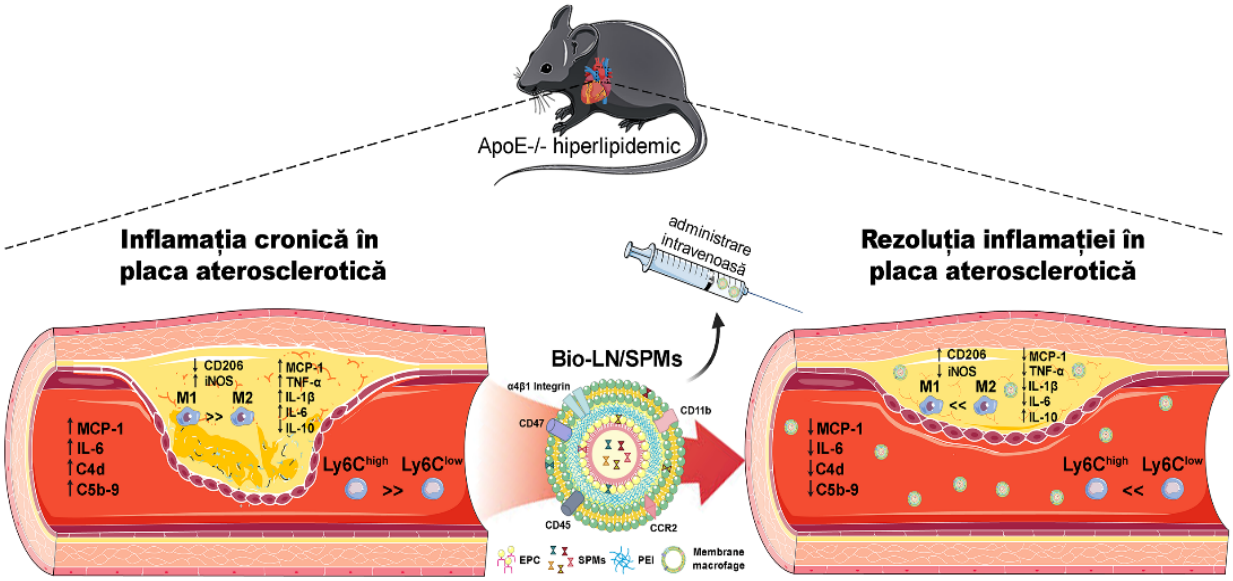

Figure 2. Schematic representation of the nanotherapeutic strategy developed in the second study to promote the resolution of vascular inflammation associated with AS. The effect of biomimetic nanoparticles loaded with specialized pro-resolving mediators (Bio-LN/SPM) on ECs, vascular SMCs, and MΦ in the hyperlipidemic ApoE−/− murine model is illustrated. Treatment with Bio-LN/SPM results in reduced expression of circulating and local inflammatory markers, induction of a reparative phenotype in MΦ, and decreased lipid accumulation in atherosclerotic lesions.

2. Confirmation of the role of inflammation resolution in AS control and validation of SPMs as viable therapeutic agents in cardiovascular nanomedicine.

E. General conclusions

This thesis makes a significant contribution to understanding and treating chronic vascular inflammation in the context of AS, proposing two complementary nanotherapeutic approaches. While MNP-Dex/PCA inhibit pro-atherogenic inflammatory pathways, Bio-LN/SPM actively promote inflammation resolution—a key process largely overlooked in current treatments. Through these strategies, the work demonstrates the applicability of nanomedicine in personalized cardiovascular therapy, opening new avenues for early and targeted intervention in AS.

