GENE REGULATION AND MOLECULAR THERAPIES LABORATORY

***Anca Violeta Gafencu**, PhD*
HEAD OF LABORATORY

STAFF
***Violeta Georgeta Trusca,** PhD / **Mădălina Dumitrescu,** PhD*
***Ioana-Mădălina Fenyő,** PhD / **Ana Văcaru,** PhD*
***Márton Fogarasi,** PhD / **Andrei Văcaru,** PhD*
***Mirel Popa,** PhD / **Irina Florina Tudorache,** PhD Student*
***Laura Georgiana Moise,** Master Student*
***Lavinia Tudor,** Master Student*
***Mihaela Bratu,** Technical assistant*

FORMER RESEARCH STAFF:
Monica Dutca, Adina Mihai,Otilia Postea,
Alexandra Robciuc, Marius Robciuc,
Irina Florea, Elena Fuior, Ana-Maria Eftimie
Simona Stavri, Corina Roman

CORE LABORATORY UNITS:
Genetic analysis
Viral transduction and transfection

GENE REGULATION AND MOLECULAR THERAPIES LABORATORY

Anca Violeta Gafencu, *PhD*
Head of Laboratory
E-mail: *anca.gafencu@icbp.ro*

Major position/appointments and professional training

• Scientific researcher I in ICBP (since 2014)
• Member of the Scientific Council of ICBP
• Member of the Doctoral School of the University of Bucharest
• Member of the Romanian Society for Cell Biology
• Visiting scientist: University of Lausanne, Switzerland (1997-1998), University of Crete Medical School, Greece (2002-2007), University of Debrecen, Hungary (2007), University of Patra, Greece (2008)

MAJOR RESEARCH INTERESTS

- **Gene expression and gene regulation**
- **Cellular and molecular therapies for non-communicable diseases**
- **Isolation, characterization and immortalization of endothelial cells**
- **Plasmalemmal domains of endothelial cells**
- **Receptors involved in endocytosis and transcytosis**

TECHNICAL EXPERTISE:

Molecular biology (PCR, RT-PCR, and Real Time PCR, cloning, sequencing, ChIP, 3C, transfection), biochemical assay (protein and nucleic acid assays, enzymatic activity, electrophoresis, chromatography, Western Blot, ELISA, etc.), adenoviral and lentiviral transduction, cell culture (primary, cell lines, mesenchymal stromal cells), optic and fluorescence microscopy, radiolabelling, flow cytometry, animal experimentation (treatment, surgery, transgenic mice, etc.), computer operating skills.

PUBLICATIONS

30 original ISI scientific articles (Scopus, > 850 citations), 9 articles in other databases, one book chapter.

Work in collaboration with Dr. Constantina Heltianu (former head of Radioizotopes laboratory), Dr. Felicia Antohe, Dr. Victor Jinga, Alexandrina Burlacu, Mihaela Stanescu, Geo Serban and Mircia Toderici.

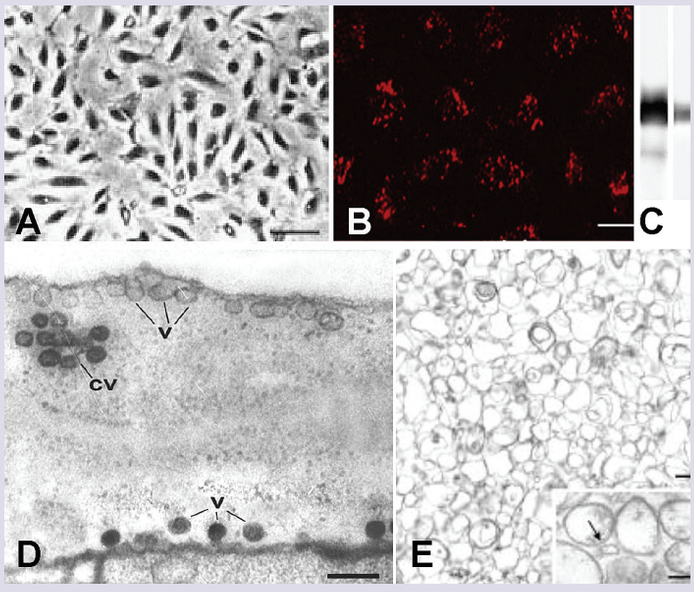
A human placental endothelial cell (EC) line was established and characterized for the cell morphology and for the expression of different markers (Jinga et al., 2000). Placental EC were immortalized by transfection with a plasmid encoding SV 40 large T antigen (Gafencu et al., 2001). This cell line was used for the characterization of the immunoglobulin G (IgG) receptors that play an important role in the transfer of antibodies from the mother to the foetus. IgG receptors expressed by the human placental EC were determined and IgG binding and internalization in these cells was characterized. The results obtained in this project showed that, beside neonatal Fc receptor (FcRn), a novel receptor for IgG is responsible for the IgG transfer from the mother to the foetus (Antohe et al., 2001; Gafencu et al., 2003). Data obtained showed the distribution of this receptor in the EC as well as some of its biochemical features. These data led to a new concept for the

maternal/foetal transfer of the antibody.

Different microdomains were isolated from a highly purified endothelial cells (EC) apical membrane fraction and identified by their protein markers. The caveolar membrane fraction was morphologically and biochemically characterized (electron microscopy -EM, protein and lipid assays). The results obtained revealed the distribution of different proteins and fatty acids between caveolar and non-caveolar domains(Gafencu et al., 1998).

The intracellular route of transferrin receptor (TfR) in EC was studied in cells transfected with a plasmid encoding TfR linked to HRP, as a reporter; by EM, TfRs were found in various intracellular structures (Heltianu et al., 1997).

The placental endothelial cell line obtained represents an important tool for the study of trans-endothelial transport of different molecules (drugs, anaesthetics, proteins, etc), which is a very important process that confers selectivity of the trans-placental transfer (Simionescu et al., 2002).

