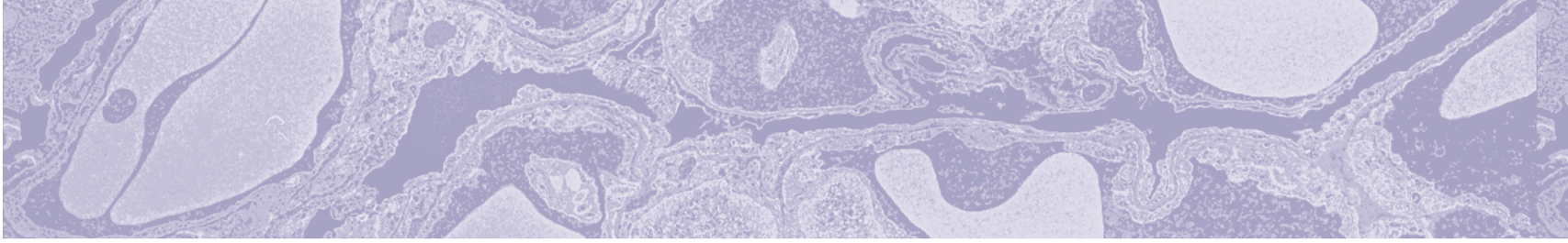
ROMANIAN ACADEMY

INSTITUTE OF CELLULAR BIOLOGY AND PATHOLOGY "NICOLAE SIMIONESCU"

ICBP 40 YEARS

AN INCREDIBLE 40-YEAR JOURNEY TO UNDERSTAND CELL'S SECRETS FOR THE BENEFIT OF HUMAN HEALTH

FUNDAȚIA NAȚIONALĂ PENTRU ȘTIINȚĂ ȘI ARTĂ
FNSA
2019
Bucharest



Credo

Cellular and molecular biology

for the benefit of the human health

ROMANIAN ACADEMY

INSTITUTE OF CELLULAR BIOLOGY AND PATHOLOGY "NICOLAE SIMIONESCU"

Center of Excellence
of the
European Community

Member Institution of
UNESCO Global Network for Molecular and Cell Biology

Center of Excellence
of the
Romanian Academy
and of the
Ministry of Education and Research

"Cultural Merit" Award - in Officer Degree
granted by the Romanian President to the
Institute of Cellular Biology and Pathology "N. Simionescu", 2004

Tribute and Honour

Pay tribute and honour
to
People and Institutions, who contributed to the
Creation, Existence and Safeguarding of ICBP

Professor ***Nicolae Simionescu***

Professor ***George E. Palade***

Professor ***Theodor Burghele***

Ambassador ***Corneliu Bogdan***

The talented Team of ICBP

National Institutes of Health, USA

Yale University, USA Columbia University, USA McGill University, Canada

Romanian Academy

Ministry of Education and Research of Romania

European Community: ICBP Centre of Excellence

A Message from the Founders

40 years of search to uncover the mysteries within the Cell

***Dear Friends**,*

It seems like yesterday, but it happened 49 years ago.

It was in 1970 when Nicolae Simionescu and I, started to do research at Rockefeller University, in New York. Facing a new culture, an untainted scientific life and a stable society we had the idea, and started to dream, to transplant the climate of a true scientific life to Romania having as model the Rockefeller University.

We aimed at creating a place where young Romanian researchers would have a chance to illustrate their talent and potential, and on a broader scale, to pioneer the emerging field of Cell Biology throughout the country.

Our idea had a short gestation phase, and a long completion period during which we had a remarkable, ten years-collaboration with Professor George Palade at Rockefeller University and Yale University, USA. It was during this time when we started to design mentally the concept of this Institute. Then we worked actively to convert the dream into reality. It was not easy.

After 9 years, the dream came true and the Institute was inaugurated on 3 September 1979. Shortly, it became a space where, under rather difficult and uninviting conditions for research, a protected scientific island was created and together with our younger collaborators, utilized all our mental power and energy to uncover the mysteries within the cell. This is because cells hide within all the secrecy of life, disease and death.

In the hostile conditions for Science and scientists during the oppressive regime, we managed to "bit the system" and were fortunate to see our dream come true and the research results valued and acknowledged.

Nicolae Simionescu left this world earlier (1995).

Dear Friends,

We present to you in this book some of our achievements of 40 years of research and where we stand today. There were difficult but rewarding and fascinating years.

I worship the past 40 years spent in the "Kingdom of Science and the World of Cells".

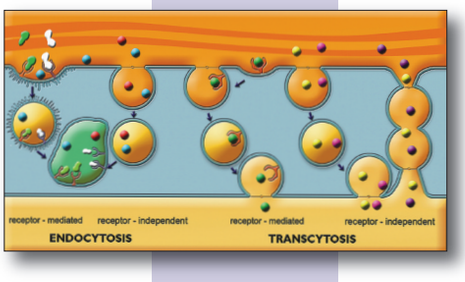
I pay reverence to all who contributed to the making, continuation and safeguarding of ICBP.

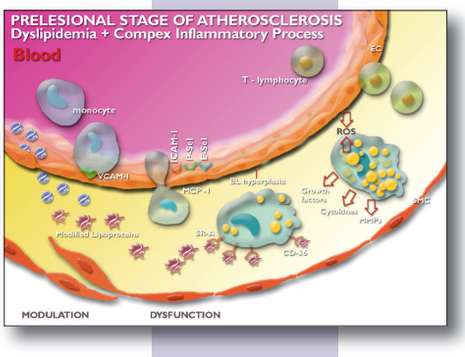
I have faith in a bright destiny for my younger collaborators and for the Institute in the years to come…

For our numerous past and present collaborators, the best wish I can think of, is to continue their inquiry into" the cell" secrets with determination and honesty and to serve Science with morals and principles. I hope they will value this as much as we have.

Acad. ***Maya Simionescu,*** *PhD*
Co-founder and Director of ICBP-NS

Summary





Werner Franke | Maya Simionescu | Gunter Blobel | Marilyn Farquhar | George Palade | Christian De Duve | Nicolae Simionescu | David Sabatini

3th September 1979

Official inauguration of ICBP

A glance into the history

1970

An idea was born in the minds of Professors Nicolae Simionescu and Maya Simionescu: a research centre for Cell Biology and Pathology should be created in Romania. They initiated this project, while in USA at the invitation of Professor George Palade with whom they had a great collaboration for 10 years at the Rockefeller University and Yale University (1970 -1979).

1971

The first draft of the Institute for Cellular Biology and Pathology (ICBP) made by Professors Nicolae Simionescu and Maya Simionescu.

1972-1979

A new building was constructed according to the design, structural and functional planning of Nicolae Simionescu and Maya Simionescu; they also obtained Fulbright fellowships for 12 young investigators to be trained in excellent laboratories in USA. Modern equipment was purchased.

1979

Official Inauguration of the Institute with a Romanian - American Workshop attended by the Nobel Prize Laureates Professors George Palade, Christian de Duve and Gunter Blobel, and by Professors Marilyn Farquhar, David Sabatini, and Werner Franke.

The Institute belonged to the Ministry of Education.

Beginning of specific projects in cell biology and pathology.

For the next 15 years, Maya and Nicolae Simionescu have maintained the position of Visiting Professors at Yale University, New Haven and Columbia University, New York, USA being for three months annually involved in teaching and research. These associations have facilitated continuation of privileged links with USA Universities and outstanding specialists in the field, keeping an open bridge for scientific exchanges and avoid isolation, as well as to obtain fellowships for ICBP researchers. During these years, numerous young investigators from ICBP were trained in prestigious American Universities.

1981

All the Romanian research funds were cut.

First application for a 3-year competitive grant to National Institute of Health (NIH)-USA was successful.

1982

Professor Nicolae Simionescu founded the Romanian Society for Cell Biology (450 members throughout the country).

First Annual Congress of the Romanian Society for Cell Biology.

1983

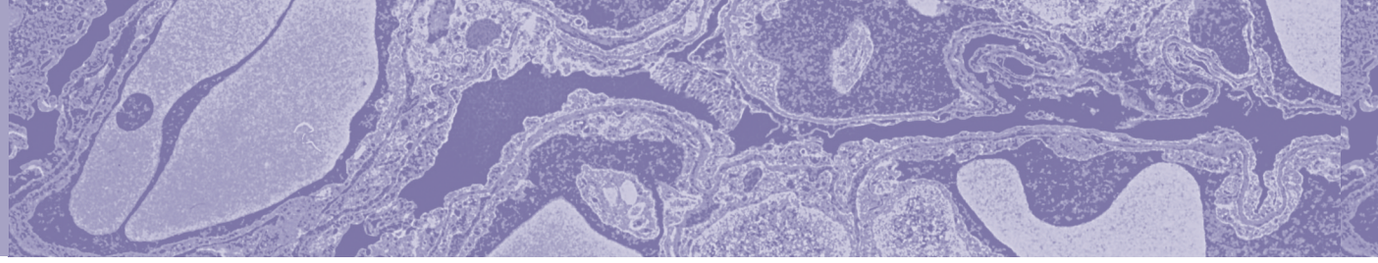
The second application for a competitive grant from NIH-USA was successful.
Second Romanian-American Workshop on "Cell Biology of the Vessel Wall".

1985

Third Romanian American Workshop on
"Cellular and Molecular Events in Atherogenesis".

1986

The third application for a competitive grant from NIH-USA was successful.



1989

***F**ourth Romanian American Workshop on "Pathobiochemistry of the Arterial Wall"*

1990

***I**CBP was affiliated to the Romanian Academy.*

***I**CBP became Member Institution of the UNESCO Global Network for Molecular and Cell Biology (UNESCO-MCBN).*

1991

***T**wo collaborative grants (for 3 years) with Prof. Samuel Silverstein and Prof. David Stern from Columbia University, New York, USA, obtained by competition from FIRCA-NIH-USA.*

Therefore, between 1981-1993 the research program of ICBP was mainly supported by competitive grants from NIH-USA.

1993

***F**unds obtained for collaborations within the European Community.*

1995

P**rofesor Nicolae Simionescu left this world. In his memory,* ***the Institute is named ICBP „Nicolae Simionescu".
***Professor Maya Simionescu became the director of the Institute**.*

1996

***T**he Institute was reconfirmed as member of UNESCO-MCBN.*

1997

***G**rant awarded by the Swiss National Science Foundation for a collaborative project.*

1999

***T**he Institute was selected Center of Excellence of the Romanian Academy.*

2000

***I**CBP "Nicolae Simionescu" was selected by competition Center of Excellence of the European Community.*

***T**he Institute was selected Center of Excellence of the Ministry of Education and Research.*

***A**dvanced Study Courses with international participation (2000-2008):"From Cellular and Molecular Biology to the Medicine of the 21st Century", Director executive: Dr. Anca Sima*

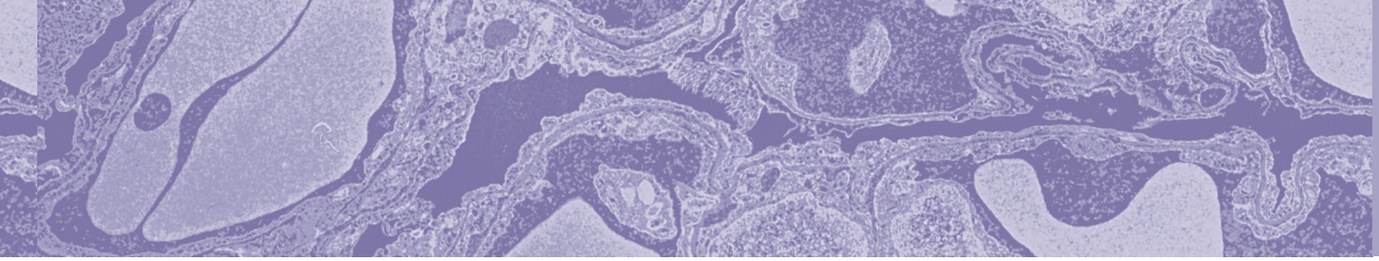
2002

***I**nternational Workshop "Cardiovascular Dysfunction in Hyperlipidemia and Diabetes" held within the framework of Center of Excellence of the European Community.*

***M**eeting of the COST Action B-17 of the European Community:" Insulin Resistance, Obesity and Diabetes Mellitus in the Elderly".*

2004

***I**nternational Anniversary Workshop - 25 years of activity of the Institute: "Cell and Molecular Biology - a key to defeat global risk diseases".*



2005

***G**rant awarded by the **E**uropean **C**ommunity FP6 Specific Support Action: "Strengthening the European Research Area by Reinforcement of Romanian Research Competency in Genomics and Proteomics of Major Global Risk Diseases: Atherosclerosis, Diabetes and its Complications"(SERA). Project Director: Maya Simionescu (950,000 Euro). Within the SERA Project (2005-2008), ICBP organized 14 international Symposia and Workshops, accommodated 113 visits of European and U.S.A. scientists to the Institute, and 83 ICBP scientists attended international congresses and inter-laboratory exchanges.*

***I**nternational Symposium "Combating Cardiovascular Diseases and Diabetes"*

***I**nternational Symposium "New Insights in Molecular Medicine"*

2006

***I**nnaugural Workshop of the "Cardio-Diabetology Research Reports and Training Unit"Combating Cardiovascular Diseases and Diabetes".*

***T**he 2nd International Congress of Cellular and Molecular Biology together with the **24**th Annual Meeting of the Romanian Society for Cell Biology.*

***I**nternational Symposium ,,Recent advances in cardio-diabetology".*

***I**nternational Symposium "Advances in Cell and Molecular Biology and Pathology".*

***I**nternational Symposium"Cell and Molecular Biology for the Benefit of Cardiovascular Disease"*

***I**nternational Symposium "Advances in gene regulation"*

***I**nternational Symposium "Molecular biomarkers of cardiovascular disease and diabetes".*

2007

***I**nternational Symposium "Advances in Gene Regulation",*

***I**nternational Symposium "Novel Trends in Cell and Molecular Biopathology"*

***I**nternational Symposium "Development of in vitro tests as an alternative to animal experiments"*

I*nternational Symposium "Stem Cells as therapeutic alternative"*

***I**nternational workshop "Inflammation-dependent vascular remodeling in atherosclerosis".*

***25**th Anniversary of the Romanian Society for Cell Biology - International Workshop "From basic Science to Therapeutic Applications".*

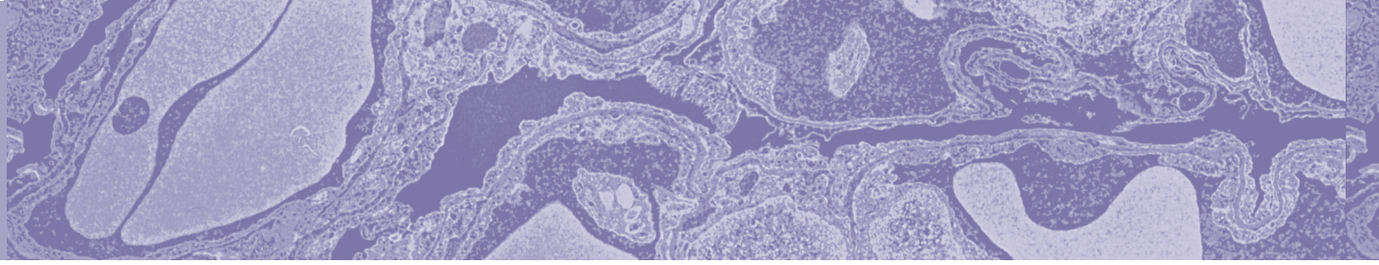
2008

***I**nternational Symposium "Translational Research in Vascular Medicine".*

***T**he international Workshop "The promise of stem cell therapy".*

***I**nternational Biomedicine Exploratory Workshop"Translation of basic research discoveries into therapeutic applications".*

***I**nternational Symposium "From gene expression and protein activation to human diseases".*



2009

The 30th Anniversary Workshop "30 Years on Route from Cell Biology to Molecular Medicine"

International Symposium "Molecular and metabolic dysfunction in diabetes" part of the COST - Action BM0602 "Adipose tissue: a key target for prevention of the metabolic syndrome"

Grant awarded by competition for the "CARDIOPRO" investment project in RDI infrastructure and related administrative capacity" ***Extension and modernization of the research infrastructure for increasing competitiveness in the field of cardiovascular diseases, diabetes and obesity****". Co-funding: European Regional Development Fund - SOP "Increase of economic competitiveness", Priority Axis 2: RTDI for Competitiveness, Operation 2.2.1., Financing contract: 17/01.03.2009, Project Director: Maya Simionescu.*

2010

2nd International Workshop „On Route from Stem Cell Biology to Clinical Applications for Cardiovascular Regeneration"

2nd International Congress and the 28th Annual Session of the Romanian Society for Cell Biology

International Biomedicine Exploratory Workshop: "Trends in Stem Cell biology and Embryological Research"

2011

3rd International Congress and the 29th Annual Session of Romanian Society for Cell Biology;

Grant awarded by FP7 ERA NET (EuroNanoMed):" Nanoparticles designed to target chemokine-related inflammatory processes in vascular diseases and cancer metastasis", Project Coordinator: Acad. Maya Simionescu, Research and Development coordinator: Dr. Manuela Calin, Partners: Center of Surface Science and Nanotechnology, University Polyethnic of Bucharest; University of Bonn, Germany; Istanbul University, Turkey; University of Zürich, Switzerland; EPO Berlin GmbH, Germany; SC Optoelectronica 2000 SRL.