F. References

1. Ahmad, M. Z., Bhatnagar, D., Ladhe, S., Kumar, D., Pathak, K., Das, R. J., Sarma, H., & Mustafa, G. (2022). Liposomes and Niosomes for Targeted Drug and Gene Delivery Systems. In *Nanotechnology in the Life Sciences*. https://doi.org/10.1007/978-3-031-12658-1_12
2. Cory, H., Passarelli, S., Szeto, J., Tamez, M., & Mattei, J. (2018). The Role of Polyphenols in Human Health and Food Systems: A Mini-Review. In *Frontiers in Nutrition* (Vol. 5). https://doi.org/10.3389/fnut.2018.00087
3. d'Aiello, A., Filomia, S., Brecciaroli, M., Sanna, T., Pedicino, D., & Liuzzo, G. (2024). Targeting Inflammatory Pathways in Atherosclerosis: Exploring New Opportunities for Treatment. *Current Atherosclerosis Reports*, *26*(12), 707–719. https://doi.org/10.1007/s11883-024-01241-3
4. Fredman, G. (2019). Can Inflammation-Resolution Provide Clues to Treat Patients According to Their Plaque Phenotype? *Frontiers in Pharmacology*, *10*(MAR). https://doi.org/10.3389/fphar.2019.00205
5. Fredman, G., & Serhan, C. N. (2024). Specialized pro-resolving mediators in vascular inflammation and atherosclerotic cardiovascular disease. In *Nature Reviews Cardiology*. https://doi.org/10.1038/s41569-023-00984-x
6. Institutul Național de Sănătate Publică. (2024). *Analiză de situație privind problematica bolilor cardiovasculare*.

EFFICIENCY AND DISSEMINATION OF RESEARCH

Papers published in ISI-indexed international journals (12 papers)

First author (5):

1. **Anghelache, M.**, Turtoi, M., Petrovici, A.R., Fifere, A., Pinteala, M., Calin, M., 2021. Development of Dextran-Coated Magnetic Nanoparticles Loaded with Protocatechuic Acid for Vascular Inflammation Therapy. Pharmaceutics 13, 1414. https://doi.org/10.3390/pharmaceutics13091414. **Impact factor at the time of publication (2021): 4.9.**

2. Turtoi, M.#, **Anghelache, M.**#, Bucatariu, S.-M., Deleanu, M., Voicu, G., Safciuc, F., Manduteanu, I., Fundueanu, G., Simionescu, M., Calin, M., 2021. A novel platform for drug testing: Biomimetic three-dimensional hyaluronic acid-based scaffold seeded with human hepatocarcinoma cells. International Journal of Biological Macromolecules 185, 604–619. https://doi.org/10.1016/j.ijbiomac.2021.06.174. **Impact factor at the time of publication (2021): 7.7.**

3. Movileanu, C.#, **Anghelache, M.**#, Turtoi, M., Voicu, G., Neacsu, I.A., Ficai, D., Trusca, R., Oprea, O., Ficai, A., Andronescu, E., Calin, M., 2022. Folic acid-decorated PEGylated magnetite nanoparticles as efficient drug carriers to tumor cells overexpressing folic acid receptor. International Journal of Pharmaceutics 625, 122064. https://doi.org/10.1016/j.ijpharm.2022.122064. **Impact factor at the time of publication (2022): 5.3.**

4. **Anghelache, M.**, Voicu, G., Deleanu, M., Turtoi, M., Safciuc, F., Anton, R., Boteanu, D., Fenyo, I.M., Manduteanu, I., Simionescu, M., Calin, M., 2024. Biomimetic Nanocarriers of Pro-Resolving Lipid Mediators for Resolution of Inflammation in Atherosclerosis. Adv Healthcare Materials 13, 2302238. https://doi.org/10.1002/adhm.202302238. **Impact factor at the time of publication (2024): 10.**

5. **Anghelache, M.**, Voicu, G., Anton, R., Safciuc, F., Boteanu, D., Deleanu, M., Turtoi, M., Simionescu, M., Manduteanu, I., Calin, M., 2025. Inflammation resolution-based treatment of atherosclerosis using biomimetic nanocarriers loaded with specialized pro-resolving lipid mediators. Materials Today Bio 32, 101733. https://doi.org/10.1016/j.mtbio.2025.101733. **Impact factor at the time of publication (2021): 8.7.**

# - authors with equal contribution

Co-author (7):

1. Turtoi, M., **Anghelache, M.**, Patrascu, A.A., Maxim, C., Manduteanu, I., Calin, M., Popescu, D.-L., 2021. Synthesis, Characterization, and In Vitro Insulin-Mimetic Activity Evaluation of Valine Schiff Base Coordination Compounds of Oxidovanadium(V). Biomedicines 9, 562. https://doi.org/10.3390/biomedicines9050562. **Impact factor at the time of publication (2021): 3.9.**