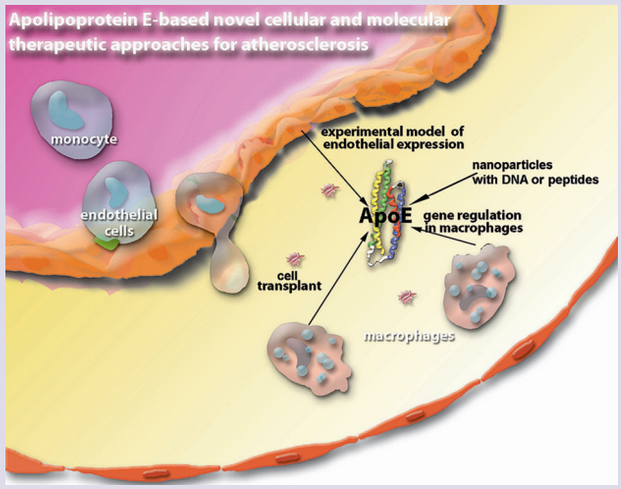


Transcytosis of IgG through placental endothelial cells. *(A). Primary culture of human placental endothelial cells (HPEC). (B) IgG endocytosis by HPEC, (C) Identification of a novel IgG receptor and FcRn in HPEC. (D) Electron micrography of IgG transcytosis through HPEC (E) Caveolae isolated from endothelial cells.*

GENE REGULATION AND MOLECULAR THERAPIES LABORATORY

CURRENT PROJECTS

1. APOLIPOPROTEINS GENE REGULATION AND MANIPULATION FOR THERAPEUTIC PURPOSES



The main directions of the project: *(A) gene regulation, (B) transplant of cells that are able to infiltrate into the athero-sclerotic plaque, (C) endothelial expression of apoE, (D) nanoparticles for delivery of DNA or peptides.*

OBJECTIVES

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

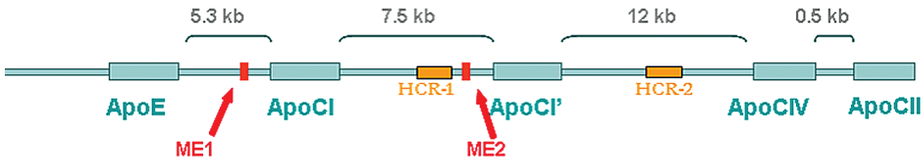
This project began in collaboration with Prof. Dimitris Kardassis (University of Crete, Medical School, Greece).

The major goal of the project is the understanding of the molecular mechanisms of apolipoproteins gene regulation in normal conditions and the identification of the alterations that affect the gene expression in pathological states.

Apolipoprotein E (apoE), a glycoprotein of 34 kDa, is a major component of the lipoprotein transport system playing important roles in lipid metabolism. ApoE gene belongs to apoE/apo-CI/apo-CIV/apoC-II cluster.

The main results concerning the gene regulation of apolipoproteins belonging to the apoE/apoCI/apoCIV/apoCII cluster showed that:

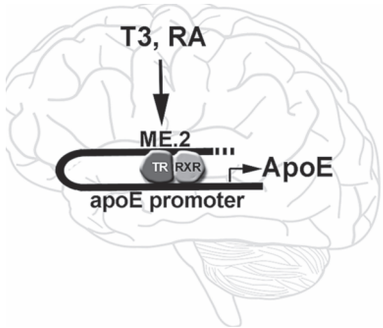
- beside proximal regulatory elements, distal enhancers play important roles in the modulation of genes located in the apoE-CII cluster (Trusca et al., 2011);
- the macrophage-specific interaction of ME.2 with the apoE promoter facilitates the transcriptional enhancement of the apoE promoter by the transcription factors STAT1 that bind on ME.2 (Trusca et al., 2011);
- STAT1 can bind on ME.2 as well as on the apoCII proximal promoter, and transactivate it; STAT1 cooperates with RXR for apoCII gene upregulation in macrophages (Trusca et al.,2012);
- apoE is strongly induced during monocytes activation by interaction of the apoE promoter and multienhancers, as revealed by 3C and transient transfection experiments (Trusca et al., 2011);
- KLF4 up-regulates apoE gene after binding on specific sites present on apoE promoter; a strong synchronized induction of KLF4 and apoE expression during macrophages differentiation was observed; the interaction of KLF4 with CREB results in an enhanced up-regulatory effect of KLF4 on apoE promoter (Stavri et al., 2015);
- the molecular signalling mechanisms



Schematic model of apoE/apoCI/apoCI'/apoCIV/apoCII gene cluster and of the known regions required for tissue-specific expression*: hepatic control region 1 and 2 (HCR-1, HCR-2), and multienhancer 1 and 2 (ME1, ME2).*

leading to apoE down-regulation under inflammatory stress involves NF-κB and AP1 transcription factors (Gafencu et al., 2007);

- metformin up-regulate apoE gene in endotoxin-stressed macrophages and the mechanism by which metformin counteracts LPS effect involves the inhibition of NF-κB (Stavri et al., 2015);
- increased concentration of homocysteine inhibited apoE expression and this negative effect is mediated *via* the activation of the proinflammatory transcription factor NF-κB (Trusca et al., 2016);
- in astrocytes, thyroid hormones upregulate apoE expression, acting on ME.2 (Roman et al., 2015).