2012

ICBP at the 33rd Anniversary "33 Years on the Road from Cell Biology to Translational and Regenerative Medicine";

Annual Workshop of the FP7 "RAMSES" project: Reinforcement of the Adult stem cell research area through Mobility and Scientific networking between Egypt, Romania and Germany. Project nr. 245691/2010-2013, Bucharest;

4th International Congress and the 30th Annual Session of Romanian Society for Cell Biology;

Workshop "Electron microscopy in Romania" organized together with "Victor Babeş" Institute;

Official presentation of the newly created RDI infrastructure, as a result of the CARDIOPRO investment project.

Grant awarded by ERC starting project-UEFISCDI: ERC-like – type 'Grant Support' - Capacity project: project ID PNII-CT-ERC-2012 - 1" "Circulating platelet microparticles and endothelial progenitor cells in vascular atherosclerosis: new pathophysiological and therapeutic implications", Coordinator: Dr. Adriana Georgescu.

2013

5th International Congress and the 31st Annual Scientific Session of Romanian Society for Cell Biology.

Grant awarded by Swiss National Science Foundation (SNSF) - UEFISCDI: "Effects of Sex Steroids on Adult/Progenitor Cell-Mediated Cardiovascular Regeneration".

2nd Training School of COST Action BM0904 (HDLnet): "HDL: Physiology, regulation and therapeutic potential".

Acad. Maya Simionescu received the highest civil and military distinction of France: Chevalier of the Legion of Honor.

34th Annual ICBP-NS Scientific Symposium.

2014

6th National Congress with International Participation and the 32nd Annual Session of Romanian Society of Cell Biology.

Grant co-funded by the European Regional Development Fund from Sectoral Operational Programme - Increasing of Economic Competitiveness: "Constitution of a New Cell Sorting and Cryopreservation Compartment for Research and Therapeutic Purposes" (SORTIS). Coordinator: Dr. Horia Maniu

35th Annual ICBP-NS Scientific Symposium.

2015

7th International Congress and the 33rd Annual Scientific Session of Romanian Society for Cell Biology.

Grant awarded by FP7 ERA NET (SIINN ERA-NET): "The effect on human health of Ag/TiO2nm-treated leathers for footwear industry" (NANO-SAFE-LEATHER), Project Coordinator: Dr. Carmen Gaidau (The National Research & Development Institute for Textiles and Leather), partners: Romania, Austria, Portugal, Responsible Partner ICBP-NS: Dr. Manuela Calin.

1st Congress of the International Society of Regenerative Medicine and Surgery.

4th International Symposium on Adipo-biology and Adipo-pharmacology.

A tribute session, In Memoriam Acad. Nicolae Simionescu (1926-1995).

36th Annual ICBP-NS Scientific Symposium.

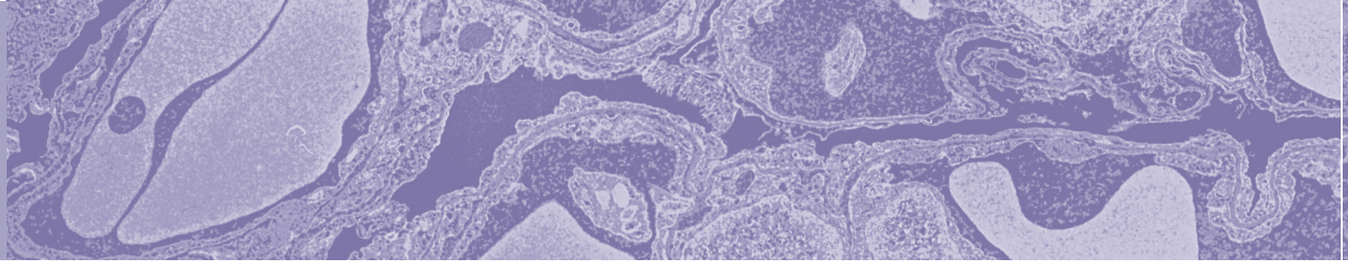
2016

8th International Congress and the 34th Annual Session of Romanian Society for Cell Biology.

Grants awarded by Competitiveness Operational Programme 2016-2020:

1. POC-A.1-A.1.1.4-E-2015: „Targeted therapies for heart valve disease in diabetes" (THERAVALDIS). Coordinator: Agneta Simionescu (USA); Executive Director: Dr. Ileana Mânduţeanu.

2. POC-A.1-A.1.1.4-E-2015: "Improve institutional competitiveness in the field of type 1 diabetes by developing an innovative concept of immunotherapy based on mesenchymal stromal cells" (DIABETER). Coordinator: Nadir Askenasy (Israel); Executive Director: Acad. Maya Simionescu and Dr. Alexandrina Burlacu.



***G**rant awarded by ERA-NET on Cardiovascular Diseases (ERA-CVD): "Exploring new pathways in age-related heart diseases" (EXPERT). Coordinator: Thomas Thum (Germany); Responsible Partner: Dr. Alexandrina Burlacu.*

***37**th Annual ICBP-NS Scientific Symposium.*

2017

***9**th International Congress and the 35th Annual Session of Romanian Society of Cell Biology.*

***2**nd Congress of the International Society of Regenerative Medicine and Surgery.*

***G**rant awarded by FRIPRO-program from The Research Council of Norway: Multifunctional microbubbles for improved image-based diagnosis and drug delivery (MULTIBUBBLE). Coordinator: Dr. Rune Hansen (Norway), Responsible Partner: Dr. Felicia Antohe.*

***W**orkshop "Advanced strategies to limit the inflammation and autoimmunity in diabetes" within DIABETER project.*

***38**th Annual ICBP-NS Scientific Symposium.*

2018

***10**th International Congress and the 36th Annual Session of Romanian Society of Cell Biology.*

***12**th Central and Eastern European Proteomic Conference (CEEPC).*

***G**rant awarded by ERA-NET on Cardiovascular Diseases (ERA-CVD): "Mechanisms of early atherosclerosis and/or plaque instability in Coronary Artery Disease" (ExploreCAD). Coordinator: Dr. Rune Hansen (Norway). Responsible Partner: Dr. Felicia Antohe.*

***G**rant awarded by UEFISCDI: PN-III-P4-IDPCCF-2016-0172 "Targeting innate immune mechanisms to improve risk stratification and to identify future therapeutic options in myocardial infarction" (INNATE-MI). Coordinator: Acad. Maya Simionescu. Partners: University of Medicine, Pharmacy, Science and Technology of Tîrgu Mureş; "CAROL DAVILA" University of Medicine and Pharmacy Bucharest.*

***G**rant awarded by UEFISCDI (international collaboration): PN-III-P4-ID-PCCF-2016-0050 "Mimicking living matter mechanisms by five-dimensional chemistry approaches" (5D-nanoP), Coordinator: Aatto Laaksonen (Institute of Macromolecular Chemistry "Petru Poni"). Resposible Partner: Acad. Maya Simionescu, Dr. Manuela Calin.*

***G**rant awarded by UEFISCDI: PN-III-P1-1.2-PCCDI-2017-0697 "Intelligent therapies for non-communicable diseases based on controlled release of pharmacological compounds from encapsulated engineered cells and targeted bionanoparticles" (INTERA). Complex project coordinator: Acad. Maya Simionescu, Component project responsible: Dr. Manuela Călin, Dr. Anca Gafencu, Dr. Elena Butoi.*

***G**rant awarded by UEFISCDI: PN-III-P1-1.2-PCCDI-2017-0527 "Development of bionanotechnologies based on extracellular vesicles for early diagnosis, prognosis and therapy of atherosclerotic disease" (BIOVEA); Complex project coordinator: Dr. Adriana Georgescu. Partners: National Institute for Research and Development in the field of Pathology and Biomedical Sciences "Victor Babeş" Bucharest; University of Medicine and Pharmacy "Carol Davila" Bucharest; University and Emergency Hospital Bucharest, Cardiology Department, Bucharest; Emergency Clinical Hospital "Pius Brînzeu" Timişoara - Research Center OncoGen.*

***39**th Annual ICBP-NS Scientific Symposium.*

2019

11th *National Congress with International Participation and the 37*th *Annual Session of Romanian Society of Cell Biology.*

S*cientific Session organized together with National Science and Art Foundation: "The future of Research & Development & Innovation in Health. Opportunities for Romania – Horizon Europe".*

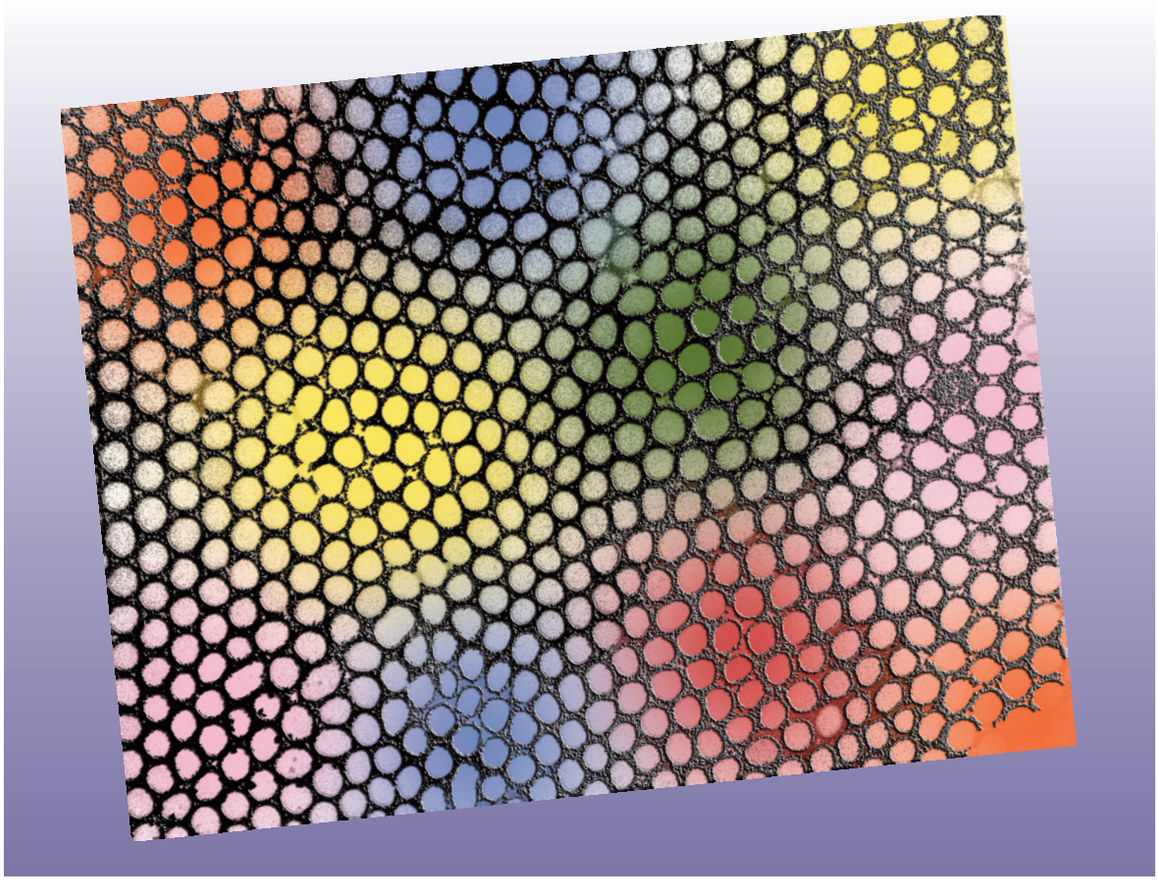
W*orkshop "Recent advances in bio-matrices for tissues-engineered heart valves" organized within the INTERA Project.*

S*ummer School "Intelligent nanoparticles for targeted delivery of bioactive compounds: preparation, characterization and applications" within the INTERA Project.*

W*orkshop "Cardiac valves disease: new targets for therapies and tissue engineering" organized within THERAVALDIS project.*

W*orkshop "Searching for a novel therapy for type 1 diabetes" organized within DIABETER project.*

I*nternational Scientific Symposium dedicated to the 40*th *Anniversary of ICBP-NS "An incredible 40-year journey to understand cell's secrets for the benefit of human health".*



NICOLAE SIMIONESCU

DIRECTOR 1979 - 1995

***Academic Degrees*: Doctor in Medical Sciences**

Major position and appointments
Vice-President of the Romanian Academy
Romanian Science Foundation President
National Committee for Molecular Biotechnology President
Romanian Society for Cell Biology President
Visiting Professor, Yale University, New Haven, USA
Ludwig Schaffer Distinguished Visiting Professor of Columbia University, N.Y. USA
Borun Visiting Professor of Cardiology, University of California, Los Angeles, USA
Visiting Professor, McGill University, Montreal, Canada
NATO Science Committee, Romanian Representative Brussels

Significant new concepts and findings internationally recognized (in collaboration)

The concept and the term ***Transcytosis*** and ***Receptor Mediated Transcytosis***
In 1979, N. Simionescu published a paper in which his new and inspired term "transcytosis" was for the first time introduced in the scientific literature (N. Simionescu, *Advances in inflammation research*, Weisman G. et al, eds. Raven Press, New York, 1979, 1: 61-70).

