# 40 years on route from cell biology to molecular medicine

# DEPARTMENT OF BIOPATHOLOGY AND THERAPY OF INFLAMMATION



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**INTERESTS** 

# Major position/appointments

- Deputy Director
- Associate member of the Romanian Academy
- Member of The Romanian Academy of Medical Sciences
- Member of the Scientific Council of ICBP "N. Simionescu"
- PhD Advisor in Biology
- Expert evaluator of the national and international grants
- Peer reviewer at national and international journals

# MAJOR RESEARCH

- To identify the specific mechanisms of valvular disease progression and the development of new nanobiotherapeutics for diabetes-aortic valve disease
- To identify relevant and specific biomarkers for vascular inflammation associated with atherosclerosis and diabetes as targets for nanotherapy
- Design of novel drug delivery systems to specifically target inflammation

### **PUBLICATIONS**

Over 80 original articles (>1100 citations) were published in Web of Sciences Core Collection journals and 5 book chapters between 1979-2019 by researchers of the Department.

# PREVIOUS PROJECTS RELEVANT PUBLICATIONS

- Surface alteration of blood platelets in diabetes mellitus (Lupu C, Calb M, Atherosclerosis, 1988; C Lupu et al., Platelets, 1992; J Mol Cell Cardiol, 1993; Platelets, 1994).
- Structure and function of valvular endothelial cells in normal pathological conditions (Mânduțeanu I. et al., J Mol Cell Cardiol, 1988).
- Interaction of valvular endothelial cells with blood cells (Mânduțeanu I. et al., J SubmicroscCytolPathol, 1992; Lupu C. et al., Platelets, 1993; Mânduțeanu I. et al., Endothelium, 1999).
- The use of liposomes as drug delivery carriers (Voinea M. et al., Vascular Pharmacol, 2002; Voinea M. et al., J Cell Mol Med, 2002; Voinea M. et al., Eur J Pharmacol, 2004; Voinea M. et al., Pharm Res, 2005; Voinea M, Călin M. et al., Cell Tiss Res, 2009; Tucureanu MM et al., Int J Nanomedicine, 2017).
- Mechanisms involved in the effects of antiinflammatory drugs on activated endothelial cells (Mânduțeanu I. et al., Pharmacology, 2002; Eur J Pharmacol 2003, Mânduțeanu I et al. Pharmacology, 2007; Dragomir E. et al., J Diab Complications, 2004).
- Modulation of MCP-1 and fractalkine expression by high glucose conditions in vascular cells: effects of anti-inflammatory drugs (Dragomir E. et al., Vascular Pharmacol, 2006; Dragomir E. et al., Thromb Haemost, 2008).

- Molecular links between chronic inflammation and accelerated atherosclerosis: role of resistin and chemokines (fractalkine and CXCL16); new avenues for targeted therapy (Mânduţeanu I et al, Biochemical and Biophysical Research Communications, 2009; Manduteanu I et al, Biochemical and Biophysical Research Communications, 2010; Stan D et al, Cell Tissue Res, 2011).
- Molecules and mechanisms involved in cytokine and chemokine-dependent vascular inflammation as targets for nanotherapeutic strategies (Butoi ED et al, 2011, Biochim Biophys Acta; Manduteanu I, Simionescu M,2012, J Cell Mol Med; Pîrvulescu M et al, 2012, Biochemical and Biophysical Research Communications Journal: Gan AM et al,2013, Cell Tissue Res; Gan AM et al, 2013, J Cell Biochem; Pirvulescu MM et al, 2014, Int J Biochem Cell Biol.; Gan AM et al, 2014, FEBS J.; Butoi E et al, 2014, Crit Rev Eukaryot Gene Expr: Simion V et al., Mediators Inflamm, 2016; Butoi E et al., BiochimBiophys Acta, 2016, *Tucureanu MM et al., Cytokine, 2016).*
- Nanoparticles designed to target chemokine-related inflammatory processes in vascular diseases and cancer metastasis (Simion V et al., Journal of Nanoparticle Research, 2013; Calin M et al., Eur J Pharm Biopharm, 2015, Roblek M et al., J Control Release, 2015, Schlesinger M et al., Int J Clin PharmacolTher, 2015, Calin M, John Wiley & Sons, Inc., Hoboken, NJ, USA, 2012, Călin M et al., European Patent no. EP 2832373).
- Toxicological studies and the inflammatory response induced by the exposure of human cells to Ag/TiO<sub>2</sub> nanoparticles developed for leather surface functionalization (in collaboration with National Institute for Research and Development of Textiles and Leather, Bucharest Romania and Minho University, Portugal) (Rebleanu D et al., Toxicology, 2019; Rodino S et al., Banat's Journal of Biotechnology, 2017, European Patent: application no: 17464014.4-1102, OSIM patent application no. A/00966).
- Investigation of cytotoxicity and gene transfection ability of non-viral vectors

- obtained bv covalent coupling hyperbranched PEI chains (Mw 2 kDa) with different core molecules using cultured cells collaboration with Institute Macromolecular Chemistry "Petru Pomi, Iasi, Romania) (Uritu CM et al., J. Mater. Chem. B. 2015a; Uritu CM et al., J. Mater. Chem. B, 2015b; Marin L et al., ACS Biomater. Sci. Eng., 2016: Dascălu AI et al., J. Mater. Chem. B. 2017; Simionescu BC et al., Mater. Sci. Eng. C. 2017; David G et al, Polym. Chem., 2018).
- MicroRNA signature of vascular cells cross-talk relevant for the atherosclerotic plaque rupture in patients with type II diabetes (Macarie RD et al., 2018)

## **PATENTS**

- European Patent no. EP2832373, inventors Bendas G, Borsig L, Calin M, Cevher E, Enachescu M, Gok MK, Hoffmann A, Mihaly M, Pabuccuoglu SK, Simionescu M, Schlesinger M, Zeisig R: "Liposome for blocking site-specifically chemokine-related inflammatory processes in vascular diseases and metastasis"
- European Patent: application no: 17464014.4-1102, inventors: Gaidau C, Călin M, Constantinescu CA, Rebleanu D, Stoica T: "Leather with anti-microbial and self-cleaning properties and process for obtaining therof"
- OSIM, application no. A/00966, inventors: Gaidau C, Călin M, Constantinescu CA, Rebleanu D, Stoica: "Leather with antimicrobial and self-cleaning properties and process for obtaining therof"
- OSIM application no A/00811, inventors Călin M, Rebleanu D, Constantinescu CA, Voicu G, Deleanu M, Mânduțeanu I: "Process for obtaining the nanocarriers for targeted delivery of interference ribonucleic acid (RNA) to aortic valve cells"
- OSIM application no A/01055, inventors: Ficai D, Ardelelean I, Ilie C, Călin M, Fuior EV, Fifere A, Pinteală M, Fundueanu-Constantin G, Ficai A, Simionescu M, Andronescu E: "Vertical magnetic (electro) separator of isomagnetic nanoparticles"