

# DEPARTMENT OF PATHOPHYSIOLOGY AND PHARMACOLOGY



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## *Major positions and appointments*

- Principal Investigator Grade I
- Member of the Scientific Council of ICBP ‘Nicolae Simionescu’
- Ph.D. Coordinator
- Supervision of Graduate Students and Postdoctoral Fellows
- Expert Evaluator of the Biology, Biochemistry and Pharmacy Commission of the National Council for the Certify of Titles, Diplomas and University Certifications (CNATDCU) (2012)
- Expert Evaluator of the National and International Grants
- Peer Reviewer for International Scientific Journals

## *MAJOR RESEARCH INTERESTS*

- **Microparticles as biomarkers, biological vectors for microRNAs and potential biomedical tools modulating atherosclerosis: role of the extracellular vesicles released from adipose tissue-derived stem cells and bone marrow mesenchymal stem cells in the macrophage polarization, and reversion of endothelial dysfunction and cardiac hypertrophy**
- **Endothelial progenitor cell dysfunction and platelet-endothelial progenitor cell interplay in atherosclerotic disease**
- **Atherosclerosis-associated diabetes mellitus and aortic valve disease: relationships between plasma biochemical parameters, circulating endothelial progenitor cells and early structural/functional alterations; establishing potential therapy**
- **Diabetes mellitus and obesity - associated cardiovascular alterations: microRNA expression profile in disease development, macrophage involvement in pancreatic beta cell response to metabolic stress**

## *PUBLICATIONS*

Over 110 original articles (>2300 citations) were published in Web of Sciences Core Collection journals, 3 books and 14 book chapters between **1979-2019** by researchers of the Pathophysiology and Pharmacology Department.

## SELECTED NEW FINDINGS OF THE DEPARTMENT

- In experimental hyperlipemia-hyperglycemia administration of L-arginine improves the microangiopathic changes of coronaries and enhances vasodilation of resistance arteries

- Enoxaparin restores the vascular reactivity of resistance arteries in ageing and diabetes

- Nebivolol has a reversible vasodilator effect on renal arteries

- Obesity alone or obesity associated with Type 2 diabetes alters human periumbilical adipose tissue arterioles in terms of structure, function and biochemistry, including diminished eNOS expression and reduced levels of IRS-1, IRS-2, PI3K and Akt in the insulin signaling pathway.

- Sera of obese type 2 diabetic patients undergoing metabolic surgery instead of conventional treatment exert beneficial effects on beta cell survival and function.

- Treatment with free fatty acids designed to limit oxidative stress, endoplasmic reticulum stress, inflammation and apoptosis may point toward novel strategies for improving beta cell function under saturated conditions.

- CO<sub>2</sub> laser increases the regenerative capacity of human adipose-derived stem cells by a mechanism involving the redox state and enhanced secretion of pro-angiogenic molecules.

- In a hypertensive-hypercholesterolemic hamster model, the endothelial progenitor cell-based therapy suppresses the development of atherosclerosis and reduces hepatic lipid and macrophage accumulation with the consequent alleviation of dyslipidemia and hypertension.

- Irbesartan administration therapeutically influences platelets activation, circulating endothelial progenitor cell and microparticle mobilization by involvement of pro-inflammatory cytokines in an atherosclerotic animal model and in patients with hypertension and dyslipidemia.

- Microparticles (microvesicles) and platelets of healthy origins improve

atherosclerotic endothelial progenitor cell dysfunction via microRNA transfer in a vitro model.

- Allogenic microvesicles administration of healthy origins to an atherosclerotic animal model (hypertensive-hypercholesterolemic hamster), can counteract diet induced detrimental effects on plasma, structural and functional parameters by biologically active miR-10a, miR-21, miR-126, miR-146a transfer to circulating endothelial progenitor cell mediating their vascular repair function in atherosclerosis processes.

- Early aortic valve dysfunction was detected by echocardiography after one week of diabetes in a murine model of atherosclerosis.

- The ratio between circulating microvesicles and endothelial progenitor cells as potential biomarker in hypertensive-hypercholesterolemic patients.

- Circulating microvesicles containing pro- or anti-angiogenic microRNAs play a key role in the development of vascular complications in patients with type 2 diabetes.