His concept on transcytosis implied that in endothelial cells, efficient and rapid transport of macromolecules from the plasma to the interstitial fluid is accomplished via vesicles, channels and fenestrae, which carries solutes throught the endothelium by a shortcut between endocytosis and exocytosis, namely by transcytosis (adsorbtive, receptor mediated transcytosis). The concept was based on work carried out with Maya Simionescu and George E. Palade. The new term and concept was extended to all epithelial cells and rapidly adopted by the international scientific community; it become so widely used for different cell systems that today very few people quote or know its original author, a common fact for classic concepts (i.e. endocytosis, exocytosis).

First identification and biochemical characterization of "*Extracellular Liposomes*" than termed "*Modified and Reassembled Lipoproteins*" as the earliest event in atherogenesis (in collaboration).

Identification and characterization of "*Albumin Binding Proteins*" on endothelial cell membrane as well as in other cell types (in collaboration).

Discovery of "*transendothelial channels*";

Discovery of „*biochemically differentiated microdomains of the Endothelial Cell surface*"

(in collaboration).

New methods in Cell Biology: galloylglucoses as mordants in electron microscopy (1976), isolation of endothelial cells from the heart microvasculature (1978), new ultrastructural permeability tracers, etc. (in collaboration)

A scientific side project: Founder together with Maya Simionescu of the Institute of Cellular Biology and Pathology

Founder of the Romanian Society for Cell Biology (1982)

PUBLICATIONS: over 600 papers in peer review jornals, numerous chapters in national and international monographs and books.

MEMBER OF SCIENTIFIC SOCIETIES

American Society for Cell Biology;
American Thyroid Association;
American Association for Advancement of Science;
International Society for Biological Rhythms;
International Society for Stereology;
International Society for Endocrinology;
European Society for Experimental Surgery; European Society for Comparative Endocrinology;
Italian Anatomical Society;
International Committee on Laboratory Animals (Governing Board);
European Artery Club (Governing Board); European Vascular Biology Association

TEACHING ACTIVITIES

Anatomy Department, Faculty of Medicine, Bucharest (20 years)

Visiting Professor, Cell Biology Course, School of Medicine, Yale University (20 years)

Advisor Ph.D and MD programs, Yale University and ICBP

Nominated in 1978 by the Ist year medical students for the Bohum Prize honoring the best professor of Yale University School of Medicine.

Lectures on Cell Biology by invitation from Universities: Columbia, New York; Mount Sinai School of Medicine, New York; SUNY Downstate Medical School, Brooklyn; NYU Medical School, New York; Massachusetts University, Worcester; Harvard University, School of Medicine, Boston; UCLA Univ., Medical School, Los Angeles; McGill University, Montreal; University of Tokyo School of Medicine, Tokyo; Faculty of Medicine, Kyoto; Faculte Xavier Bichat, Paris; Faculty of Medicine, Lisabona.

Invited speaker, chairman and organizer of over 50 International Congresses (USA, Europe, Mexico, Japan, Canada)

MEMBER IN EDITORIAL BOARDS

Thrombosis Research; Journal of Submicroscopic Cytology and Pathology; Science et Techniques de l'Animal de Laboratoire; Cell Differentiation; Endothelium.

CONSULTANT TO INTERNATIONAL SCIENTIFIC INSTITUTIONS

WHO expert on experimental endocrinology
Expert, Thyroid Cancer Group of the International Union Against Cancer
National Institutes of Health (NIH), Bethesda, MD, USA (grant applications)
National Science Foundation, Washington, D.C., USA (grant applications)
Dept. Experimental Medicine, Pharmacia Biotechnology, Uppsala, Sweden
Cardiology Institute of Texas, Houston, TX, USA
Medical Research Council (MRC), London, England (grant applications)
Medical Research Council of Australia, Adelaide, Australia (grant applications)
Medical Research Council of New Zealand, Auckland, New Zealand
Member of the Planning and Programme of Biblioteca Universalis and of the International University: Pax et Veritas, Szentes, Hungary

Legacy of a distinguished scientist

PROFESSOR NICOLAE SIMIONESCU

Director of ICBP: 1979-1995

*"**N**icolae Simionescu had a meteoric career. In ten years, starting with a good mind and a good general education, he became an accomplished, generally recognized authority in the cell biology of the vascular endothelium. In the next decade or so, under uncertain and difficult conditions of social and political nature, he organized a research institute and trained a whole team of capable investigators and in the next five years he assumed a position of leadership in the Romanian Academy, the highest institution guiding the creative activities of the country.*

At every step in this rapid evolution, he left behind a lasting heritage:

- his research accomplishments;

- the Institute of Cellular Biology and Pathology;

- two generations of well-trained investigators and a demanding but luminous vision for the future of nature sciences in Romania."

Professor George Emil Palade
University of California, San Diego, USA

*"**N**icolae Simionescu was a citizen of the world, but was in the first place a Romanian through and through, down to his last red blood cell. He gave all his energies to build in Romania an island of excellence - on a world scale - and he did so despite enormous difficulties, pain, and personal danger. Shielded by his extraordinary presence, his scientific stature, his inspiring imagination, he fought for the future of young Romanians at his own risk, day after difficult day.*

Nicolae has permanently enriched our lives. For those who had the privilege of knowing him personally, cherished memories will include flashes of his unbeatable sense of humour, which never left him even under the hardest circumstances. Although to the international scientific community he was the quintessence of a „pure" researcher, in his private life he found the time to compose music at the keyboard, to paint and to write poetry; in this too he was an admirable role model for his younger associates. Among tangible gifts, Nicolae Simionescu left us a living monument - the ICBP - with a scientifically beautiful name and a beautiful mission. And above all, for Romanians and for scientists the world over, his example of uncompromising courage will live on; heroes are needed more than ever in the difficult times that we are still living.

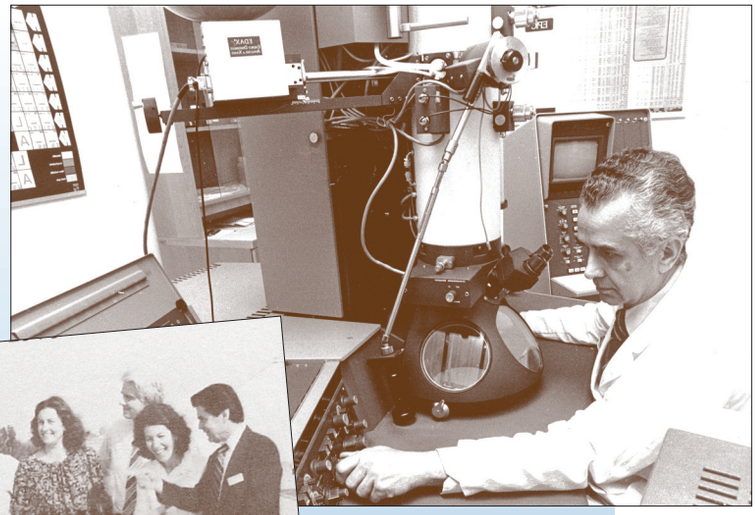
Romania has lost a most distinguished son - but also acquired a precious legacy."

Professor Guido Majno
University of Massachusetts, Worcester, USA

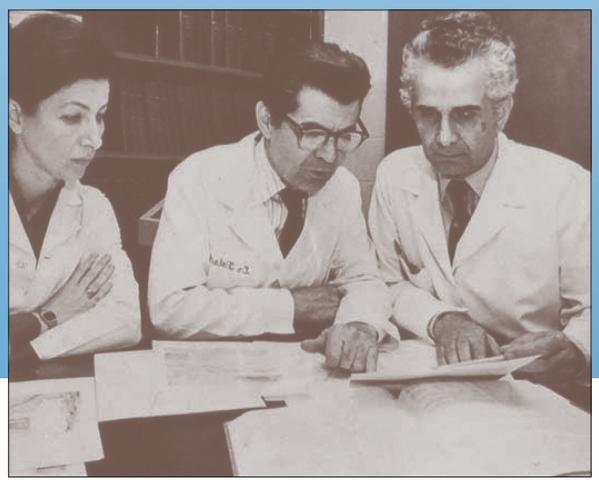
***F**or us, Professor Nicolae Simionescu was a breath of fresh air in the hard time of the communist regime. He was a complete and complex personality in which the scrupulous scholar, the genuine scientist, the authentic educator and teacher and the veritable patriot combined to bestow a remarkable human being. We have learned from our Magister the marvel of research, the meaning of the dedication to science, the ways to meet the success and failure, the sense of responsibility, the rigour, the ethics and the greatness of intellectual grace and moral values that should complement a genuine scientist.*

Infinite gratitude to our Professor.

ICBP - Collaborators




J.DE DUVE C.DE DUVE
G.E.PALADE
D.SABATINI



MAYA SIMIONESCU

DIRECTOR - SINCE 1995

***Academic Degrees*: Doctor in Biology**

Major position and appointments
Vice-President of the Romanian Academy (1996 – 2005)
President of the Romanian Society for Cell Biology
President of the Section of Biological Sciences - Romanian Academy
Vice-President of the European Life Scientist Organization
Visiting Professor: Yale University, School of Medicine, New Haven, USA;
McGill University, School of Medicine, Montreal, Canada;
Columbia University, New York, USA; University of California-Los Angeles, Los Angeles, USA

MEMBER OF SCIENTIFIC SOCIETIES

American Society for Cell Biology;
European Cell Biology Organization;
European Life Scientist Organization (Vice-President);
Romanian Society for Cell Biology (President).

MAJOR RESEARCH INTEREST

Cellular and molecular biology and pathology of the cardiovascular system, with special emphasis on atherosclerosis and diabetes**.** Structural-functional correlation of microcirculation and large blood vessels, endothelial cells, lung cells plasma cells, stem cells, lipoproteins.

MAIN ACHIEVEMENTS

PUBLICATIONS: 450 scientific papers published in international peer review journals 55 chapters in international handbooks and monographs Co-editor at two monographs published by Plenum Press, one monograph by The Publishing House of the Romanian Academy and one monograph in Romanian.
ISI Citation of papers: 7000; Hirsh Index: 50

NOVEL CONTRIBUTIONS *(in collaboration)*

● Discovery of transendothelial channels and their role in the exchange of macromolecules across endothelial cell (EC).

● First identification of biochemically and structurally differentiated microdomains on the luminal and abluminal plasmalemma of endothelial cells.

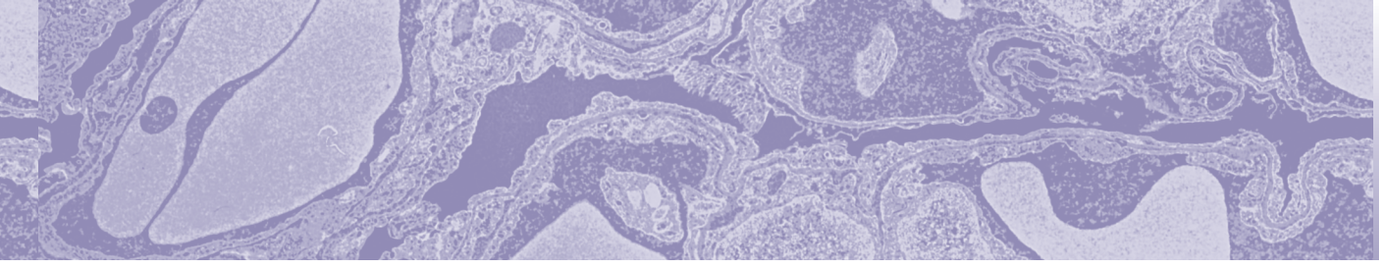
● Plasmalemmal vesicle membrane: distinct chemical composition and receptors that carry out fluid phase, adsorbtive or receptor-mediated transcytosis.

●First report on the existence of albumin and histamine receptors in EC.

●Discovery of intimal deposition ofmodified and reassembled lipoproteins asthe first event occurring in the arterialwall and heart valves at the inception ofatherosclerosis..

●Structural, biochemical and functional characterization of modified lipoproteins isolated from the arterial intima of hypercholesterolemic animal models.

●Transcytosed lipoproteins amass within the subendothelium as modified and reassembled lipoproteins



● Pathobiochemistry of combined diabetes and atherosclerosis studied on an original animal model, hyperlipemic/hyperglycemic hamster.

● Detection of the effect of high glucose on endothelium and of glycated proteins on lipoproteins that may account for accelerated atherosclerosis in diabetes.

TEACHING EXPERIENCE IN CELL BIOLOGY

19 years at Yale University, Medical School, USA: Cell Biology Course (Visiting Professor)
5 years at the University of Bucharest and "Ovidius University", Constanța, România

A SCIENTIFIC SIDE PROJECT

Co-founder of the Institute of Cellular Biology and Pathology together with Professor Nicolae Simionescu.

AWARDS AND HONORS

Louis and Arthur Lucian International Award for Research in Circulatory Diseases, McGill University, Montreal, Canada (shared with Prof. N. Simionescu), 1978

***Medal of the Institute of Clinical Electron Microscopy*,** Bologna, Italy, 1987

Ludwig Schaefer Distinguished Professor, Columbia University, USA, 1990-1991

***Borum Professor of Cardiology*,** University of California, Los Angeles, USA, 1990

Corresponding Member of the Romanian Academy, 1990

Member of the Romanian Academy, 1991

Vice-President of theRomanian Academy, 1998

Member of theAcademy of Medical Sciences, Romania, 1998

Sanofi Thrombosis Prize for Atherosclerosis and Thrombosis Research, 1998

Award "Serviciul credincios" - Marea Cruce, of the Romanian Presidency, 2000

Honorary Member, Academy of Sciences of Moldova Republic, 2001

Award "Rio Branco – Comendador", of the Brazilian Presidency, 2001

UNESCO - L'Oreal Special Honor Award for Women in Science, 2001

"Ion Pavel" Prize of the Romanian Academy of Medical Sciences and of the Romanian Society for Diabetes, Nutrition and Metabolic Diseases, 2004

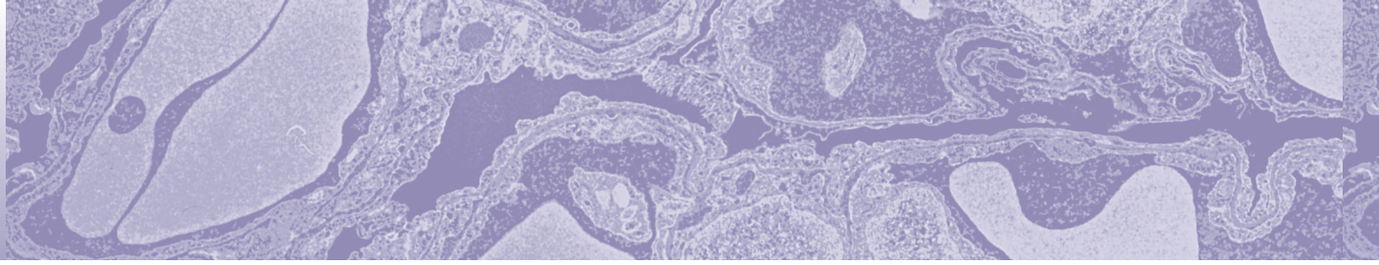
Académica Correspondiente de la Reial Acadèmia de Doctors, Universitat de Barcelona, 2005

Doctor Honoris Causa: ***University "Ovidius"***, Constanța, România, 2000; ***University of Medicine "Gr.T.Popa"***, Iași, România, 2000; ***West University***, Timișoara, România, 2006; ***„Vasile Goldiş" University,*** Arad, România, 2011

"Romanian Star" Order of the Romanian Presidency, 2008

"Opera Omnia" Prize, of the Romanian Ministry of Education and Research, 2008

Gold medal – EUREKA, Bruxelles, 2013; Prize AGEPI (State Agency for Intellectual Property) for Innovation INNOVA and " Romanian Innovation Awards, 3M PREMIAZĂ



INOVAȚIA, 2014, for patent applications: *Nervous conductors made of collagen and process for preparing the same*. *Inventors*: Albu M. G., Lascăr I., Zamfirescu D., Simionescu M., Zegrea I., Titorencu I., D. Popescu M., Bumbeneci G., 2013.