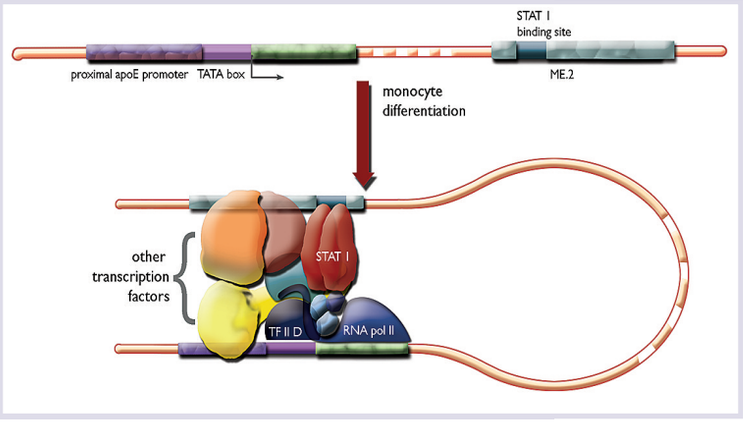


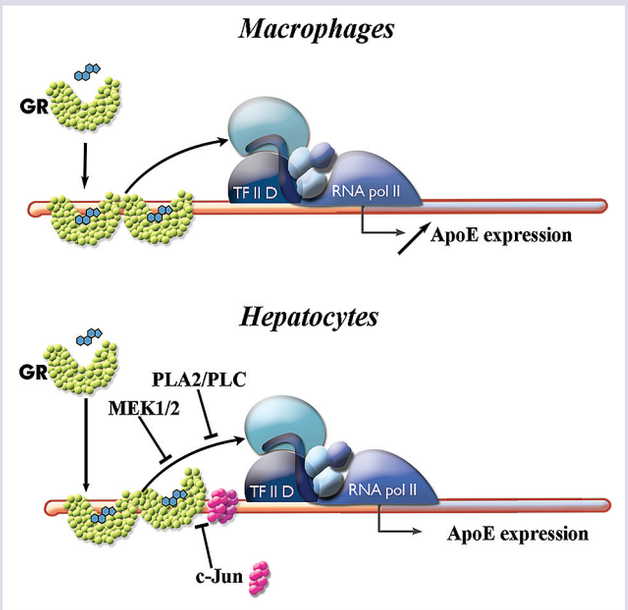
ApoE gene expression in the brain is modulated by ligand-activated TRβ/RXRα heterodimers.

The binding site of TRβ/RXRα is located on the distal regulatory element ME.2 that interact with apoE promoter to enhance the expression (Roman et al., 2015).

STAT1 interaction with the transcription initiation machinery, leading to the modulation of apoE gene expression.

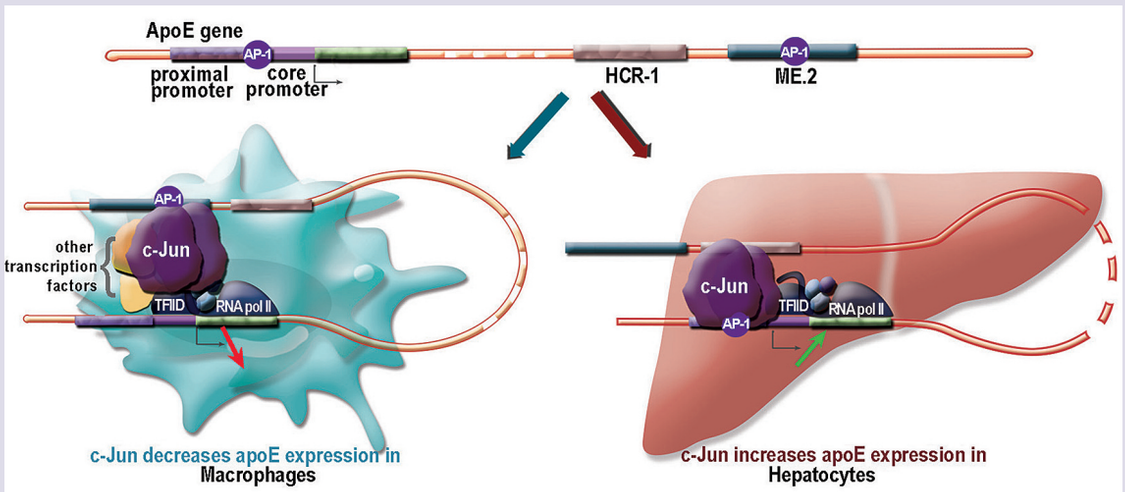
After DNA bending that probably takes place during monocyte differentiation, STAT1 bound on ME.2 interacts with the transcription initiation complex, leading to the activation of apoE expression (Trusca et al., 2011).





***Cell-specific modulation of apoE gene expression by ligand-activated glucocorticoid receptors (GR)**. In macrophages, ligand-activated GR binds to its specific site located on apoE proximal promoter leading to an increase in apoE promoter activity and enhancing apoE transcription. In hepatocytes, despite the direct interaction between dexamethasone-activated GR and apoE promoter, GR cannot modulate apoE transcription. The binding of c-Jun on its specific site located next to the GR binding site inhibits only partially GR binding. MEK1/2 and PLA2/PLC signaling also contributes to the inhibition of GR action on apoE gene (Trusca et al., 2016).*

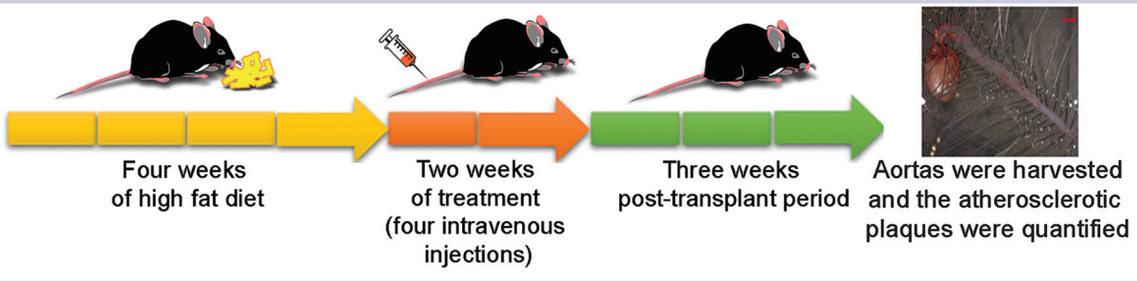
- glucocorticoids differentially target apoE gene expression, increasing its level specifically in macrophages, while a combinatorial effect of different pathways leads to the inability of glucocorticoid receptors to modulate apoE expression in hepatocytes (Trusca et al., 2017);
- c-Jun transcription factor has an opposite effect on apoE gene regulation in hepatocytes and macrophages (Trusca et al., 2019);



