BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: **Maiseyeu, Andrei**
eRA COMMONS USER NAME (credential, e.g., agency login): **maiseyeu01**
POSITION TITLE: Assistant Professor of Medicine

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Lomonosov Moscow State University, Russia	BS and MS	06/2002	Chemistry
Lomonosov Moscow State University, Russia	PHD	06/2007	Organic Chemistry
Bruker BioSpin Corp., Billerica, MA	Internship	11/2007	Magnetic Resonance Imaging
Ohio State University, Columbus, OH	Postdoctoral Fellow	09/2012	Cardiovascular Nanobiomedicine

A. Personal Statement

My formal education and training is originally in organic chemistry and multi-step synthesis.[1] I have had more than 15 years of experience in small molecule design and synthesis while working on my Masters and PhD degrees at Lomonosov Moscow State University. In 2007, I undertook postdoctoral training in cardiovascular biomedicine, during which I was involved in both developing new nanomaterials for drug delivery and studying health effects of environmental nanoparticles. Wearing two hats gave me perspective on how nano-sized objects behave on single-cell- and organism-level, and how bio-analytical methods may tackle molecular mechanisms nanoparticles' interactions with biological systems. Leveraging my chemistry background, I have developed numerous methods to track and characterize nanoparticles (with MRI, various microscopy methods and mass-spectrometry),[2,3] while close interaction with colleagues from various medical and public health backgrounds has helped me to sharpen my understanding of critical biological processes such as signal transduction,[3][4] lipoprotein metabolism,[4] and physiology of metabolic disease.[3]

1. Moiseev AM, Balenkova ES, Nenajdenko VG. Thiophene 1, 1-dioxides as unique building blocks in modern organic synthesis and materials chemistry. *Russ Chem Rev*. 2006;75:1015.

2. Bagalkot V, Badgeley MA, Kampfrath T, Deiuliis JA, Rajagopalan S, Maiseyeu A. Hybrid nanoparticles improve targeting to inflammatory macrophages through phagocytic signals. *J Control Release*. 2015 Nov 10;217:243–255. PMID: **26386437**

3. Shah Z, Kampfrath T, Deiuliis JA, Zhong J, Pineda C, Ying Z, Xu X, Lu B, Moffatt-Bruce S, Durairaj R, Sun Q, Mihai G, Maiseyeu A, Rajagopalan S. Long-term dipeptidyl-peptidase 4 inhibition reduces atherosclerosis and inflammation via effects on monocyte recruitment and chemotaxis. *Circulation*. 2011 Nov 22;124(21):2338–2349. PMCID: **PMC4224594**

4. Maiseyeu A, Yang H-Y, Ramanathan G, Yin F, Bard RL, Morishita M, Dvonch JT, Wang L, Spino C, Mukherjee B, Badgeley MA, Barajas-Espinosa A, Sun Q, Harkema J, Rajagopalan S, Araujo JA, Brook RD. No effect of acute exposure to coarse particulate matter air pollution in a rural location on high-density lipoprotein function. *Inhal Toxicol*. 2014 Jan;26(1):23–29. PMCID: **PMC4445365**

B. Positions and Honors

Positions and Employment

2007 - 2010	Post-Doctoral Researcher, The Ohio State University, Heart and Lung Research Institute
2010 - 2012	American Heart Association Post-Doctoral Fellow, The Ohio State University, Heart and Lung Research Institute
2012 - 2013	Research Assistant Professor, The Ohio State University, Division of Cardiovascular Medicine
2013 -	Assistant Professor of Medicine (Tenure Track), The University of Maryland, Baltimore, Division of Cardiovascular Medicine

Other Experience and Professional Memberships

2010 -	Professional Member, American Heart Association

Honors

1996	Silver Award, National Chemistry Olympiad, Belarus
1997	Bronze Award, XXXI International Mendeleev Chemistry Olympiad
2010	Distinguished Post-Doc Award, Heart and Lung Research Institute
2010	Post-Doctoral Fellowship Award, American Heart Association