***"Légion d'Honneur" National Order of the French Republic**, 2013.*

Award for Excellence in Research - Romanian Society of Cardiology: L.S. Niculescu, N. Simionescu, G.M. Sanda, A.C. Popescu, M.R. Popescu, A. Vlad, D.R. Dimulescu, M. Simionescu, A.V. Sima; the 55th National Congress of Cardiology, Sinaia, 2016

"Omnia" Diploma of Excellence, Romanian Medical Association, 2017

Medal "Centenar Pierre Werner", The Institute of Economic Research "Costin C. Kirițescu", 2017

Honorary Member of the Romanian Society of Cardiology, 2017

EDITORIAL BOARDS

European Journal of Cell Biology; Differentiation; Cell and Tissue Research;
Journal of Cellular and Molecular Medicine; Microvascular Research;
Sciences et Techniques de l'Animal de Laboratoire;
Journal of Submicroscopical Cytology and Pathology; Biomedical Reviews.

Member Expert Panel, European Research Council Peer Review Evaluation

Peer Reviewer to International Grants application and Journals

Chairperson, invited speaker and co-organizer at over 60 scientific meetings in USA, Europe, Japan, Mexico.

Director of European Community FP5 Grant awarded by competition to ICBP - Centre of Excellence of the European Community *Blood Vessels*: "*Function and dysfunction of blood vessels: transcytosis in normal/pathological states, alterations in atherosclerosis and diabetes; their therapeutic control*"

Director of European Community FP6 Specific Support Action - grant awarded by competition: "*Strengthening the European Research Area by Reinforcement of Romanian Research Competency in Genomics and Proteomics of Major Global Risk Diseases: Atherosclerosis, Diabetes and its Complications*" (2005-2008)

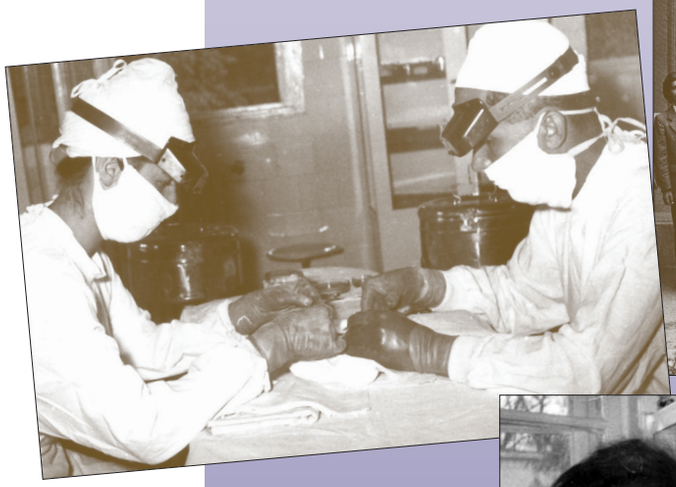
Member in the Management Committee of the COST Action B 17 of the European Community "*Insulin Resistance, Obesity and Diabetes Mellitus in the Elderly*" Coordinator of the WG5 (2001-2003)

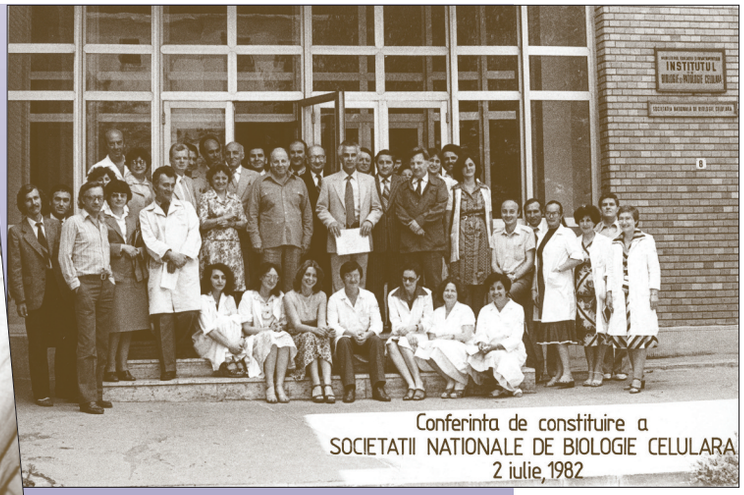
Member in the Management Committee of the COST Action BM0602 "*Adipose Tissue: A Key Target for Prevention of the Metabolic Syndrome*" (2008-2011)

Member in the Management Committee of the **COST Action CA17129. "***Catalyzing Transcriptomics Research in Cardiovascular Disease***": The CardioRNA** (2019-2022)

Director of the "CARDIOPRO" investment project in RDI infrastructure and related administrative capacity, "*Extension and modernization of the research infrastructure for increasing competitiveness in the field of cardiovascular diseases, diabetes and obesity*".

e-mail: maya.simionescu@icbp.ro





Conferinta de constituire a
SOCIETATII NATIONALE DE BIOLOGIE CELULARA
2 iulie, 1982

DEPUTY DIRECTORS AND SCIENTIFIC SECRETARIES OF ICPB-NS

DEPUTY DIRECTORS OF ICBP-NS

1979 - present

Constantin Neacșu, PhD
(1979-1984)

Theodor Constantinescu, PhD
(1984-1990)

Victor V. Jinga, PhD
(1990-2012)

Ileana Mânduțeanu, PhD
member of the Romanian Academy
(2012-Prezent)

SCIENTIFIC SECRETARIES OF ICBP-NS

1979 - present

Doina Popov, PhD, Academician
(1979-2016)

Anca Sima, PhD, Academician
(2016-Prezent)

MAJOR GOALS

►***Biomedical Research***:
cellular and molecular biology and pathobiochemistry of the cardiovascular system;

►***Teaching and Education***:
Master and PhD. programs, specialization, post-universitary training courses.

►***Promotion of modern Cell Biology and Pathology*** *in Romania by in-depth training of young investigators; foundation of the* ***Romanian Society for Cell Biology;***

►***International collaborations***
and ***exchanges***.

OUR MISSION

►***To uncover at the cellular and molecular level the pathobiochemical alterations occurring in the heart and blood vessels which lead to atherosclerosis, diabetes, ageing, metabolic syndrome;***

►***To translate the knowledge from "bench to bedside" for patients benefit: prevention, early diagnosis, better therapeutic control, and ultimately cure of cardiovascular diseases.***

ORGANIZATION

DIRECTOR AND COORDINATOR OF RESEARCH PROGRAM

Acad. ***Maya Simionescu***, *PhD*

SCIENTIFIC COUNCIL

Maya Simionescu /President/,
Ileana Mânduțeanu /Deputy Director/,
Anca Sima /Scientific Secretary/,
Members:
Felicia Antohe, Monica Raicu, Horia Maniu, Manuela Călin, Anca Gafencu, Alexandrina Burlacu, Adrian Manea, Adriana Georgescu, Irina Titorencu

We are a team of 100 individuals: senior and young investigators (biochemists, biophysicists, chemists, biologists, physicists) trained in prestigious laboratories in United States and Europe, technicians and administrative staff.

The Institute occupies a five-floor building of ~4,000 m2 out of which ~3,000 m2 reside in laboratory space. Laboratories are organized in a technological flow that consists of specialized units, core laboratories, central facilities and services.

ICBP-NS has 4 specialized departments, 4 laboratories and modernised core laboratory units and other facilities.

DEPARTMENTS

1. Department of proteomics
2. Department of lipidomics
3. Department of pathophysiology and pharmacology
4. Department of biopathology and therapy of inflammation

LABORATORIES

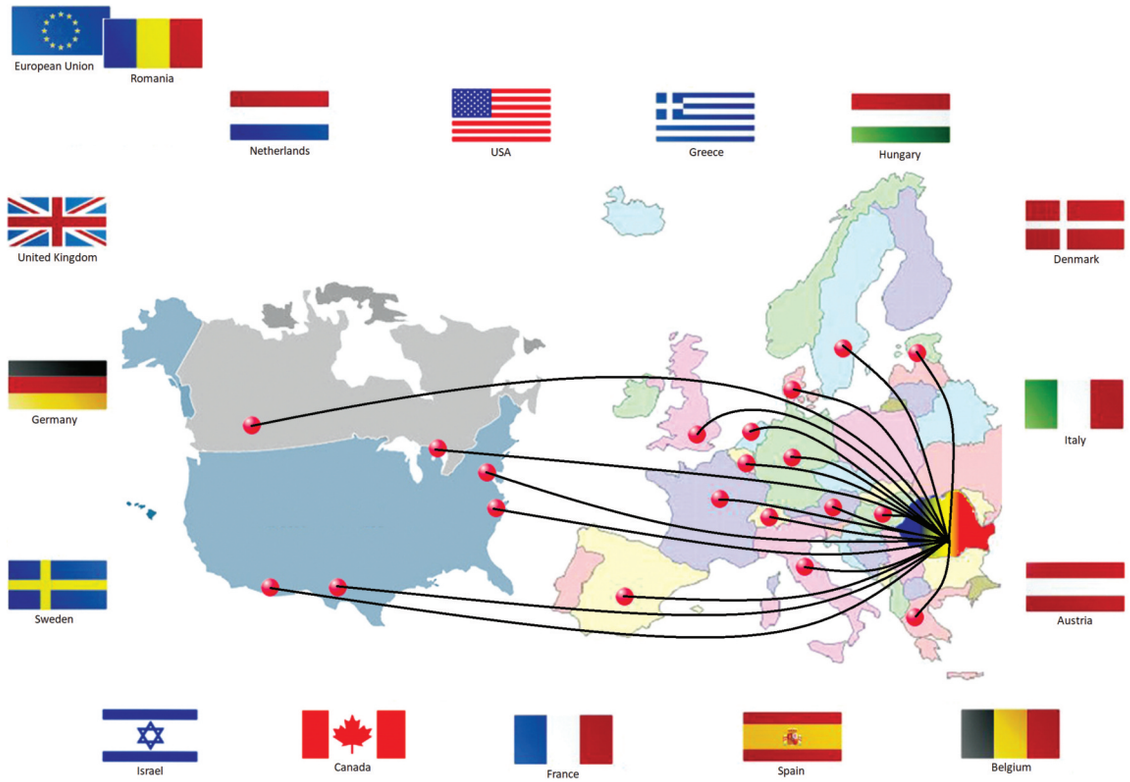
1. Gene regulation and molecular therapies
2. Molecular and cellular pharmacology - functional genomics
3. Stem cell biology
4. Cell and tissue engineering

CORE LABORATORY UNITS

Cell culture; Genetic analysis; Viral transfection;
Liquid and gas chromatography; Mass spectrometry; Flow cytometry;
Cell adhesion; Laser microdissection; Myography;
Exploratory imagistics; Bioinformatics; 3D Bio-printing;
Confocal microscopy; Bioarchive; Experimental modelling platform.

INTERNATIONAL AND NATIONAL COOPERATION

The Institute has strong ongoing collaborative projects
/see individual departments/



THE ROMANIAN SOCIETY FOR CELL BIOLOGY

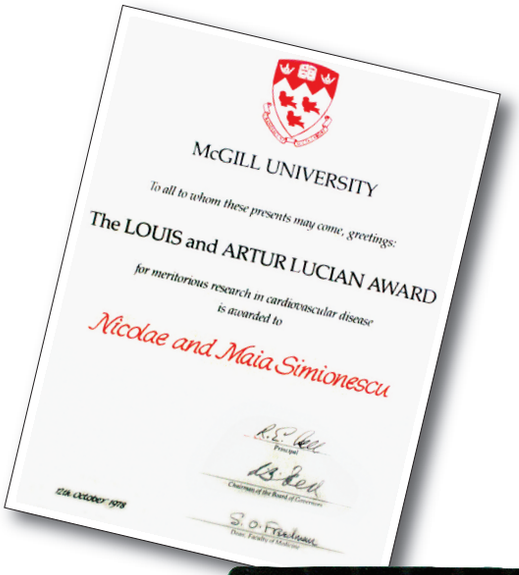
The Romanian Society for Cell Biology was founded in 1982 as a national scientific organization under the auspices of the Institute of Cellular Biology and Pathology.

The Society includes 13 regional branches acting in the major academic centres and has 500 registered members.

The papers presented at the meetings are yearly published in extenso in the Annals of the Romanian Society for Cell Biology.

AWARDS GRANTED TO ICBP "N. SIMIONESCU"

- ***Center of Excellence of the European Community***
- ***Member Institution of UNESCO Global Network for Molecular and Cell Biology***
- ***Center of Excellence of the Romanian Academy and of the Ministry of Education and Research***
- ***"Cultural Merit" of the Romanian Presidency, in Officer Degree, conferred at the 25th Anniversary (2004)***
- ***"Conceived in Romania" Excellence Diploma of the Ministry of Education and Research***


McGILL UNIVERSITY

To all to whom these presents may come, greetings:

The LOUIS and ARTUR LUCIAN AWARD

for meritorious research in cardiovascular disease

is awarded to

Nicolae and Maia Simionescu


Președintele României

Dorind a răsplăti meritele

Institutului de Biologie și Patologie Celulară

al Academiei Române,

Conferă Ordinul „Meritul Cultural"

în gradul de Ofițer categoria H „Cercetare științifică"

Dat în București la 7-IX-2004

Președintele României

Cancelarul Ordinelor

Ministrul Culturii și Cultelor

Decret nr. 666

Brevet MC/ nr.