***Cell-specific effects of c-Jun on apoE gene expression.** In macrophages, c-Jun binding to the apoE core promoter downregulated apoE expression, in conjunction with other transcription factors. ME.2 distal regulatory element was brought into the proximity of the apoE promoter, and the functional AP-1 binding site on ME.2 additionally potentiated c-Jun repression of apoE. In hepatocytes, the HCR-1 distal regulatory element interacted with the apoE promoter, but apoE expression was upregulated by c-Jun through binding to the site located at -94/-84 in the apoE proximal promoter (Trusca et al., 2019).*

2. Transplant of cells that are able to infiltrate into the atherosclerotic plaque.

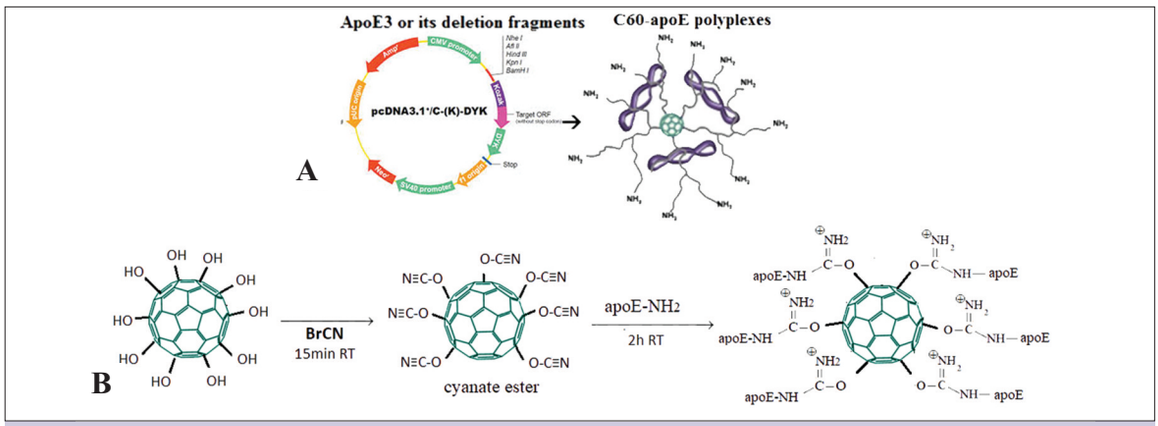
ApoE overexpressing RAW 264.7 monocytes/macrophages were transplanted into apoE deficient mice previously fed with a high fat diet for one month. The quantification of the aortic plaques area revealed a significant decrease in the mice transplanted with ApoE-expressing RAW 264.7 cells, as compared with those transplanted with unmodified RAW 264.7. Taken together, our results sustain the involvement of apoE released by transplanted macrophages in the regression of the atherosclerotic plaque (Dumitrescu et al., 2016).



Experimental design of monocytes transplant. *After four weeks of atherogenic diet, the apoE deficient mice were injected four times during two weeks with apoE stably transfected or non-transfected RAW 264.7 cells or vehicle alone. After a period of three weeks, the animals were sacrificed and the aortas were isolated and analyzed.*

3. Fullerene-based vectors for DNA encoding apoE or apoE protein for atherosclerosis innovative therapies.

The central hypothesis of this project is that targeting apoE at the site of atherosclerotic plaque using novel biotechnologies will provide an efficient cholesterol efflux from the lipid loaded cells, having significant benefits in the fight against atherosclerosis. The main goal of this project is to use plasmids encoding apoE or recombinant apolipoproteins attached together with transferrin / anti-TfR to fullerene nanoparticles to increase the cholesterol efflux from foam cells, leading to the regression of the atherosclerotic plaques.

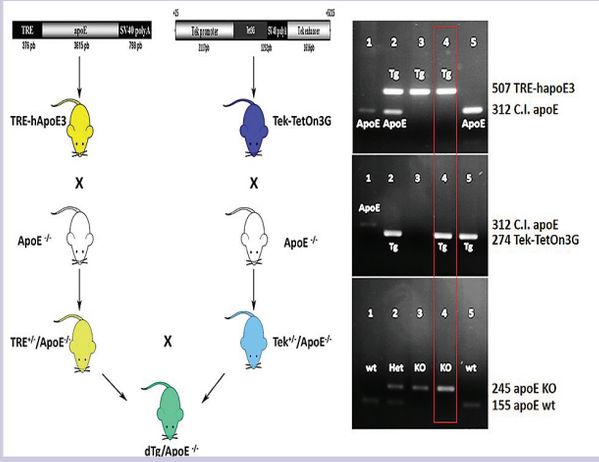


Obtaining fullerene nanoparticles with apoE-encoding DNA or ApoE protein. ***A.*** *Coupling apoE encoding plasmids to C60-PEI conjugates;* ***B.*** *Hydroxyl groups of fullerenol are activated to cyanate ester groups (FullCN) which interact with the amino groups of ApoE protein.*

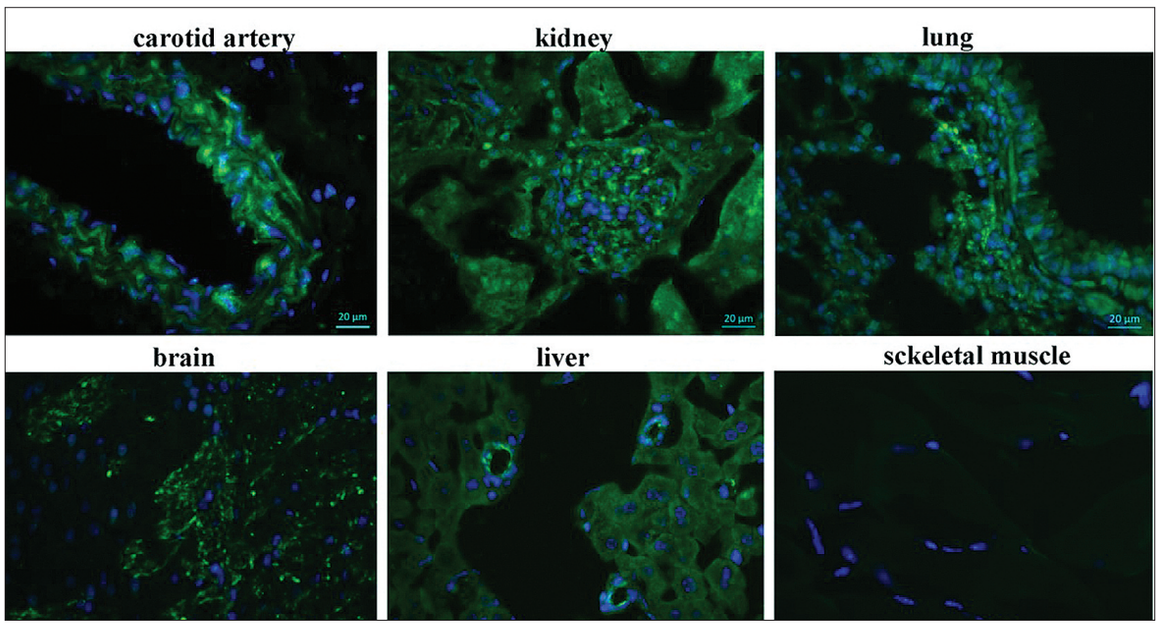
4. Transgenic mice with conditional and selective apoE expression in the endothelium