2. Popescu, I., Turtoi, M., Suflet, D.M., Dinu, M.V., Darie-Nita, R.N., **Anghelache, M.**, Calin, M., Constantin, M., 2021. Alginate/poloxamer hydrogel obtained by thiol-acrylate photopolymerization for the alleviation of the inflammatory response of human keratinocytes. International Journal of Biological Macromolecules 180, 418–431. https://doi.org/10.1016/j.ijbiomac.2021.03.082. **Impact factor at the time of publication (2021): 7.7.**

3. Fundueanu, G., Constantin, M., Turtoi, M., Bucatariu, S.-M., Cosman, B., **Anghelache, M.**, Voicu, G., Calin, M., 2022. Bio-Responsive Carriers for Controlled Delivery of Doxorubicin to Cancer Cells. Pharmaceutics 14, 865. https://doi.org/10.3390/pharmaceutics14040865. **Impact factor at the time of publication (2022): 4.9.**

4. Turtoi, M., **Anghelache, M.**, Patrascu, A.A., Deleanu, M., Voicu, G., Raduca, M., Safciuc, F., Manduteanu, I., Calin, M., Popescu, D.-L., 2022. Antitumor Properties of a New Macrocyclic Tetranuclear Oxidovanadium(V) Complex with 3-Methoxysalicylidenvaline Ligand. Biomedicines 10, 1217.

https://doi.org/10.3390/biomedicines10061217. **Impact factor at the time of publication (2022): 3.9.**

5. Voicu, G., Mocanu, C.A., Safciuc, F., **Anghelache, M.**, Deleanu, M., Cecoltan, S., Pinteala, M., Uritu, C.M., Droc, I., Simionescu, M., Manduteanu, I., Calin, M., 2023. Nanocarriers of shRNA-Runx2 directed to collagen IV as a nanotherapeutic system to target calcific aortic valve disease. Materials Today Bio 20, 100620. https://doi.org/10.1016/j.mtbio.2023.100620. **Impact factor at the time of publication (2023): 8.7.**

6. Voicu, G., Mocanu, C.A., Safciuc, F., Rebleanu, D., **Anghelache, M.**, Cecoltan, S., Droc, I., Simionescu, M., Manduteanu, I., Calin, M., 2024. VCAM-1 targeted nanocarriers of shRNA-Smad3 mitigate endothelial-to-mesenchymal transition triggered by high glucose concentrations and osteogenic factors in valvular endothelial cells. International Journal of Biological Macromolecules 281, 136355. https://doi.org/10.1016/j.ijbiomac.2024.136355. **Impact factor at the time of publication (2024): 7.7.**

7. Motelica, L., Voicu, G., Chircov, C., Surdu, A.V., Trusca, R.D., Vasile, B.S., Ficai, D., Oprea, O.C., Marta, D.S., Peteu, V.-E., **Anghelache, M.**, Ficai, A., Calin, M., 2025. Aspartic acid functionalized magnetic nanoparticles for enhanced internalization in tumoral cell. J Aust Ceram Soc 61, 265–283. https://doi.org/10.1007/s41779-024-01102-x. **Impact factor at the time of publication (2021): 1.8.**

Abstracts published in ISI-indexed journals – 4 (1 first author)

1. **Anghelache, M.**, Deleanu, M., Anton, R., Turtoi, M., Voicu, G., Mândușeanu, I., Simionescu, M., Călin, M., 2023. Pro-resolving lipid mediator-loaded biomimetic nanoparticles as promising carriers for inflammation resolution in atherosclerosis. Talks. FEBS Open Bio 13, 2–60. https://doi.org/10.1002/2211-5463.13645.