THE AMERICAN THYROID ASSOCIATION

FOUNDED 1923

In acknowledgement of his interest in the study of the Thyroid Gland the

American Thyroid Association

has elected

Nicolae Simionescu, M. D.

to

Corresponding Membership

June 25, 1970

PRESIDENT

SECRETARY

FUNDING SOURCES */SELECTION/*

Competitive Grants from:

- National Institute of Health (NIH) of United States of America (1980-1989)

- Romanian Academy (since 1990)

- Fogarty International Research Collaborative Award-NIH (1991-1994)

- Ministry of Education and Research (since 1995)

- National Research Programs: CNCSIS, CERES, VIASAN, BIOTECH

- European Community (since 1993)

- Swiss National Science Foundation (1996-1998)

- UNESCO Global Network for Molecular and Cellular Biology (1995-1998)

- PECO Program, European Community, coordinator: Prof. M.J. Mulvany (1995-1996)

- Collaborative Grant from Swiss National Science Foundation (1996-1998), coordinators: Prof. W. Hunziker (University of Lausanne) and Dr. M. Simionescu, ICBP, Romania;

- INCO Program, European Community, Center of Excellence, coordinator: Dr. M. Simionescu (2000 – 2003)

- Collaborative linkage Grant NATO Science Programme (2002-2004), coordinators: Prof. V. Zannis, Boston Univ., USA - Dr. M. Simionescu, ICBP, Romania

- COST Action B 17 of the European Community "Insulin Resistance, Obesity and Diabetes Mellitus in the Elderly", coordinator: Prof. P. Csermely, Hungary; (2001-2003) WG 5 coordinator: Dr. M. Simionescu

- COST Action BM0602. Coordinator: Prof. J. Eckel, Germany, Dr. M. Simionescu, member in the Management Committee (2008-2011)

- European Community Structural Funds, POS-CCE: "Extension and modernization of the research infrastructure in order to increase competitiveness in the field of cardiovascular diseases, diabetes and obesity" CARDIOPRO. Project Director: Maya Simionescu.

- FP7 ERA-NET (EuroNanoMed),"Nanoparticles designed to target chemokine-related inflammatory processes in vascular diseases and cancer metastasis and implementation of a biosensor to diagnose these disorders" NANODIATER, (2011-2014), Project Director: Acad. Maya Simionescu

- European Community FP7 Research Potential REGPOT-2009-2: Reinforcement of the Adult stem cell research area through Mobility and Scientific networking between Egypt, Romania and a German consortium for Strengthening the international scientific competency (RAMSES). (2010-2013). Project Coordinator: Prof. Konrad Brockmeier (Germany). Romanian Team Coordinator: Dr. Maya Simionescu, Romanian Team Scientific Coordinator: Dr. M. Lupu. Common workshops and training events held in Cairo (2010), Köln (2011), and Bucharest (2012).

- ERC Starting Grant – UEFISCDI: ERC-like – type 'Grant Support' - Capacity project: project ID PNII-CT-ERC-2012 - 1", "Circulating platelet microparticles and endothelial progenitor cells in vascular atherosclerosis: new pathophysiological and therapeutic implications" (2012-2014), Project Director: Adriana Georgescu

- Swiss National Science Foundation (SNSF) - UEFISCDI:" Effects of Sex Steroids on Adult/Progenitor Cell-Mediated Cardiovascular Regeneration" (2013), Project Director: Acad. Maya Simionescu.

● European Regional Development Fund from Sectoral Operational Programme - Increasing of Economic Competitiveness: "Constitution of a New Cell Sorting and Cryopreservation Compartment for Research and Therapeutic Purposes" (SORTIS), (2014-2015) Project Director: Horia Maniu

● FP7 ERA NET (SIINN ERA-NET), "The effect on human health of Ag/TiO2nm-treated leathers for footwear industry" (NANO-SAFE-LEATHER), Project Coordinator: Dr. Carmen Gaidau (The National Research & Development Institute for Textiles and Leather), (2015-2018) partners: Romania, Austria, Portugal, Responsible Partner ICBP-NS: Dr. Manuela Călin.

COMPETITIVENESS OPERATIONAL PROGRAMME 2016-2020:

● 1. POC-A.1-A.1.1.4-E-2015: „Targeted therapies for heart valve disease in diabetes" (THERAVALDIS). Coordinator: Agneta Simionescu (USA); Executive Director: Dr. Ileana Mânduţeanu.

● 2. POC-A.1-A.1.1.4-E-2015: "Improve institutional competitiveness in the field of type 1 diabetes by developing an innovative concept of immunotherapy based on mesenchymal stromal cells" (DIABETER). Coordinator: Nadir Askenasy (Israel); Executive Directors: Acad. Maya Simionescu and Dr. Alexandrina Burlacu.

● ERA-NET on Cardiovascular Diseases (ERA-CVD): "Exploring new pathways in age-related heart diseases" (EXPERT), (2017-2020). Coordinator: Thomas Thum (Germany); Responsible Partner: Dr. Alexandrina Burlacu.

● ERA-NET on Cardiovascular Diseases (ERA-CVD): "Mechanisms of early atherosclerosis and/or plaque instability in Coronary Artery Disease" (ExploreCAD), (2017-2020) Coordinator: Dr. Rune Hansen (Norway). Responsible Partner: Dr. Felicia Antohe.

● UEFISCDI: PN-III-P4-IDPCCF-2016-0172 (international collaboration): "Targeting innate immune mechanisms to improve risk stratification and to identify future therapeutic options in myocardial infarction" (INNATE-MI) (2018-2020). Coordinator: Acad. Maya Simionescu.

● UEFISCDI: PN-III-P4-ID-PCCF-2016-0050 (international collaboration): "Mimicking living matter mechanisms by five-dimensional chemistry approaches" (5D-nanoP), Coordinator: Aatto Laaksonen (Institute of Macromolecular Chemistry "Petru Poni"). Resposible Partner: Acad. Maya Simionescu.

● UEFISCDI: PN-III-P1-1.2-PCCDI-2017-0697 (multi-laboratories project) "Intelligent therapies for non-communicable diseases based on controlled release of pharmacological compounds from encapsulated engineered cells and targeted bionanoparticles" (INTERA). Coordinator: Acad. Maya Simionescu.

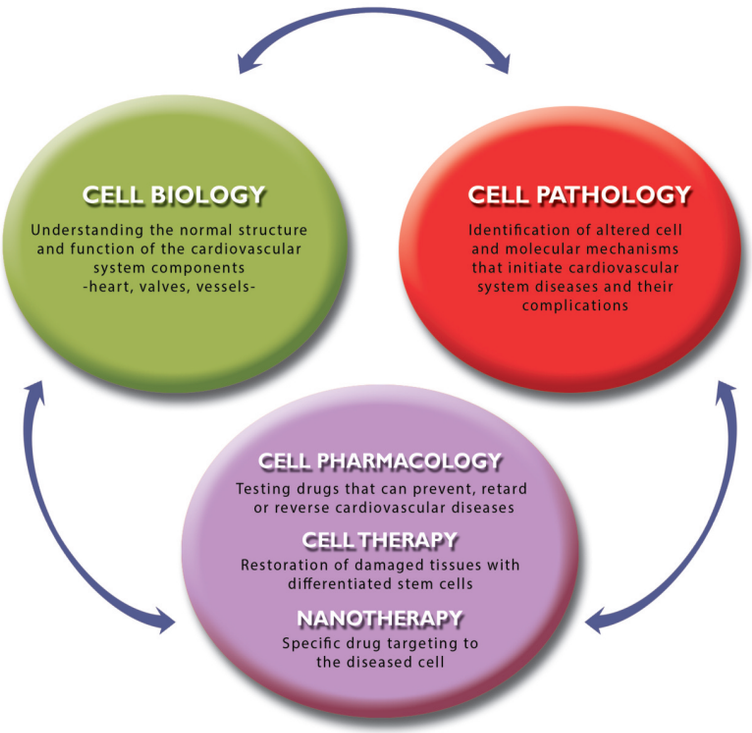
● UEFISCDI: PN-III-P1-1.2-PCCDI-2017-0527 (multi-laboratories project) "Development of bionanotechnologies based on extracellular vesicles for early diagnosis, prognosis and therapy of atherosclerotic disease" (BIOVEA); Coordinator: Dr. Adriana Georgescu.

Other grants obtained from Executive Unit for Financing Higher Education, Research, Development and Innovation (UEFISCDI) (PED, PCCF, PCCE, PCCDI programs) are presented at individual departments.

Cellular and Molecular Mechanisms Implicated in the Functioning of Cardiovascular System in Health and Malfunctioning in Diseases; Therapeutic Control.

Cardiovascular disease represents more than 45-60% of the world-wide death rate. The World Health Organisation predicted that by 2020 cardiovascular maladies will be the leading global cause of total disease burden. In the case of atherosclerosis, the first signs appear in young individuals but in time, as a function of numerous risk factors and genetic determinants, they evolve towards advanced atherosclerotic plaques. The plaques finally impede partially or totally the blood flow through a territory of the heart or brain, leading to myocardial infarction or stroke. .

Uncovering the critical events and the pathobiochemistry of vascular diseases will provide the tools and the markers for clinical screening, early diagnosis and efficient treatment of these maladies.



► CELL BIOLOGY
– the baseline and the terrain for uncovering the physiological mechanisms;

► CELL PATHOLOGY
– detecting of insults – induced altered molecules and cellular mechanisms;

► CELL PHARMACOLOGY AND CELL THERAPY
– finding remedy to correct and treat cardiovascular diseases.

NANOTHERAPY
– specific drug targeting to the diseased cell; part of Nanomedicine

CELL BIOLOGY

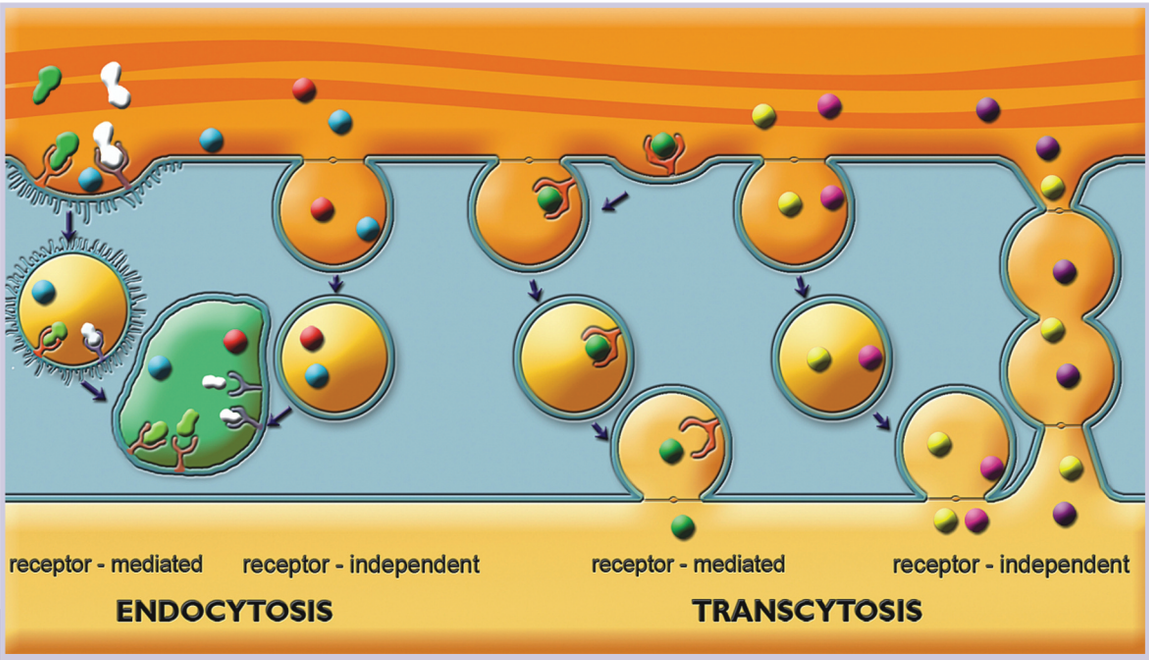
I. Mechanisms of transcytosis of macromolecules through the vascular endothelium in normal and pathological conditions.

Transcytosis is a process utilized by plasma molecules, hormones, proteins, immuno-globulins or drugs to cross the vessel's lining - the endothelial cells – in order to reach the target cells and tissues.

The various mechanisms that monitor transcytosis of molecules - fluid phase, adsorptive, receptor-mediated transcytosis – highlight the role of endothelial cells in the control of selective transport as well as in the permeability alterations occurring in pathological conditions.

Some projects on transcytosis (original concept of ICBP):

- *Albumin transcytosis; specific receptors - Albumin Binding Proteins*
- *Transcytosis of Low Density Lipoproteins*
- *Transcytosis of ß-Very Low Density Lipoproteins*
- *Transport of Reversibly and Irreversibly Glycated Albumin*
- *Materno-fetal transport of Immunoglobulin G.*



Deciphering the molecular events, the modulating factors and the magnitude of varied mechanisms that monitor transcytosis of molecules could explain how macromolecules or intravascularly injected drugs reach their target cells, as well as the permeability alterations occurring in pathological conditions.

(M. Simionescu et al., 2009)

II. Molecular mapping of the endothelial cell surface and its microdomains

The primary interaction of plasma molecules and cells with the blood vessel wall occurs at the luminal surface of endothelial cells. We search for the surface exposed proteins, glycoproteins, glycolipids and proteoglycans, and their distinct distribution on the differentiated microdomains (original concept) of endothelial plasmalemma.

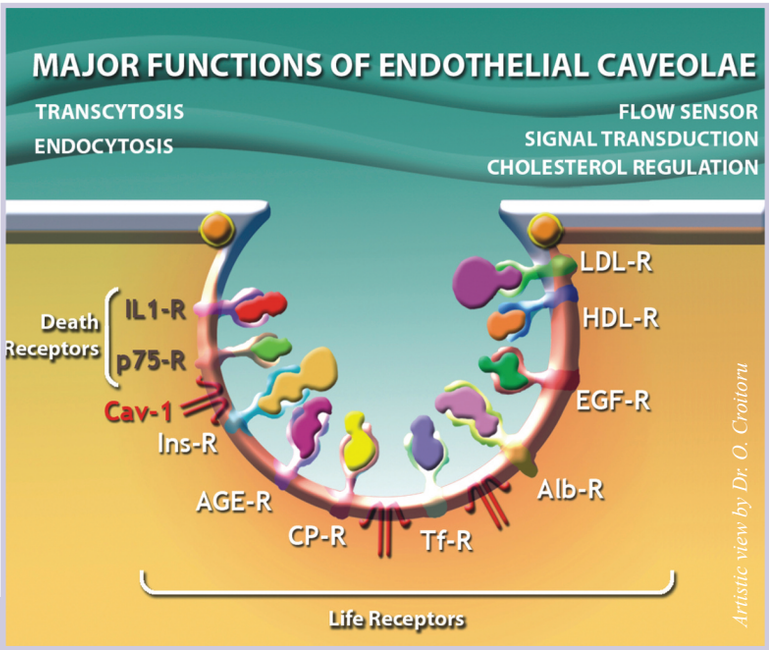
The specific endothelial surface molecular properties may explain the sorting of molecules, the localised leukocyte recruitment and migration, preferential localization of metastases and others.

Among the topics studied:

- *Selective radiolabeling of endothelial cell (EC) luminal membrane microdomains;*
- *Protein and fatty acid composition of endothelial vesicles (caveolae);*
- *Biochemical characterization of endothelial plasma membrane domains; receptors localized in caveolae;*
- *2-D map of normal and endothelial-derived foam cell proteins*
- *Proteomic analysis of endothelial cells in normal and pathological conditions: membrane microdomains (lipid rafts and caveolae).*

III. Lectins of blood platelets membrane

The molecular components of blood platelets and their modifications in pathological conditions.



Identification of molecules that are particular to a given vascular bed, constitutively expressed or induced in pathological conditions could be the targets for tissue or cell-specific drug delivery, a goal of molecular medicine.