We hypothesized that induction of *apoE* gene expression in the endothelium might contribute to an elevation of ApoE concentration in the atherosclerotic plaque, where it could participate to cholesterol efflux from lipid-loaded cells found in the atheroma. We obtained double transgenic mice as described below. Under doxacycline treatment apoE expression is induced in the endothelial cells of various organs.

We greatly acknowledge the help of Dr. Serban Morosan and Dr. Sébastien Dussaud (Fac. Med. Pierre et Marie Curie, Paris) for the pronuclear injection and the obtaining of the transgenic founders.



Generation of the transgenic mice with inducible endothelial-specific expression of ApoE3 (EC-ApoE3 Tg mice). *This mouse model was obtained by cross-breeding two transgenic mice (i) one carrying the reverse tetracycline transactivator expressed under an endothelial specific promoter (Tek-rtTA) in the apoE null mouse (Tek-rtTA apoE null), and (ii) one carrying the apoE3 variant driven by the promoter provided with a modified tetracycline-responsive element (TRE-apoE), expressed also in the apoE-/- mouse -TRE-apoE apoE null (Fenyo et al., 2016).*



Endothelial-derived apoE distribution in different organs of the transgenic mice. *Under doxycycline treatment, apoE is expressed in the carotid artery, kidney, lung, brain and liver. By contrast, no staining was observed in the muscle (unpublished).*

2. ENCAPSULATED CELLS SECRETING ANTI-INFLAMMATORY FACTORS

The multi-laboratories complex project (INTERA, coordinated by Maya Simionescu) aims to develop innovative therapeutic methods to ameliorate the pathological progression by reducing the inflammatory process.

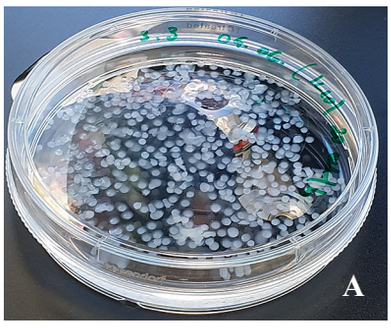
The multidisciplinary studies proposed by INTERA can create and define new nano- or micro-medical devices usable for smart and innovative anti-inflammatory therapies.

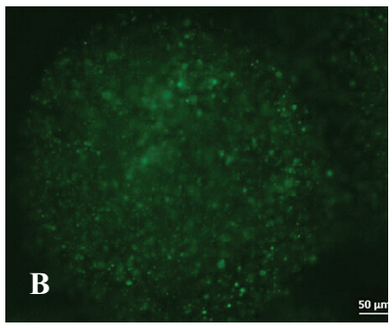
There are two sub-projects in which the laboratory is involved: "Cell-encap-sulation of genetically manipulated eukaryotic cells for controlled release of pharma-cologically active products "and "Polymeric conjugates to induce efficiently the expression of genes of interest with applicability in cellular therapy".

The project on cell encapsulation is performed in a collaboration with a team from "Petru Poni" Institute of Macromolecular Chemistry, Iasi, led by Dr. Gheorghe Funduianu, and a team from the Polytechnic University of Bucharest, led by Dr. Anton Ficai.

Cell encapsulation allows the delivery of molecules of interest for a longer period as cells release these molecules continuously. The capsule maintains the cell immobilized and do not allow the spreading of the cells. Moreover, the encapsulation protects the cells from the host's immune system.

So far, we have obtained stably transfected cells expressing IL-10 and GFP, cells which were encapsulated in alginate using a cell encapsulator from Nisco (Switzerland).





Cell encapsulation
(A) *Alginate capsules;*
(B) *GFP-labelled encapsulated cells*

3. TRANSPLANT OF THE KILLER MESENCHYMAL STROMAL CELLS - AN APPROACH TO CURE TYPE 1 DIABETES (PART OF THE MULTI-LABORATORIES DIABETER PROJECT)

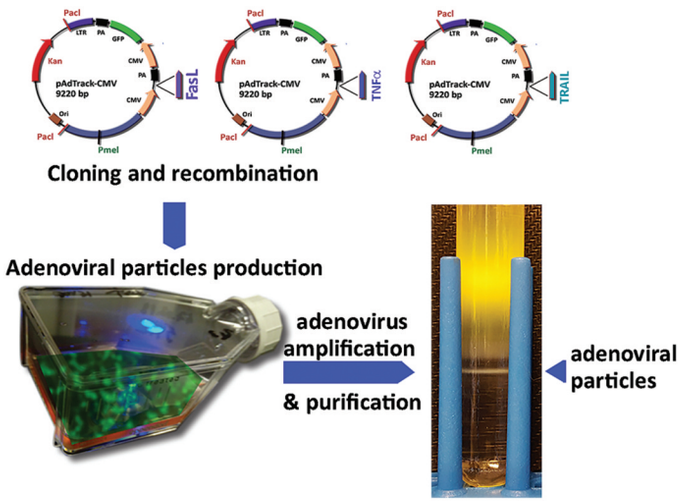
This multi-laboratory project is led by Dr. Nadir Askenasy (Frankel Laboratory of Experimental Bone Marrow Transplantation, Petach Tikva, Israel).