C. Contribution to Science

I. *Pioneered "Eat-Me" Nanomedicine for Atherosclerosis.*

"Eat-me" signals are molecular cues displayed on the surface of apoptotic debris (dying cells, apoptotic bodies, microparticles) that signal to phagocytic cells of the innate immune system such as macrophages to engage in engulfment and rapidly clear the debris. Phosphatidylserine and oxidized lipids had been known for decades to serve as "eat-me" signals; however, I was one of the first to demonstrate they can efficiently guide nano-sized MRI contrast agents to the sites of cardiovascular disease. I designed, synthesized, and tested "eat-me" probes to show that they are consumed rapidly by macrophages residing in the plaque lesions of atherosclerosis.[5,6] Imaging macrophages through atherosclerosis-directed probes based on "eat-me" signaling opens new possibilities for non-antigenic targeting of nanomedicines. Such drug- and imaging probe-delivery approaches are expected to have lower cost than their antibody-based analogs and to circumvent the obstacles associated with many biologics, for example immunogenicity (for proteins) and mutagenicity (for viral vectors). Since the publication of my original study in 2009,[5] there have been many others that have followed similar strategy for drug delivery and imaging of macrophages in cardiovascular disease, cancer, autoimmune disease, and HIV/AIDS.[7]

5. Maiseyeu A, Mihai G, Kampfrath T, Simonetti OP, Sen CK, Roy S, Rajagopalan S, Parthasarathy S. Gadolinium-containing phosphatidylserine liposomes for molecular imaging of atherosclerosis. *J Lipid Res*. 2009 Nov;50(11):2157–2163. PMCID: **PMC2759821**

6. Maiseyeu A, Mihai G, Roy S, Kherada N, Simonetti OP, Sen CK, Sun Q, Parthasarathy S, Rajagopalan S. Detection of macrophages via paramagnetic vesicles incorporating oxidatively tailored cholesterol ester: an approach for atherosclerosis imaging. *Nanomedicine*. 2010 Nov;5(9):1341–1356. PMID: **21128718**

7. Bagalkot V, Deiuliis JA, Rajagopalan S, Maiseyeu A. "Eat me" imaging and therapy. *Adv Drug Deliv Rev*. 2016;99:2–11. PMID: **26826436**

II. *Defined Mechanisms of Action of Environmental Nanoparticles in Atherosclerosis.*

Our laboratory is on the forefront of interrogating correlations between cardiovascular health and anthropogenic particulate pollution. We were first to demonstrate that inhaled particulate matter (PM 2.5) could lead to oxidation of lipids in the lung, resulting in oxidative stress and inflammation concomitant with accelerated atherosclerosis. We developed mass-spectrometry methods that identify oxidation-associated lipids (such as 7-ketocholesterol and oxidized phospholipids) and discovered that mice exposed to air pollution express increased levels of oxidized lipids in atherosclerosis (as compared with mice inhaling filtered air), which, in turn, serve as potent signaling molecules to initiate inflammation via toll-like receptor 4 (TLR4) signaling.[8] We also showed that the signaling cascade through which oxidized lipids are deposited in plaque macrophages is likely to involve lipid-influx transporter CD36.[9] These findings offer identify of new, previously unknown relationships between particulate matter and its deleterious effects on cardiovascular health. Moreover, knowledge of molecular mechanisms obtained from these studies may offer insights into nanoparticle-induced toxicity of synthetic nanoparticles used in industry and manufacturing, including nanomaterials used for drug delivery.

8. Kampfrath T, Maiseyeu A, Ying Z, Shah Z, Deiuliis JA, Xu X, Kherada N, Brook RD, Reddy KM, Padture NP, Parthasarathy S, Chen LC, Moffatt-Bruce S, Sun Q, Morawietz H, Rajagopalan S. Chronic fine particulate matter exposure induces systemic vascular dysfunction via NADPH oxidase and TLR4 pathways. *Circ Res*. 2011 Mar 18;108(6):716–726. PMID: **21273555**

9. Rao X, Zhong J, Maiseyeu A, Gopalakrishnan B, Villamena FA, Chen L-C, Harkema JR, Sun Q, Rajagopalan S. CD36-dependent 7-ketocholesterol accumulation in macrophages mediates progression of atherosclerosis in response to chronic air pollution exposure. *Circ Res*. 2014 Oct 10;115(9):770–780. PMCID: **PMC4275116**

III. *Developed New Tools to Assess Cholesterol Metabolism*

My team and I looked into cholesterol efflux measured in humans as a metric of cardiovascular risk from PM exposure. The aim was to demonstrate whether air pollution impairs high-density lipoprotein's (HDL) ability to remove excess cholesterol. Although we did not find any functional HDL abnormalities in subjects exposed to airborne PM, this study represents an attempt to identify high risk individuals in the population exposed to particulate pollution.[4] Importantly, over the course of many experiments testing HDL function, I realized that the current methods of cholesterol efflux assessment are outdated. Drawing upon my nanotechnology expertise, I engineered a nanoparticle-based sensor that provides researchers with much more accurate and useful cellular cholesterol flux information.[10] Emerging evidence from our lab and our collaborators indicates that HDL's ability to shuttle cholesterol for disposal in liver may have an unexpected dependence on function of liver endothelial cells (LSECs). Using new nanometer resolution microscopy tools, we were the first to demonstrate that an HDL receptor, SR-B1, that was long thought to be expressed in liver hepatocytes, is actually highly expressed in LSECs. Paradoxically, we show that hepatocytes express negligible levels of SR-B1.[11]