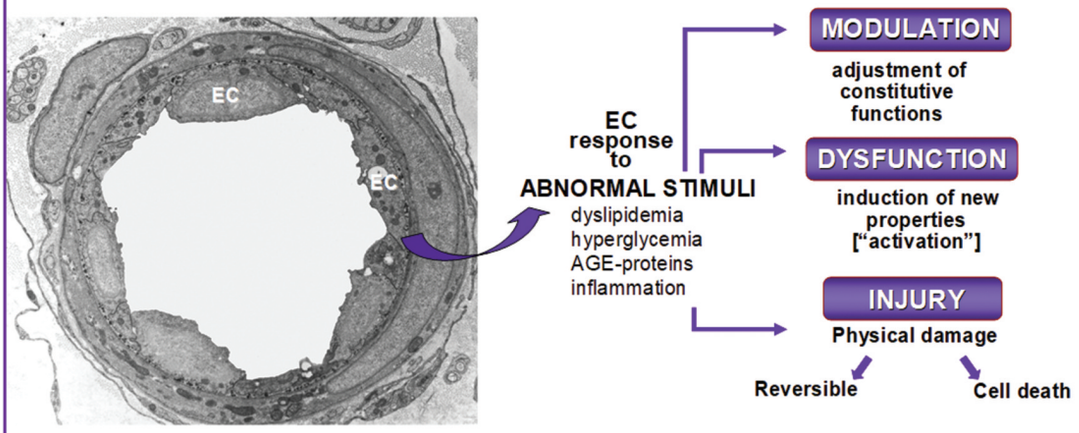
(M. Simionescu et al., 2009)

CELL PATHOLOGY

Atherosclerosis is a multifactorial disease that implyies a complex inflammatory process and a lipid disorder, which induce alterations of the vessel wall, ultimately leading to atheroma formation, vessel's obstruction and generation of myocardial infarction, and cerebral stroke.

The potential therapeutic implications of decoding the altered intimate processes leading to cardiovascular diseases fully justify the efforts to understand their cellular and molecular mechanisms. Uncovering the events taking place at the commencement of the plaque formation is the best approach for anticipation and prevention of the lesions.

At the inception of atherogenesis, the key cell actor is the endothelial cell, whose numerous physiological functions are disturbed by insults from the plasma, interstitial fluid and the underlying cells. To insults, endothelial cells respond initially by **modulation** of their con¬stitutive functions, then by **dysfunction**, and ultimately by **injury** and apoptosis.



The vital role of EC in health and disease generated a complex discipline:

- ▶**ENDOTHELIOLOGY**: investigation of mechanisms used to preserve homeostasis;
- ▶**ENDOTHELIOPATHY**: search for mechanisms alterations in vascular diseases
- ▶**ENDOTHELIOTHERAPY**: quest for novel drugs targeted to dysfunctional EC

M. Simionescu, 2004

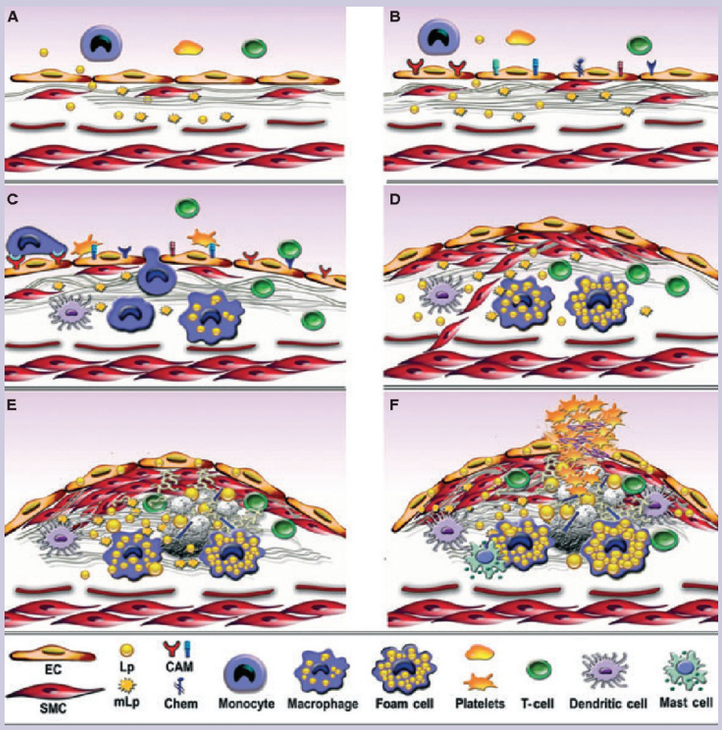
I. Atherosclerosis: pathobiochemical events

A) Atherosclerosis: pathobiochemical events

- *Identification of early structural-functional modifications occurring in the cardiac valves, coronary arteries, aortic arch (lesion-prone areas).*
- *Biochemical characterization (in vivo and in vitro) of modified and reassembled lipoproteins, accumulated in the the subendothelial space, the initial event in atherogenesis.*
- *Interaction of modified and reassembled lipoproteins with the cells of the vessel wall*
- *Diapedesis of monocytes through the vascular endothelium: role of adhesion molecules*
- *Role of monocytes / macrophages in lesion formation in hyperlipidemia*

B) The lesional stage of atherosclerosis

- *Role of monocytes / macrophages in lesion formation in hyperlipidemia*
- *Correlation between lipoprotein deposits, monocyte and smooth muscle cell recruitment and migration*
- *Pathobiochemistry of the atheroma*
- *Involvement of the oxidative stress and NADPH oxidases*
- *Molecular events leading to foam cell formation*
- *The relationship between endothelial cells and macrophages in the atherosclerotic plaques progression*
- *Effect of hyperlipemia on cerebral blood vessels and amyloid deposition*
- *Modulation and role of chemokines and cytokines*



Current concept on the sequence of events occurring during plaque formation in athero-sclerosis. *Consecutive arbitrary stages taking place in the development of atherosclerotic lesion. A hypothetical diagram - based on our data and from literature.* ***Stage I.*** *Endothelial cell (EC) activation/modulation of constitu-tive functions: increased transcytosis of plasma lipoproteins (Lp), and the switch to a secretory phenotype accountable for the hyperplasic basal lamina. Lp by interaction with extracellular matrix (ECM) components become atherogenic - oxidised modified lipoproteins (mLp).* ***Stage II.*** *EC dysfunction: initiation of an inflammatory process - expression of new or more cell adhesion molecules, cytokines and chemokines.* ***Stage III.*** *Recruitment of blood immune cells and commencement of a robust inflammatory reaction. Adherence of blood monocytes and T-cells to EC and diapedesis; platelets and neutrophils assist leukocytes migration. In the intima, monocytes become activated macrophages, take up mLp, turn into foam cells. Activation of lymphocytes.* ***Stage IV.*** *Formation of the fibrous cap by proliferation of intima-resident SMC and SMC migrated from the media and increased synthesis of ECM components.* ***Stage V.*** *Generation of a calcified fibro-lipid plaque: SMC, foam cells, apoptotic cells-derived lipids and calcification centres form a lipid loaded necrotic core rich in cholesterol crystals.* ***Stage VI.*** *Physical rupture of the unstable fibro-lipid plaque and thrombosis: thinning of the fibrous cap, EC apoptosis and erosion. The direct contact between tissue factor, blood platelets and coagulation components trigger thrombus formation that partially or totally impede the blood flow.*

(Mânduţeanu I. and Simionescu M., J Cell Mol Med, 2012)

II. Diabetes and its main complication - accelerated atherosclerosis

- *Modifications of plasma components, cells and tissues most affected by hyperglicaemia (myocardium, cardiac valves, retina, kidney, blood vessels), employing the hyperglycemic-hyperlipemic hamster, an original animal model*

- *Mechanisms involved in the altered reactivity of resistance arteries in hyperglycemic and/or hyperlipemic hamster*

- *The oxidant - antioxidant imbalance in diabetes associated / or not with obesity;*

- *The effects of high glucose on signal transduction pathways within the cells of the arterial wall;*

- *Signalling pathways activated by high glucose, AGE-albumin, Angiotensin II in the aortic endothelium and smooth muscle cells;*

- *MCP-1, Fractalkine, Resistin - major contributors to the inflammatory process associated with diabetes;*

- *Effect of AGE-LDL on human vascular cells: lipid loading, oxidative and inflammatory stress;*

- *Effect of homocysteine on calcium concentrations and platelet function in type 2 diabetes.*

III. Metabolic Syndrome and related disorders

- *Apolipoprotein E and apolipoprotein A¬V genes - risk factors in Metabolic Syndrome; impact on obesity;*

- *Lipolysis/lipogenesis imbalance in obesity; studies on adipocytes;*

- *Protein Tyrosine Phosphatase-1B, a key negative regulator of insulin signalling;*

- *Cardiac remodeling and glomerular cell dysfunction in hypertension;*

- *Transcription factors NF-kB and AP-1 involvement in the regulation of oxidative stress in inflammatory process in diabetes-associated hypertension;*

- *Platelets and circulating microparticles contribution to hypercoagulability*

IV. Gene regulation and polymorphism

- *Gene regulation of apolipoproteins belonging to the apoE/apo-CI/apo-CIV/apoC-II cluster;*

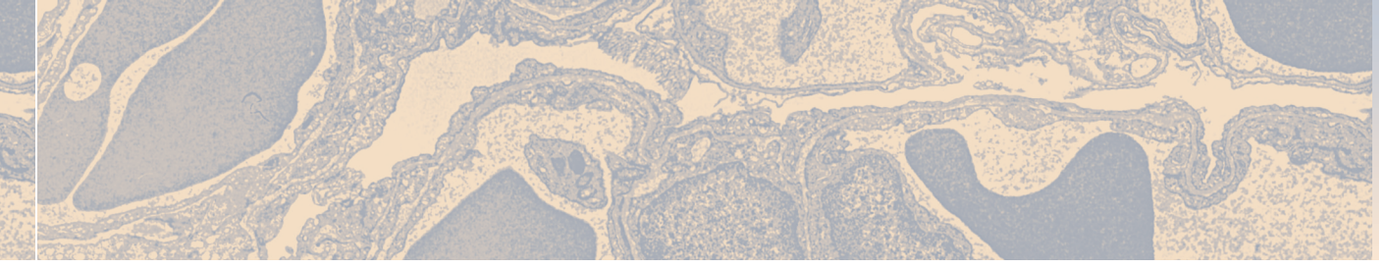
- *Stress inducible factors and inflammatory signaling pathways that regulateApoE gene expression in macrophages;*

- *eNOS gene variants in atherosclerosis, diabetes and Fabry's disease*

- *I/D gene polymorphism of ACE in atherosclerosis and diabetes*

- *Role of eNOS - TT894GG genotype in type 1 diabetic neuropathy.*

- *Leptin and leptin receptor gene polymorphisms in obesity and Type 2 diabetes.*



CELL PHARMACOLOGY

Uncovering the cellular and molecular mechanisms and the sequence of events occurring in diseases has as final goal interventions that could prevent, arrest or reverse the pathologic process.

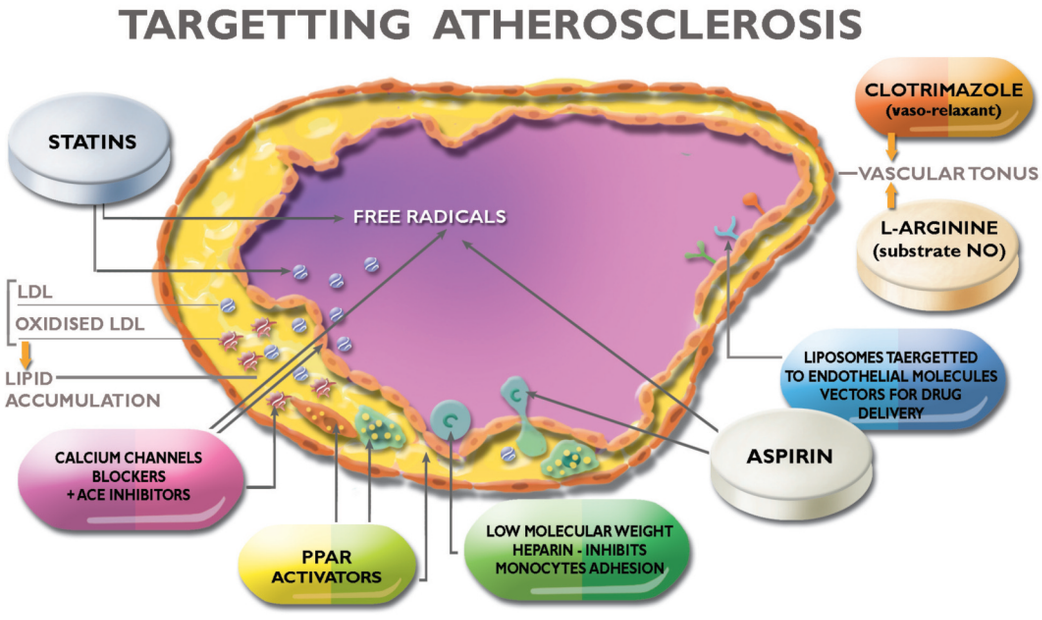
Experimental models and cultured cells are employed to determine the effect of various drugs and active principles at the level of organs, tissues, cells and molecules.

Some of the topics:

- *Molecular mechanisms involved in the protective effect of natural antioxidants on lipoprotein peroxidation;*
- *The effect of calcium channel blockers and inhibitors of angiotensin converting enzyme on the evolution of atherosclerosis;*
- *The effect of pro-oxidants and anti-oxidants on microvascular dysfunction;*
- *Effect of clotrimazole and enoxaparin on the vascular tone of resistance arteries;*
- *Liposomes targeted to endothelial receptors as vectors for drug delivery;*
- *A novel attribute of enoxaparin: inhibition of monocyte adhesion to endothelial;*
- *Modelling and therapeutic control of oxidative stress in endothelial and smooth muscle cells;*
- *Arresting and reversing the cardiovascular diseases by probiotic compounds;*
- *Effects of nutraceuticals (polyphenols and carotenoids) on gelatinases expression and activity; possible role in prevention and treatment of cardiovascular diseases;*
- *The antioxidant capacity of Zofenoprilin;*

Modulation of the oxidants-antioxidants balance by PPAR/RXR system;

- *Effect of anti-inflammatory drugs on chemokines expression in vascular cells exposed to hyperglycemia;*
- *Effect of AT1 receptor antagonist, irbersartan in experimental hypertension and hypercholesterolemia*
- *Modulation of gene expression and exploitation of molecular engineering for development of novel therapeutic anti-atherosclerotic strategies.*



CELL THERAPY

Traditional approach to restore a failing organ function is organ donation. Today, cell therapy is envisaged to provide an alternative solution to substitute diseased cells with functional cells.

Stem cells are endowed with the capacity to renew themselves and differentiate into a variety of specialized cell types. Once transplanted into patients, these cells are expected to interact intimately with, and be influenced by the microenvironment of the recipient organ.