Type 1 diabetes is an inflammatory reaction against pancreatic islets triggered by extrinsic precipitating factors in subjects with particular genetic configurations favorable to autoimmunity.

Despite intensive interest in etiology, pathogenesis and mechanisms of this inflammatory reaction, reliable curative therapies are yet to be developed.

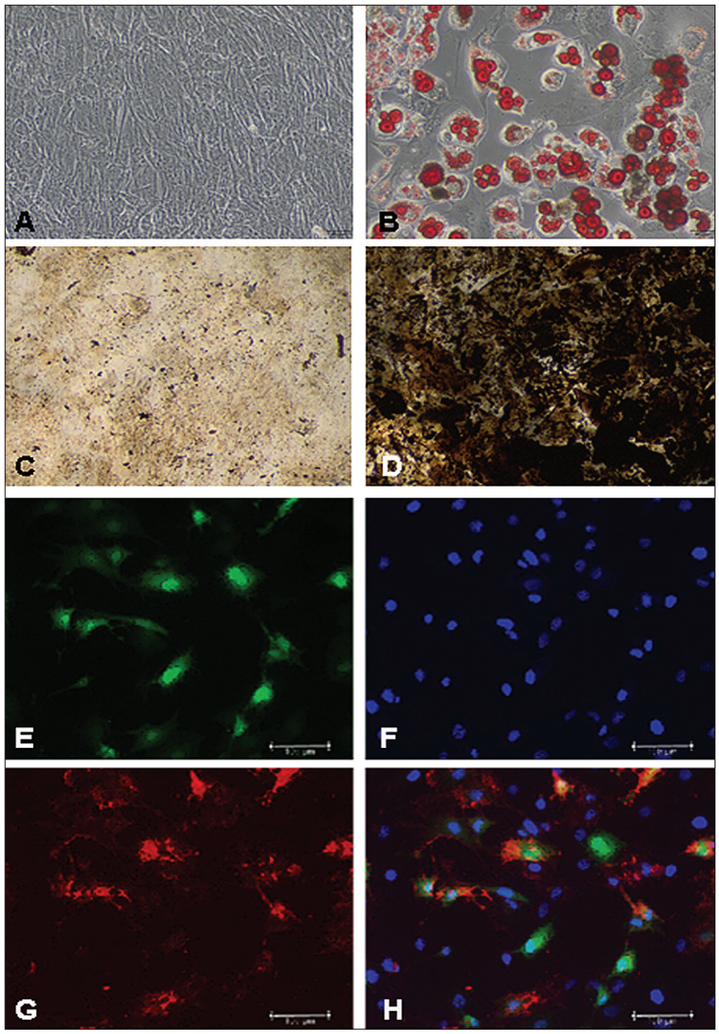
The **goal** of the proposed studies is to design, refine, consolidate and simplify a clinically-relevant cell therapeutic approach to cure type 1 diabetes using mesenchymal stromal cells (MSC).

To this purpose, we designed and produced the adenoviruses for TNF-family ligands for MSC transduction. Large amounts of the adenoviruses were produced by amplification in AD293 cells, that were modified to confer resistance to apoptosis. The adenoviruses were purified by ultracentrifugation on CsCl gradient.



We greatly acknowledge the help of Dr. Kyriakos Kypreos (Univ. Patras, Greece) for his advices concerning the adenoviral technology.

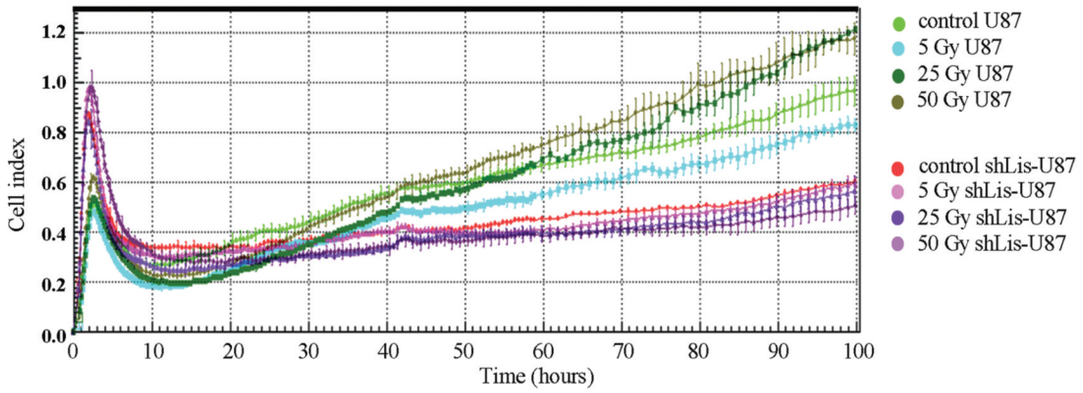
Mesenchymal stromal cells were isolated from bone marrow and checked for their ability to differentiate into adipocytes, chondrocytes and osteoblasts. The expression of TNF-family members was induced on MSC by adenoviral transduction.



Differentiation of mesenchymal stromal cells and FasL expression induced by adenoviral transduction. *Adipogenic differentiation of m*esenchymal stromal cells (*MSC) showed lipid loaded cells stained with OilRedO (B) as compared with control cells (A). Osteogenic differentiation showed matrix mineralization of MSC (D) as compared with the control cells (C). MSC transduced with the adenovirus that induces FasL and GFP expression. After transduction, cells express GFP (E). The anti-FasL antibody stained the transduced cells in red (G). Nuclei were stained with Hoechst 33258 (F). Merged staining contains: red- FasL, green– GFP; blue– nuclei (H).*