10. Rajagopalan S, Badgeley MA, Maiseyeu A. Cholesterol Efflux Assay Probe Formulations, Methods of Making and Using. *US Patent. 20130272963:A1*, 2013 [cited 2016 Feb 22]. Available from: http://www.google.com/patents/US20130272963

11. Ganesan LP, Mates JM, Cheplowitz AM, Avila CL, Zimmerer JM, Yao Z, Maiseyeu A, Rajaram MVS, Robinson JM, Anderson CL. Scavenger receptor B1, the HDL receptor, is expressed abundantly in liver sinusoidal endothelial cells. *Sci Rep*. 2016;6:20646. PMID: **26865459**

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/andrei.maiseyeu.1/bibliography/9384884/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

05/01/2016-04/30/2021
1R01HL130516-01A1, National Heart, Lung, and Blood Institute
Andrei Maiseyeu (PI)
Probing Cardiovascular Actions of GLP-1 Using Nanoparticles
Role: PI

Objective: The goal of this proposal is to elucidate the molecular mechanisms of glucagon-like peptide-1 (GLP-1) in cardiovascular disease through the use of nanoparticle probes that target and image atherosclerosis. We posit that GLP-1 may directly regulate immune cell behavior by activating its receptor, GLP-1R, thereby reducing monocyte recruitment to the plaque, potentiating macrophage and cholesterol exit, and resolving inflammation. We propose to investigate locus-specific actions of GLP-1 with the use of engineered nanoparticles that will image lesional and blood leukocytes simultaneously delivering a payload of a GLP-1 mimetic within plaque.

Pending Research Support

09/01/2016-08/31/2021
1U01ES027267-01, National Institute of Environmental Health Sciences
Andrei Maiseyeu (PI), Sanjay Rajagopalan (PI), Lung-Chi Chen (PI)
Systemic Health Effects of Engineered Nanomaterials
Role: Co-PI

Objective: The broad goals of this proposal are to provide comprehensive biological response profiles for consortium ENMs using in vitro and in vivo models of inhalation and to provide a clear picture of their molecular, biochemical and pathophysiological effects with a focus on metabolic alterations. The unprecedented rise in chronic non-communicable diseases (NCD) such as diabetes and obesity and the concordance of this epidemic with exposure to protean environmental influences such as endocrine disruptors has clearly focused attention on the potential chronic effects of entities such as ENMs that may persist in the body for long periods. We have previously provided a large body of data linking particulate air pollution with metabolic abnormalities. The ultimate goal of this proposal is to enhance our understanding of the health effects of a range of ENMs. Through the use of custom high-throughput approaches, relevant acute physiologic assays and chronic models of inhalational exposure in susceptible animal models, we hope to provide a comprehensive profile of their chronic effects.

Completed Research Support

01/01/2013-12/31/2016
13SDG14500015, American Heart Association – National Center
Andrei Maiseyeu (PI)
Nanoparticle-Aided Modulation of Inflammation in Atherosclerosis
Role: PI

Objective: In this proposal we ask the following questions: 1) how can we deliver experimental agents to the sites of disease minimizing off-target side effects of therapeutic agents? 2) What are the requirements for clinical grade agents and how can we make our probes translatable? To address these questions we propose: 1) to develop highly specific, translatable mAb against Myeloid Related Protein (Mrp), which will bind to the target protein in inflammatory plaques, while minimizing off-target accumulation. 2) We will develop clinically translatable nanoparticle formulations, composed of FDA approved “Intralipid” and signaling lipids, which can exert additional effects on inflammation. We envision that strategies combining Mrp-targeted imaging probes have the potential for use in a variety of inflammatory diseases.

2010/01/10-2012/06/30
GRT00019104, American Heart Association – Great Rivers Affiliate Postdoctoral Fellowship Program
Andrei Maiseyeu (PI)
Novel polyvalent multimodal macrophage targeting strategies for imaging and therapy of atherosclerosis
Role: PI

Objective: The goal of this work is to develop novel nanoparticle-based strategies to target atherosclerosis. We propose multivalent nanoparticles directed against chemokine (C-C motif) ligand 2 (CCL2). These nanoparticles will be engineered, fabricated and tested *in vitro* and *in vivo* using models of experimental atherosclerosis.