Among the topics studied:

- *Differentiation of adult mesenchymal cells from human bone marrow into osteoprogenitor cells-osteoblasts;*
- *Molecular signals involved in stem cell differentiation;*
- *Development of cell therapies using endothelial progenitor cells derived from human placental tissueand Wharton Jelly;*
- *Establish a Stem Cell Bank.*

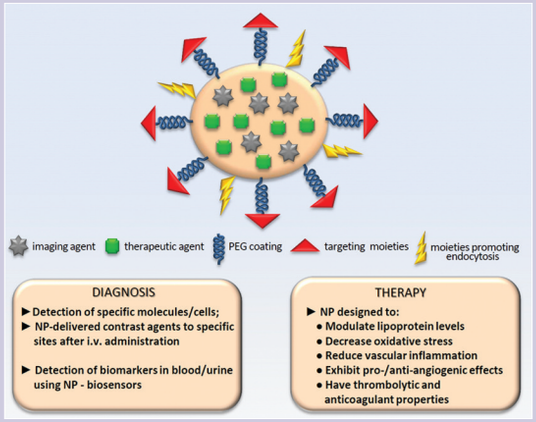
NANOTHERAPY

Recently, the emergence of nanotechnology uses in medicine (i.e., nanomedicine) has opened a new prospect for the development of targeted therapies for atherosclerosis based on drug nanocarriers. Our research interest is focused on the development of advanced targeted therapies based on nanotechnology to mitigate the inflammatory process associated with cardiovascular disease and cancer. The aim is to develop new and effective targeted drug delivery systems based on nanoparticles.

Among the topics studied:

- *Endothelial- and monocyte/macrophages-targeted nanotherapy designed to reduce inflammation in experimental models of atherosclerosis (small pharmaceutical agents, siRNA/shRNA delivery);*
- *Investigation of cytotoxicity and intracellular response induced by nanomaterials in human cells;*
- *In vivo toxicity and immunology studies after administration of nanoparticles;*
- *Testing of biomimetic structural and functional entities able to act as gene transfection vehicles.*

Multifunctional nanoparticle (NP)



*Hypothetical model of a multifunctional nanoparticle developed so as to exhibit one or more of the following characteristics: (**1**) ability to avoid the uptake by the mononuclear phagocyte system; (**2**) targeted delivery of encapsulated imaging or therapeutic agents by coupling of appropriate targeting moieties on the surface, and (**3**) if need be, the ability to promote the intracellular uptake.*
(Călin M. et al., Springer International Publishing 2016, editor H. Mureșian)

ORIGINAL CONCEPTS

- *Transcytosis of molecules and its mechanisms: fluid phase, adsorptive and receptor mediated;*
- *Histamine receptors expressed preferentially on venular endothelial cells (EC);*
- *Hyperglycemia induced - increased atherogenicity of lipoproteins contribute to accelerated atherosclerosis in diabetes;*
- *Albumin binding proteins expressed by endothelial cells, cardiomyocytes and other cells;*
- *The initial event in atherogenesis: the accumulation of modified lipoproteins within the subendothelial space of aorta, cardiac valves, coronary arteries (humans and experimental animals);*
- *Endothelial cell response to aggressors; modulation, dysfunction, injury;*
- *Specific patterns of alarmins identified by mass spectrometry may be favorable molecular biomarkers that could discriminate between different chronic non-communicable diseases (atherosclerosis, diabetes, cancer).*

ORIGINAL ANIMAL MODELS

- *The hyperlipemic hamster*
- *The hyperglycemic / hyperlipemic hamster*
- *L-NAME-induced hypertensive hamster*
- *Hypertensive/hyperlipemic hamster*
- *New Zeeland white rabbit model of atherosclerosis induced by high fat diet under sustained treatment with statins and inhibitors for PCSK9.*

NEW CELL LINES

- see the Collection of the Cell Culture Laboratory -

ADVANCED BIOMEDICAL TRAINING

- *Ph.D. program in cellular and molecular biology*
- *Postdoctoral training of scientists from Romania and abroad*
- *National and International Congresses of the Romanian Society for Cell Biology*
- *Annual Advanced Study School "From Cell and Molecular Biology to the Medicine of 21st Century", under auspices of the Romanian Academy (2000-2008).*

UNIUNEA EUROPEANĂ

Instrumente Structurale 2014-2020

COMPETITIVENESS OPERATIONAL PROGRAMME 2014-2020
PRIORITY AXIS 1 – RESEARCH, TECHNOLOGICAL DEVELOPMENT AND INNOVATION (RD&I) TO SUPPORT ECONOMIC COMPETITIVENESS AND BUSINESS DEVELOPMENT
ACTION 1.1.4 Attracting high-level personnel from abroad in order to enhance the RD capacity
Project Type: Attracting high-level personnel from abroad
MY SMIS: 104362, Financing contract 115/13.09.2016 (Budget: 8.657.500 lei); Period: 2016-2020

THERAVALDIS project - a multi-laboratories project

Title: TARGETED THERAPIES FOR DIABETES-RELATED AORTIC VALVE DISEASE

Coordinator: Dr. Agneta Simionescu, Clemson University, USA
Romanian Coordinator: Dr. Ileana Mânduțeanu, ICBP "N. Simionescu"

STATE OF THE ART:

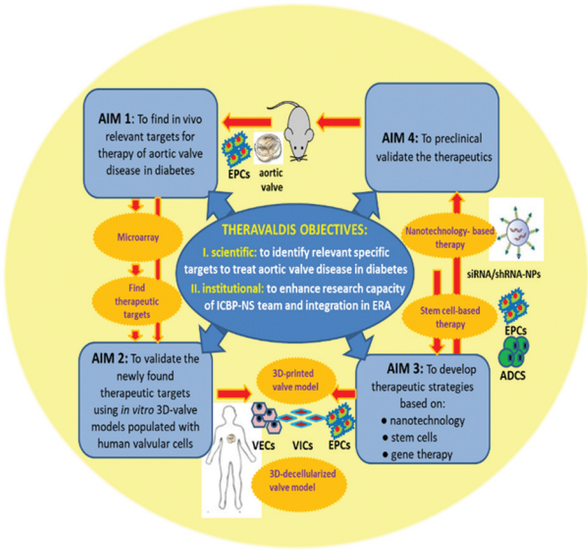
Aortic valve disease and especially calcific aortic valve disease (CAVD) is a global health burden in all aging societies, including the Romanian population. It is known that the presence of diabetes accelerates CAVD, and is predictive of poor prognosis in valve disease and of faster degeneration of implanted bio-prosthetic aortic valves. To our knowledge, a clinically pharmacological therapy for valve disease is still not available, the only alternative being the invasive and costly valve replacement. This urges the need for additional research to identify distinctive mechanisms of valve disease progression.

GOAL: to increase Romanian research at EU level in the field of medical and pharmaceutical biotechnology by creating a nucleus for research in nanotechnologies in ICBP "N Simionescu".

OBJECTIVE: to identify the specific mechanisms of valvular disease progression and the development of new nano-biotherapeutics for diabetes-aortic valve disease.

Schematic plan of the THERAVALDIS project objectives and aims for achieving its goal are:

EXPECTED RESULTS: (**I**) increase of the scientific performance and excellence of ICBP-NS (ISI papers, patents) and implementation of translational medicine; (**II**) new solutions to treat diabetes-related valve diseases contributing to improved efficiency of medical services and socially, to the health problem of the population; (**III**) integrating ICBP in the European Area of Research by enhancing and creating new collaboration with European partners (program „Horizon 2020") and with private medical-pharmaceutics and bio-medical industry; (**IV**) better and efficient exploitation of human potential in ICBP, motivate young people by creating new jobs, reducing „brain-drain" and attracting researchers from abroad.



UNIUNEA EUROPEANĂ

Instrumente Structurale 2014-2020

CCOMPETITIVENESS OPERATIONAL PROGRAMME 2014-2020
PRIORITY AXIS 1 – RESEARCH, TECHNOLOGICAL DEVELOPMENT AND INNOVATION (RD&I)
TO SUPPORT ECONOMIC COMPETITIVENESS AND BUSINESS DEVELOPMENT
ACTION 1.1.4 Attracting high-level personnel from abroad in order to enhance the RD capacity
Project Type: Attracting high-level personnel from abroad
MY SMIS: 104969, Financing contract: 118/16.09.2016 (8.630.843,2 lei, from which:
FEDR reimbursable contribution 7.254.108 lei)

DIABETER

DIABETER project - a multi-laboratories project

Title: IMPROVE INSTITUTIONAL COMPETITIVENESS IN THE FIELD OF TYPE 1 DIABETES BY DEVELOPING AN INNOVATIVE CONCEPT OF IMMUNOTHERAPY BASED ON MESENCHYMAL STROMAL CELLSE

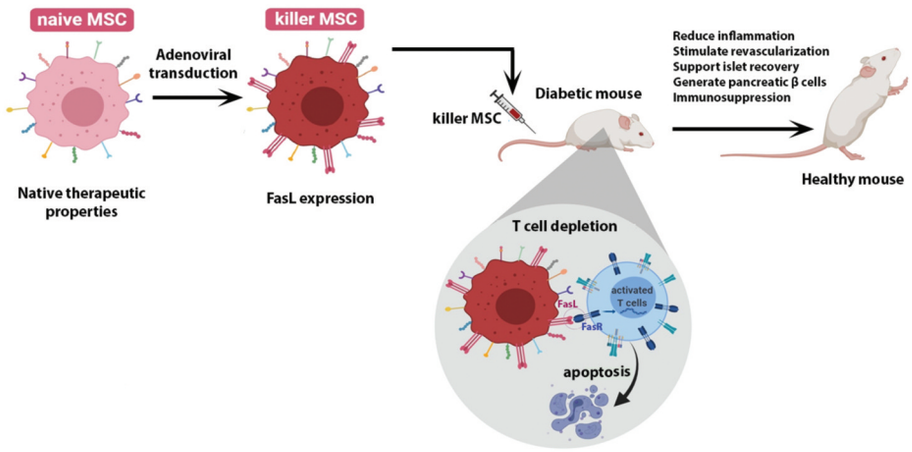
Coordinator: Dr. Nadir Askenasy, Schneider Children's Medical Center, Israel
Romanian Coordinators: Acad. Maya Simionescu and **Dr. Alexandrina Burlacu,** ICBP "N. Simionescu"

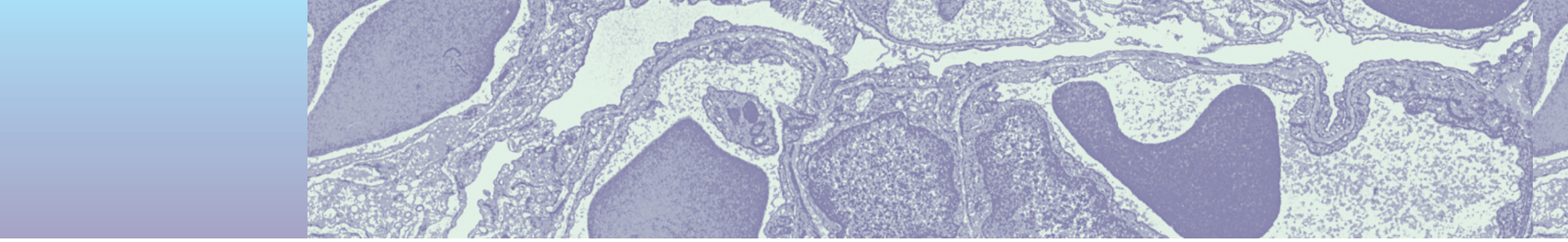
STATE OF THE ART:

Diabetes is a major public health problem in modern society, causing morbidity, disability and premature mortality, due to late complications. Previous studies have documented the need to deplete pathogenic T cells in order to restore self-tolerance. As systemic immunosuppressive therapy has detrimental consequences due to disease recurrence during rebound recovery from lymphopenia, other approaches should be developed by which autoreactive T cells are specifically depleted. This project is grounded on previous studies of Dr. Askenasy in the field of immunomodulatory therapy, showing that targeted delivery of T regulatory cells (Treg) carrying death ligands to the site of inflammation results in stabilization of glucose levels and reduces the pancreatic inflammation in animal models.

OBJECTIVE: to design a clinically relevant cell approach to cure diabetic autoimmunity by delivery of apoptotic signals using mesenchymal stromal cells as vehicles.

EXPECTED RESULTS: DIABETER aims to explore MSC capacity to cure type 1 diabetes in three mechanistic stages: arrest diabetic autoimmunity, restore self-tolerance and reconstitute insulin-producing capacity. The ambition, aspiration and **the strategic objective of DIABETER project** is to further develop our scientific skill and increase the long-standing involvement of ICBP team in the research areas of diabetic and cardiovascular pathophysiology.





INNATE-MI project - a multi-laboratories project

Title: TARGETING INNATE IMMUNE MECHANISMS TO IMPROVE RISK STRATIFICATION AND TO IDENTIFY FUTURE THERAPEUTIC OPTIONS IN MYOCARDIAL INFARCTION

Project code: PN-III-P4-ID-PCCF-2016-0172; Contract number: 5PCCF/2018 (2018-2022)

WEB page: http://www.icbp.ro/static/en/en-networking_grants-grants-national_grants/innatemi.html

Project Coordinator: Acad. Maya Simionescu, ICBP "N. Simionescu"

PARTNERS:

University of Medicine and Pharmacy of Târgu Mureş (Coordinator **Dr. Alexandru Șchiopu**);

"Carol Davila" University of Medicine and Pharmacy, Bucharest (Coordinator **Prof. Dr. Dragoș Vinereanu**).

STATE OF THE ART:

Myocardial infarction (MI) is a major cause of morbidity and mortality. At present, clinicians lack specific biomarkers for an accurate post-MI risk stratification and therapeutic tools to modulate myocardial inflammation and to promote efficient recovery. Innate immune processes mediated by polymorphonuclear neutrophils (PMN) and macrophages (MAC) in the immediate post-MI period determine the extent of myocardial damage but also induce repair.

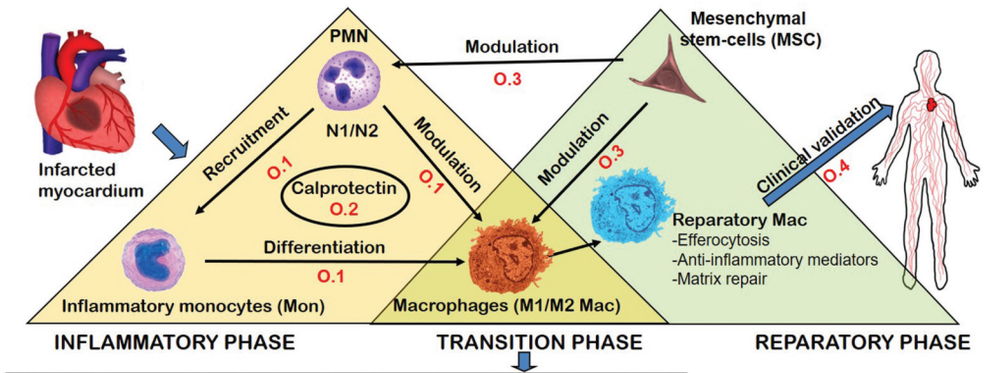
EXPECTED OUTCOME:

To find biomarkers that can be used to accurately identify patients at high risk to suffer new myocardial events. MSC therapy or S100A8/A9 blockade could improve recovery of MI patients and reduce morbidity and mortality in this large patient group.