4. NOVEL BIOMARKERS AND TARGETS FOR GLIOBLASTOMA

By a multi-omics approach, we search for relevant biomarkers of glioblastoma, in the frame of an ERA-NET project led by Prof. Joerg Walter Bartsch, Philipps University Marburg. Until now, we found that Lissencephaly-1 (Lis1) expression colocalize with CD133 in a subset of glioma cells. Lis1 gene expression is increased up to 60-fold in CD133 positive cells isolated from primary cultures of glioblastoma and U87 cell line as compared to CD133 negative cells. In U87 with silenced Lis1 gene (shLis1-U87) we noticed a significant decrease of CD133+ cells fraction as compared with control cells. Moreover, CD133+ cells isolated from shLis1-U87 were two times less adhesive, migratory and proliferative, as compared with control transfected U87 CD133+ cells. Lis1 silencing decreased the proliferative capacity of irradiated U87 cells, an effect attributable to the lower percentage of CD133+ cells. Our data show that a preferential expression of Lis1 gene is found in CD133+ glioblastoma cells, and reveal a role of Lis1 in regulating CD133+ glioblastoma cells function. This work was done in collaboration withDr. Felix Brehar from Bagdasar - Arseni Emergency Hospital, Bucharest, Romania.



Proliferation of irradiated U87 and shLis-U87 cells. *Cells having Lis1 silenced (shLis-U87) or not (U87) were irradiated with X-ray doses from 5 to 50 Gy. Cells seeded in E-plates were followed for 100 hours in xCelligence RTCA instrument. Data show that irradiated U87 cells recovered better their proliferative capacity after irradiation than shLis-U87 cells (Brehar et al., 2016).*

GRANTS AWARDED BY COMPETITION (1996-2019)

• **2019-2021**: *Integrative Personal Omics Profiles in Glioblastoma Recurrence and Therapy Resistance* – ERA-NET PerMed grant, supported by UEFISCDI and European Commission, Coordinator for Romanian team: Dr. Anca Gafencu.

• **2018-2020**: *Intelligent therapies for non-communicable diseases based on the controlled release of pharmacological compounds from encapsulated cells after genetically manipulated or vectorized bionanoparticles* PN-III-P1-1.2-PCCDI-2017-0697 (acronym INTERA), Project Director: Acad. Maya Simionescu, Coordinator for ICBP: Dr. Anca Gafencu

• **2018-2020**: *Evaluation of the therapeutic potential of non-viral apolipoprotein E gene transfer to limit progression of atherosclerosis* PN-III-P1-1.1-PD-2016-1942 (acronym Nano ApoE), Coordinator: Dr. Violeta Trușcă

• **2017-2020**: *Improve institutional competitiveness in the field of type 1 diabetes by developing an innovativeconcept of immunotherapy based on mesenchymal stromal cells* POC-A.1-A.1.1.4-E-2015 (ID: P_37_668, acronym DIABETER), Coordinator: Dr. Nadir Askenasy

• **2015-2017:** *Combined hormonal treatment-induced gene transactivation of anti-atherosclerotic proteins as an innovative therapeutic approach for atherosclerosis* PN-II-RU-TE-2014-4-2660 (AterTE), Coordinator: Dr. Violeta Trușcă

• **2015-2017**: *Genetically engineered apolipoproteins immobilized on nanoparticles: a Molecular Trojan horse targeting atherosclerotic plaque* (Acronym: APGEN) PN-II-RU-TE-2014-4-2143, Projects for Young Research Teams, supported by CNCSIS Romania, Coordinator: Dr. Anca Gafencu.

• **2011-2016**: *Apolipoprotein E-based novel anti-atherosclerosis cell-therapy approaches* Exploratory research projects, project PN-II ID_PCE-2011-3-0591, supported by CNCSIS Romania, 2011-2016, Coordinator: Dr. Anca Gafencu.

• **2009-2011**: *Novel strategies employing genetic engineering to increase plasma HDL-*

the protective lipoproteins in atherosclerosis, Exploratory research projects:1307 supported by CNCSIS Romania, Coordinator: Dr. Anca Gafencu.

- **2005-2007**: *Regulation of apolipoprotein gene clusters- an innovative therapeutic approach of neurodegenerative and cardiovascular diseases* "Excellence Research Program: Projects for Young Researchers" supported by the Romanian Ministry of Research, Coordinator: Dr. Anca Gafencu.

- **2003-2005**: *ApoE gene regulation - therapeutic target in cardiovascular and neurodegenerative diseases* Grant awarded by the Romanian Ministry of Research, National Research Program for Biotechnology "BIOTECH", Coordinator: Dr. Anca Gafencu.

- **2002-2004**: *Role of ApoE in cholesterol and triglyceride homeostasis* - Collaborative linkage Grant NATO Science Programme, coordinators: Prof. V. Zannis, Boston Univ., USA - Dr. M. Simionescu, ICBP, Romania.

- **2001-2003**: *Characterization of albumin and IgG receptors, expressed by the endothelial cells in normal and pathologic states,* Grant awarded by the Romanian Ministry of Research- National Research Program for fundamental research "CERES", Coordinator: Anca Gafencu.

- **2000**: *Functional analysis of the IgG receptors in endothelial cells*, supported by the Romanian Research Ministry, Coordinator: Anca Gafencu.

- **1999:** *Identification of FcR in human placental endothelial cells* supported by the Romanian Academy, Coordinator: Anca Gafencu.

- **1998**: *Immortalization of endothelial cells,* supported by the Romanian Academy, Coordinator: Anca Gafencu.

- **1997**: *Lipid composition of the microdomains of the endothelial cell membrane,* Grant awarded by the Romanian Academy, Coordinator: Anca Gafencu.

- **1996-1999**: *Biochemical and functional characterization of the endothelial plasmalemma,* Grant awarded by the Romanian Research Ministry, 1996- 1999, Coordinator: Anca Gafencu.