## PREVIOUS RESEARCH PROJECTS/ RELEVANT PUBLICATIONS

- **Biochemical mapping of endothelial cell surface: evidence for differentiated microdomains** (Ghinea N. and Simionescu N., J. Cell Biol 1985; Ghinea N. et al., J Submicrosc Cytol Pathol 1987; Leabu M. et al., J Submicrosc Cytol Pathol 1987)

- **Detection of Albumin Binding Proteins** (Ghinea N. et al., J Cell Biol 1988; Popov D., J Mol Cell Cardiol 1992)

- **Interaction of AGE-albumin with normal and diabetic capillary endothelium** (Schmidt A.M. et al., Proc Natl Acad Sci USA, 1994; Popov D. and Simionescu M. Arch Physiol Biochem 2006; Simionescu M. et al., Cell Tiss Res 2009)

- **Pathomorphological changes of micro- and macrovasculature in diabetes** (Popov

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D. et al., Acta Diabetol 1996, 1997; Simionescu M. et al., Am J Pathol 1996; Popov D. and Simionescu M., Eur Respir J 1997; Mompeo B. et al., J Submicrosc Cytol Pathol 1998; Costache G. et al., J Submicrosc Cytol Pathol 2000; Popov D. et al., Cell Tiss Res 2002; Popov D. et al., Diabetologia 2003)

• **Vascular reactivity of resistance arteries in hyperlipemia associated with hyperglycaemia** (Georgescu A. and Popov D., J Am Aging Assoc 2000; Georgescu A. et al., Fundam Clin Pharmacol 2001, 2003; Georgescu A. et al., Vasc Pharmacol 2003, 2006)

• **Mechanisms involved in nebivolol effects on renal artery in diabetes associated with hypertension** (Georgescu A. et al., Eur J Pharmacol 2005, 2008; Georgescu A. et al., Pharmacology 2007, 2008)

• **Polymorphisms of the leptin and leptin receptor gene** (Constantin A. et al., Biochem Biophys Res Commun 2010)

• **Effect of high glucose concentration/diabetes mellitus on human blood platelets** (Alexandru N. et al., Platelets 2007; Alexandru N. et al., J Cell Mol Med 2008; Alexandru N. et al., Clin Chem Lab Med 2008, Alexandru et al., Trends Cardiovasc Med 2010)

• **Contribution of circulating microparticles and platelets to human peripheral venular dysfunction: focus on chronic venous insufficiency** (Georgescu A. et al., J Thromb Haemost 2009; Alexandru N. et al., Clin Lab 2011)

• **Dysfunction of human subcutaneous fat arterioles in obesity alone or obesity associated with Type 2 diabetes** (Georgescu A. et al., Clinical Science 2011)

• **Circulating microparticles, endothelial progenitor cells and platelet activation in atherosclerosis; effects of irbersartan** (Alexandru N. et al., J Thromb Haemost 2011; Georgescu A. et al., J Thromb Haemost 2012; Alexandru N. et al., Thromb Res 2012;

Alexandru N. et al., PloS One 2013; Georgescu A. et al., Eur J Pharmacol 2013; Badila E. et al., Farmacia 2014, Andrei E. et al., Exp Clin Cardiol 2014)

• **Studies designed to find new and better ways to treat patients with diabetes: PTP1B protein expression in human aortic smooth muscle cells exposed to high glucose concentration; enoxaparin effects on adrenergic contraction of resistance arterioles; activation profile of dorsal root ganglia Iba-1 (+) macrophages** (Popov D. et al., Biochem Biophys Res Commun 2009; Georgescu A. et al., Blood Coagul Fibrin 2011; Thi Ton B-H et al., Acta Histochem 2013; Badila E. et al., Eur J Pharmacol 2015)

• **CO<sub>2</sub> laser increases the regenerative capacity of human adipose-derived stem cells by a mechanism involving the redox state and enhanced secretion of pro-angiogenic molecules** (Constantin A. et al., 2017)

• **Endothelial progenitor cells - based therapies on vascular dysfunction in diabetes and atherosclerosis** (Georgescu A. et al., Eur J Pharmacol 2011; Georgescu A. World J Diab 2011; Alexandru N. et al., Biol Cell 2015; Georgescu A. et al., Biol Cell 2016)

• **Circulating microparticles and microRNAs as biomarkers and diagnostic tools in hypertension, atherosclerosis and diabetes** (Sadri C. et al., Diabetes 2010; Alexandru N. and Georgescu A. World J Hematol 2013; Orbe J et al., Thromb Res 2015; Alexandru N. et al., Biochem Biophys Res Commun 2016; Nemezc et al., Curr Hypertens Rep 2016; Alexandru N. et al., Curr Stem Cell Res Ther 2017; Stępień EŁ. et al., Theranostic 2018; Georgescu A. et al., Acta Physiol 2018)

• **Microparticles and platelets of healthy origins improve endothelial progenitor cell dysfunction via microRNA transfer in an atherosclerotic hamster model** (Alexandru N. et al., Acta Physiol 2017)