INNATE-MI project GOALs - OBJECTIVEs - METHODOLOGY

- Identify key immune mediators that can be used to monitor cardiac recovery and assess prognosis in MI patients

- Develop novel immuno-modulatory therapies to limit the inflammatory damage and promote myocardial repair



O.1 Investigate the dynamic crosstalk between PMN and Mon/Mac sub-populations that mediate the inflammation/repair balance post-MI

O.2 Assess blockade of the PMN mediator calprotectin (S100A8/A9) as a p.tential therapy to inhibit inflammation and promote cardiac repair post-MI

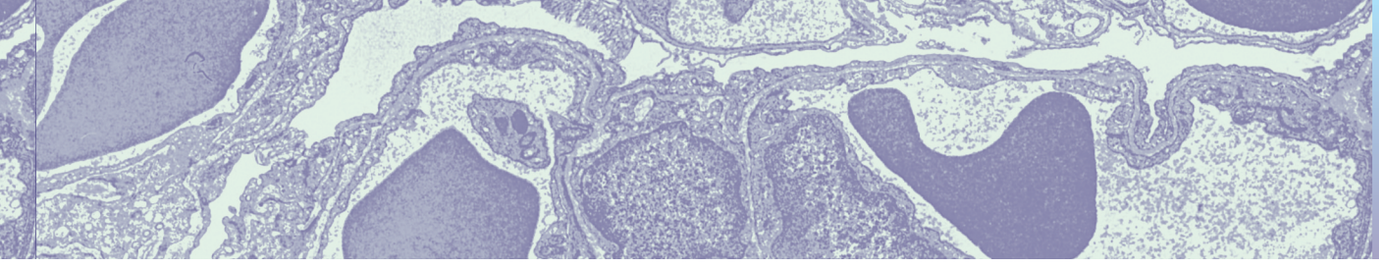
O.3 Develop a cellular therapy based on the immuno-modulatory properties of MSC, aimed to control inflammation and promote myocardial recovery post-MI

O.4 Identify and clinical validate key innate immune mediators as potential biomarkers reflecting cardiac remodeling and prognosis in MI patients

In-vivo - experimental MI
- Assess cell population dynamics
- Test effects of cell/pharmacological therapy on heart function and structure

In-vitro
- Investigate cellular crosstalk
- Identify key soluble mediators
- Identify key transcription factors

Clinical study – MI patients
- Dynamics of plasma mediators
- Cardiac remodeling (echo)
- Prognosis – Follow-up of CV events



INTERA project - a multi-laboratories project
Title: INTELLIGENT THERAPIES FOR NON-COMMUNICABLE DISEASES BASED ON CONTROLLED RELEASE OF PHARMACOLOGICAL COMPOUNDS FROM ENCAPSULATED ENGINEERED CELLS AND TARGETED BIONANOPARTICLES

Funded by UEFISCDI, code: PN-III-P1-1.2-PCCDI-2017-0697: 2018-2020

Project Coordinator: Acad. Maya Simionescu, ICBP "N. Simionescu"
PARTNERS:
*ICBP "N. Simionescu" (partner responsible: **Anca Gafencu**);*
*University Politehnica of Bucharest (partner responsible: **Ecaterina Andronescu**);*
*National Institute of Materials Physics (partner responsible: **Mădălina Bârsan**);*
*"Petru Poni" Institute of Macromolecular Chemistry (partner responsible: **Gheorghe Fundueanu**).*

STATE OF THE ART:

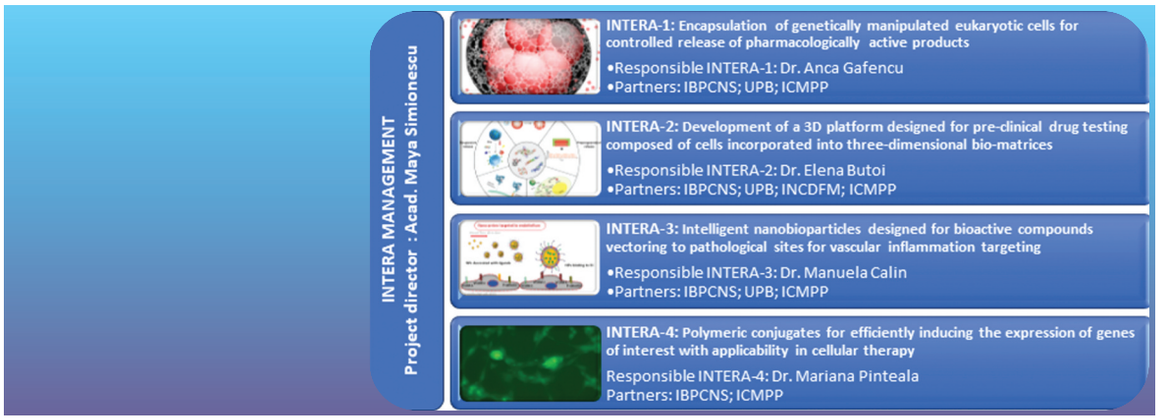
Chronic non-communicable diseases (atherosclerosis, diabetes, obesity, cancer), a major cause of mortality in the developing countries, are characterized by an associated inflammatory process. The complex project INTERA aims to develop innovative therapeutic methods to ameliorate the pathological progression by reducing the inflammatory process.

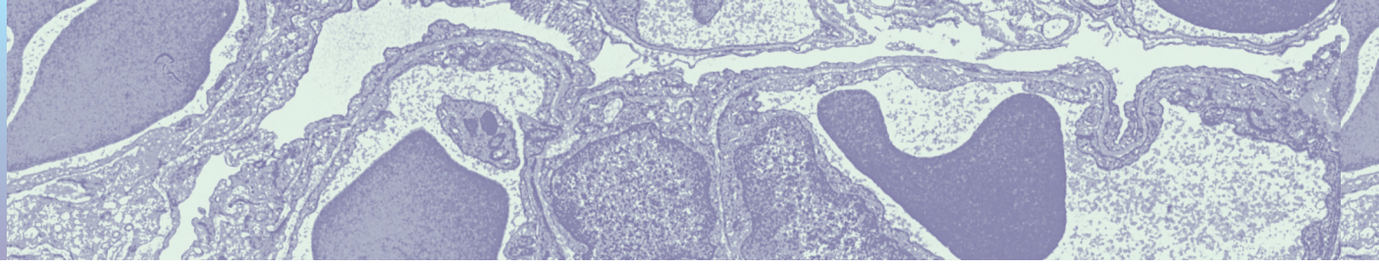
OBJECTIVE: INTERA project will provide the support to strengthen the scientific and technical competencies of the partner research units in the Bioeconomic domain. INTERA includes the development of multidisciplinary studies that only together can create and define new nano- or micro-medical devices for smart and innovative anti-inflammatory therapies

EXPECTED RESULTS:

(1) Attracting 10 young researchers to each partner teams; (2) Training of young researchers (training courses, knowledge transfer, 2 specialization schools and 2 workshops; (3) Consolidation and expansion of scientific and technical competencies; (4) Technological products and new or improved services will be the basis for a more effective interaction with the economic environment; (5) Better capitalization and dissemination of knowledge, competences and research results, by filing patent applications and publishing the data obtained in scientific journals.

The four sub-projects that compose the complex INTERA project are shown below:





BIOVEA project - a multi-laboratories project

Title: DEVELOPMENT OF BIONANOTECHNOLOGIES BASED ON EXTRACELLULAR VESICLES FOR EARLY DIAGNOSIS, PROGNOSIS AND THERAPY OF ATHEROSCLEROTIC DISEASE

Funded by UEFISCDI, code: PN-III-P1-1.2-PCCDI-2017-0527; 2018-2020

Project Coordinator: Dr. CSI Adriana Georgescu , ICBP "N. Simionescu"

PARTNERS:

National Institute for Research and Development in the field of Pathology and Biomedical Sciences "Victor Babeş" Bucharest (INCDVB) - partner responsible: ***Dr. CSI Mihaela Gherghiceanu****; University of Medicine and Pharmacy "Carol Davila" Bucharest (UMF) - partner responsible:* ***Prof. Dr. Dragoş Vinereanu****; Emergency Clinical Hospital "Pius Brînzeu" Timişoara - Research Center OncoGen (OncoGen) - partner responsible:* ***Prof. Dr.Virgil Păunescu****.*

STATE OF THE ART:

Various biomarkers have been proposed for the diagnosis and prognosis of acute coronary syndrome, however not for stable coronary disease. Identification of biomarkers that augment established clinical indicators, may allow earlier diagnosis of coronary disease, as well as improved recognition of the risk of complications and cardiovascular death. Additionally, this would pave the way for biomarkers, such as extracellular vesicles, to be employed as precise therapeutic agents in these diseases.

OBJECTIVE:

To develop and implement new technologies to identify extracellular vesicles that can be used for early diagnosis, monitoring and treatment of stable coronary disease.

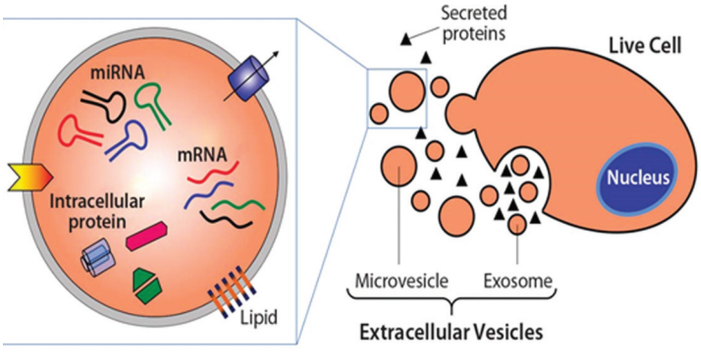
Such promising approaches are in their infancy in many areas of clinical medicine, therefore key contributions to existing knowledge are of strategic priority in medicine.

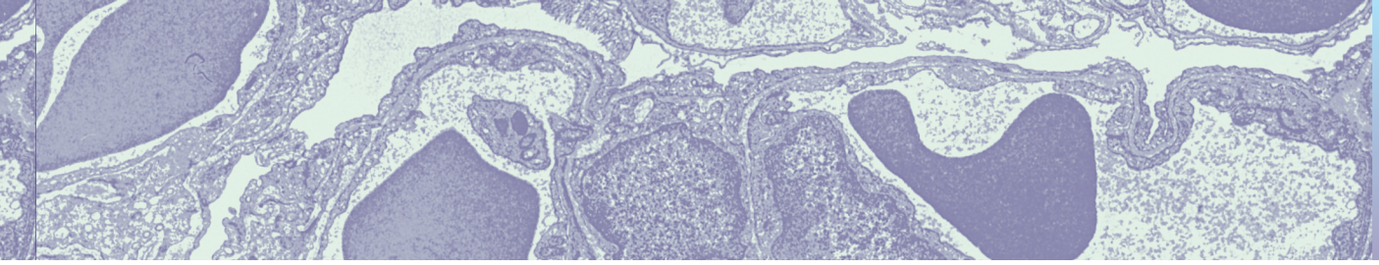
SPECIFIC AIMS:

(1) identification and analysis of circulating extracellular vesicles, as potential biomarkers in experimentally induced atherosclerotic coronary disease; **(2)** validation of extracellular vesicles as biomarkers for the early diagnosis and prognosis of stable coronary disease in human patients; **(3)** in vitro establishment of a cell-line that can efficiently generate vesicles to be used as therapeutic agents in atherosclerotic coronary disease; **(4)** investigation of therapeutic potential of extracellular vesicles in experimental models for cardiac hypertrophy and coronary atherosclerosis.

EXPECTED OUTCOME:

Is the creation of a competitive, multidisciplinary consortium focusing on the application of leading-edge technologies in the diagnosis, monitoring and treatment of cardiovascular disease. It is expected that the study will deliver extracellular vesicle-based nanotechnologies to be employed in a clinical setting.





NANODIATER project - a multi-laboratories project

Title: NANOPARTICLES DESIGNED TO TARGET CHEMOKINE-RELATED INFLAMMATORY PROCESSES IN VASCULAR DISEASES AND CANCER METASTASIS AND IMPLEMENTATION OF A BIOSENSOR TO DIAGNOSE THESE DISORDERS

Funded under the frame of EURONANOMED ERA-NET project FP7 scheme, 2011-2014

Project Coordinator: Acad. Maya Simionescu, ICBP "N. Simionescu"

PARTNERS:

România: *ICBP "N. Simionescu" - project responsible: **Manuela Călin**;*
*University Politehnica of Bucharest - project responsible: **Marius Enăchescu**;*
*SC OPTOELECTRONICA 2001 - project responsible: **Theodor Necşoiu**;*
Germany: *University of Bonn - project responsible: **Gerd Bendas**;*
*EPO GmbH Berlin - project responsible: **Reiner Zeisig**;*
Switzerland: *University of Zurich - project responsible: **Lubor Borsig**;*
Turkey: *Istanbul University - project responsible: **Erdal Cevher**.*

STATE OF THE ART:

Inflammatory processes and endothelial expression of chemokines and cell adhesion molecules accompany atherosclerotic plaque formation and cancer cell metastasis. Therefore, therapeutic blockage and early diagnosis of inflammation may prevent these pathological events.

OBJECTIVE:

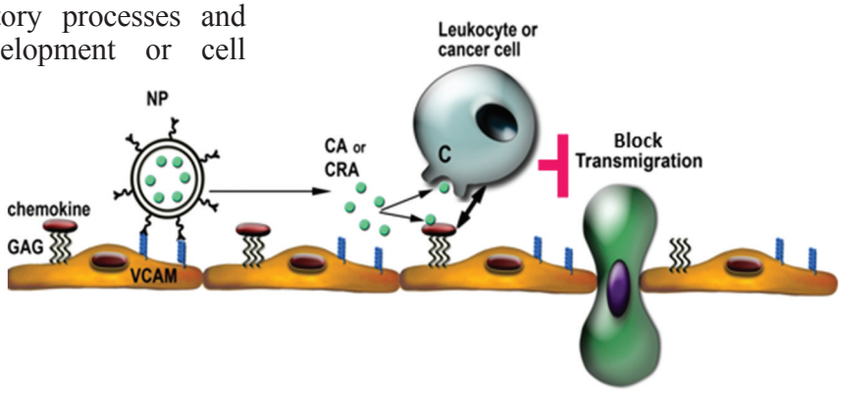
To design nanoparticles (NP) as "cell sensors" for tumorigenic or inflammatory cells and for targeted drug delivery to the inflammatory site.

WORKING HYPOTHESIS:

The NP targeting exclusively activated endothelium will carry chemokine antagonists or chemokine receptor antagonists, will bind specifically and release the antagonists, thus blocking the inflammatory processes and prevent atheroma development or cell metastasis in cancer.

RESULTS:

- European patent (EP2832373):"Liposome for blocking site-specifically chemokine-related inflammatory processes in vascular diseases and metastasis";
- 13 peer-reviewed ISI articles;
- 2 reviews;
- 1 book chapter;
- 26 communications to scientific congress;
- 3 PhD dissertation thesis;
- In 2019, the NANODIATER project was selected as one of the successful EuroNanoMed project and Dr. Manuela Călin was invited to present the project' results at the EuroNanoMed3 review seminar for funded projects in Bratislava, Slovakia, 28-29th May 2019.



ICGEB 40 YEARS

AN INCREDIBLE 40-YEAR JOURNEY TO UNDERSTAND CELL'S SECRETS FOR THE BENEFIT OF HUMAN HEALTH