2. Voicu, G., **Anghelache, M.**, Deleanu, M., Turtoi, M., Safciuc, F., Anton, R., Mândușeanu, I., Simionescu, M., Călin, M., 2023. Dual targeting of resolvins-loaded nanoparticles to VCAM-1 and collagen IV assure their delivery to the aorta of

atherosclerotic mice, 2023. FEBS Open Bio 13, 61–258. https://doi.org/10.1002/2211-5463.13646

3. Boteanu, D., **Anghelache, M.**, Turtoi, M., Călin, M., 2025. Enhancing tumor drug delivery: targeting nucleolin with liposomes for improved therapeutic efficacy. SEE J Immunol 8, 067. https://doi.org/10.3889/seejim.2025.6130.

4. Turtoi, M., **Anghelache, M.**, Voicu, G., Safciuc, F., Deleanu, M., Călin, M., 2025. Innovative vanadium (V)-based drug: preliminary in vitro and in vivo antitumor investigations. SEE J Immunol 8, 078. https://doi.org/10.3889/seejim.2025.6141.

REGISTERED PATENTS

1. Patent application no. A/00388, filed with the State Office for Inventions and Trademarks (OSIM) on 20.07.2023, titled "Smart magnetic nanosystems for cellular vectorization of bioactive compounds", authors: Movileanu C., Ficai D., Ficai A., Calin M., **Anghelache M.**, Gafencu A., Fundueanu-Constantin G., Pinteala M., Simionescu M., Andronescu E.
(https://osim.ro/images/Publicatii/Inventii/2025/bopi_inv_01_2025.pdf).

PRESENTATIONS AT INTERNATIONAL SCIENTIFIC EVENTS:

Oral Presentations (3):

1. **Maria Anghelache**, Preparation and characterization of macrophage-membrane coated nanoemulsions for delivery of specialized pro-resolving lipid mediators of inflammation, 38th Annual Scientific Session of The Romanian Society for Cell Biology, 4 November 2021.

2. **Maria Anghelache**, Pro-resolving Lipid Mediators-loaded Biomimetic Nanoparticles as Promising Carriers for Inflammation Resolution in Atherosclerosis, The 47th FEBS Congress, Oral presentation, Tours, France, 8-12 July 2023.

3. **Maria Anghelache**, Macrophage Membranes-Functionalized Lipid Nanoemulsions as Promising Carriers of Pro-Resolving Lipid Mediators to Atherosclerotic Lesions, 40th Annual Scientific Session of The Romanian Society for Cell Biology, Oral presentation, 16-17 November 2023.

Posters (5):

1. **Maria Anghelache**, Florentina Safciuc, Geanina Voicu, Mihaela Turtoi, Cornelia Ioana Ilie, Anton Ficai, Manuela Calin, Chitosan-coated iron oxide nanoparticles as a promising nanocarriers for gallic acid targeted delivery, "International Conferences & Exhibition on Nanotechnologies, Organic Electronics & Nanomedicine", Thessaloniki, 06-09 July 2021.
2. **Maria Anghelache**, Mariana Deleanu, Mihaela Turtoi, Geanina Voicu, Manuela Calin, Preparation and physico-chemical characterization of specialized pro-resolving lipid mediators (SPMs)-loaded nanoemulsions as nanocarriers for inflammation resolution, "International Conferences & Exhibition on Nanotechnologies, Organic Electronics & Nanomedicine", Thessaloniki, 6-9 July 2021.
3. **Maria Anghelache**, Mariana Deleanu, Mihaela Turtoi, Geanina Voicu, Manuela Calin, Development of Biomimetic Nanocarriers for delivery of Specialized Pro-Resolving Lipid Mediators (SPMs) to atherosclerotic plaque, "Materials, Methods & Technologies", Burgas, Bulgaria, 19-22 August 2022.
4. **Maria Anghelache**, Mariana Deleanu, Ruxandra Anton, Mihaela Turtoi, Geanina Voicu, Ileana Manduteanu, Maya Simionescu, Manuela Calin, Development of Biomimetic Nanocarriers for Delivery of Pro-Resolving Mediators to Atherosclerotic Plaque, "The 39th Annual Scientific Session of The Romanian Society for Cell Biology", 21-23 October 2022.
5. **Maria Anghelache**, Mariana Deleanu, Ruxandra Anton, Mihaela Turtoi, Geanina Voicu, Ileana Manduteanu, Maya Simionescu, Manuela Calin, Specialized pro-resolving mediators (SPMs)-loaded Nanoemulsions as promising biomimetic nanocarriers for inflammation resolution, The 47th FEBS Congress, Tours, France, 8-12 July 2023.