- **1996-1998**: *Role of IgG receptors in human placental endothelial cells* - Collaborative Grant from Swiss National Science Foundation (1996-1998), coordinators: Prof. Walter Hunziker (University of Lausanne) and Dr. M. Simionescu (ICBP, Romania)

SUPPORT GRANTS:

- **2012-2014**: *Prospects for novel therapies of cardiovascular disease that are based on the transcriptional regulation of the apoE gene,* **Bilateral cooperation Romania-Greece**, Coordinator for ICBP: Acad. Maya Simionescu / Dr. Anca Gafencu, and Prof. Dimitris Kardassis for University of Crete

- **2009-2012:** *The extension and modernization of research infrastructure in order to increase the competitiveness in the field of cardiovascular diseases, diabetes and obesity* -CARDIOPro; **Structural Funds Project**, coordinator Dr. M. Simionescu

- **2009-2013: European Cooperation in Science and Technology:** COST Action BM0904: Project title: "HDL: From Biological Understanding to Clinical Exploitation". **Acronym**: HDLnet, Dr. Anca Gafencu – member in the Management Committee (2009-2013)

- **2005-2008:** *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), **FP6 grant** 016873/2005, coordinator Dr. M. Simionescu, Executive Manager of the project - Dr. Anca Gafencu

- **2005-2007**: *Regulation of the expression*

of the human apolipoprotein E gene in macrophages and the brain: new approaches for the treatment of dyslipidemias and Alzheimer's Disease, **Bilateral cooperation Romania-Greece,** Support for collaboration and exchanges in the framework of the project, Greek team coordinator: Prof. Dimitris Kardassis, Coordinator for ICBP: Dr. Anca Gafencu.

• **2001-2005**: *Function and dysfunction of blood vessels: transcytosis in normal/ pathological states, alterations in atherosclerosis and diabetes; their therapeutic control*, **FP5 INCO** project "Centre of Excellence" grant ICA1-CT-2000-70020, coordinator Dr. M. Simionescu, Administrative manager -Dr. Anca Gafencu

PATENTS

• Adenovirus containing murine FasLmini-genefor induction of the functional FasL expression in transduced cells, MădălinaDumitrescu,Violeta Georgeta Truscă, Alexandrina Burlacu, Maya Simionescu, Nadir Askenasy, Anca Violeta Gafencu – OSIM A/00512/26.08.2019

• Polymer vesicles and tubes and related technology of manufacturing, DenisaFicai, AndreeaIliev, Anton Ficai, Violeta Georgeta Trusca, Anca Violeta Gafencu, Sanda-Maria Bucatariu, Fundueanu Constantin Gheorghe, Maya Simionescu, EcaterinaAndronescu-OSIM A/01 054/05.1 2.2018

• Device for modifying the cell culture plate, and the real-time measurement method a displacement of cells in ex vivo system. Mirel Popa, Cristina Mihai. Patent No. 131463/2018.

AWARDS

• **Prize of Excellency awarded by the National Foundation for Science and Art**, Anca Violeta Gafencu, 2007

• **Prize awarded by CNCSIS** for the results obtained in the frame of the grant "Regulation of apolipoprotein gene clusters-an innovative therapeutic approach of neurodegenerative and cardiovascular diseases" Project category:" Young researchers -Excellent Projects", Coordinator Dr. Anca Gafencu, 2007

• **Special prize of the Jury awarded by UNESCO-L'Oréal** - Competition "Women in Science", Violeta Trusca, 2012

• **Prize for the poster** entitled "Fullerene-based nanoparticles conjugates with apolipoprotein E encoding DNA for gene therapy purposes", presented at the Romanian Society for Cell Biology Congress, Constanta, 2019

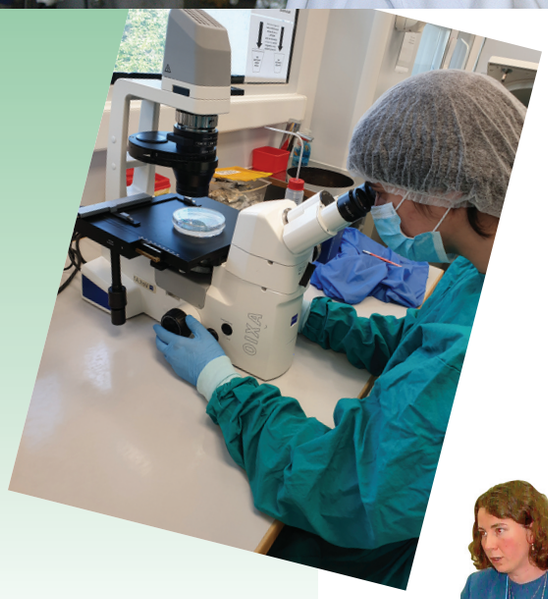
• **Third Prize Best Poster Award**- IM Fenyo, A-M Eftimie, AV Gafencu. Generation of a murine transgenic model for in vivo endothelial-specific and conditional expression of human apolipoprotein E3. 13th FELASA Congress, Brussels, Belgium, June 2016

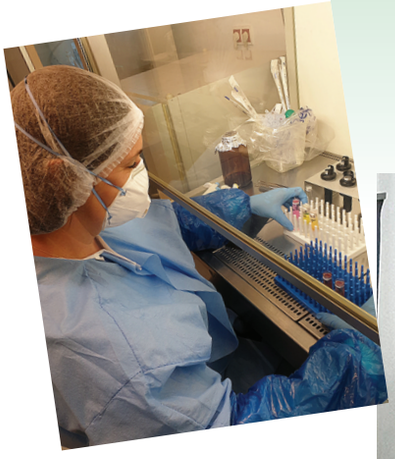
• **Prize for the Best Poster** "The interaction between the promoter and distal regulatory elements modulates the apoE expression in macrophages", International Conference of the Romanian Society for Cell Biology, Bistrita, 2009

• **Prizes awarded by the National Council for Scientific Research in the Higher Educational System (CNCSIS)** for **7** ISI publications, in the period 2007-2018.

• **Special Prize of Romanian Association for Alternative Technologies** (A.R.T.A), Sibiu 2019

• **Excellence Award and Gold Diploma** at "EuroInvent 11th Edition European Exhibition of Creativity and Innovation for: "Polymer vesicles and tubes and related technology of manufacturing" D. Ficai, A. Iliev, A. Ficai, VG. Truşcă, AV. Gafencu, SM. Bucatariu, FC. Gheorghe, M. Simionescu, E. Andronescu, 2019





GENE REGULATION AND MOLECULAR THERAPIES LABORATORY