AWARDS OBTAINED DURING THE DOCTORAL PROGRAM

1. **Gold Medal –** Smart nanoparticle systems for cellular internalization, Authors: Movileanu C., Ficai D., Ficai A., Calin M., **Anghelache M.**, Gafencu A., Fundueanu-

Constantin G., Pinteala M., Simionescu M., Andronescu E.; Traian Vuia International Exhibition of Inventions and Innovations, 12–14 October 2021, Timișoara, Romania.

2. **Gold Medal** – Smart nanoparticle systems for cellular internalization, Authors: Movileanu C., Ficai D., Ficai A., Calin M., **Anghelache M.**, Gafencu A., Fundueanu-Constantin G., Pinteala M., Simionescu M., Andronescu E.; International Exhibition of Scientific Research, Innovation and Inventions "PRO INVENT" – 19th Edition, 20–22 October 2021, Cluj-Napoca, Romania.
3. **Gold Medal –** Inventions, Plant Varieties, Industrial Design – Smart nanoparticle systems for cellular internalization**,** Autori: Movileanu C., Ficai D., Ficai A., Calin M., **Anghelache M.**, Gafencu A., Fundueanu-Constantin G., Pinteala M., Simionescu M., Andronescu E.; International Specialized Exhibition "INFOINVENT 2021" – 17th Edition, 17–20 November 2021, Chișinău, Republic of Moldova.

SPECIALIZATIONS AND COURSES COMPLETED DURING THE DOCTORAL PROGRAM

1. The course „**Flow Cytometry Training School**". Romanian Cytometry Association, Bucharest, 14–15 December 2020.
2. 9th International Lab Animal Course Crete (**FELASA**), Crete, Heraklion, May–June 2023.
3. **Secondment – CARDIOSCOPE:** "Comprehensive and personalized assessment of acute coronary syndrome by multiomic approach and artificial intelligence strategy", HORIZON-MSCA-2021-SE-01, Multimedica, Milan, 12 March – 11 April 2025.

SCHOLARSHIPS OBTAINED DURING THE DOCTORAL PROGRAM

1. Doctoral scholarship: Romanian Academy (SCOSAAR): 2020–2025
2. Scholarship for participation in the FEBS Congress (2023)

COLABORĂRI ÎN PROIECTE DE CERCETARE

1. **PN-II-P4-ID-PCE-2020-2465** – "Targeted nanocarrier-based therapy for inflammation resolution in atherosclerosis (NANORES)", project director Dr. Manuela Calin.
2. **PN-III-P1-1.2-PCCDI-2017-0697** – "Smart therapies for non-communicable diseases, based on controlled release of pharmacological compounds from encapsulated cells after genetic manipulation or targeted bionanoparticles (INTERA)", project director: Acad. Maya Simionescu, component project 3 "Smart nanobioparticles designed for the vectorization of bioactive compounds for vascular inflammation therapy" coordinator: Dr. Manuela Calin.
3. **PNRR-III-C9-2022-I8-CF93** – "New nanotherapeutic strategies targeting mechanisms involved in fibroblast-to-myofibroblast transition for the treatment of cardiac fibrosis (HeartCure)", project director Dr. Rostyslav Billy, scientific coordinator of the host institution Dr. Manuela Calin.
4. **ERANET-NANOTECMEC-Ctr. nr. 92/2025** – "Nanovehicles for Ago/antagomiR delivery used for immunomodulation: a potential approach in cancer and lung transplant therapy (SAIL)", project director Dr. Rostyslav Billy.
5. **H2020-EU.1.2.-AMD-861878-17 (2025)** – „Development of "smart" amplifiers of reactive oxygen species specific to aberrant polymorphonuclear neutrophils for treatment of inflammatory and autoimmune diseases, cancer and myeloablation (NeutroCure)", project director Prof. Dr. Andriy Mokhir.