# **College of Engineering Computing and Applied Sciences**

# **RESUME** Agneta Simionescu

#### PERSONAL DATA

Assistant Professor Department of Bioengineering Clemson University Clemson, SC 29634 864-656-3729 Arad, Romania US Citizen

## **EDUCATION**

Ph.D., Institute for Cell Biology, Romanian Academy, Bucharest, Romania, 2001, in Biochemistry/Cell Biology "Matrix metalloproteinases in cardiovascular pathology", advisors Professors Maya Simionescu, Doina Velican, Doina Popov, Radu Deac.

B.S., University of Bucharest, Bucharest, Romania, 1981, Biochemistry

## PROFESSIONAL EXPERIENCE

Clemson University, Bioengineering, 2012-present, Assistant Professor Clemson University, Bioengineering, 2011-2012, Visiting Lecturer Clemson University, Bioengineering, 2007-2011, Research Assistant Professor

Clemson University, Bioengineering, 2003-2007, Post-doctoral fellow, advisor Professor Narendra Vyavahare

Mures Heart Center, Targu Mures, Romania, 1995-2003, Principal Research Investigator and Director of the Transplant Immunology Lab. Medical Research Center, Targu-Mures, Romania, 1981-1995, Research Scientist, advisor Professor Radu Deac

## **MEMBERSHIPS**

Member, Tissue Engineering and Regenerative Medicine International Society, TERMIS, (2006-present).

Member, Biomedical Engineering Society, BMES, (2004-present).

Member, American Heart Association, AHA, (2017)

Member, Society for Biomaterials, SFB, (2003-present).

Member, International Society for Applied Cardiovascular Biology, ISACB, (1988-present).

Executive Board Member, International Society for Applied Cardiovascular Biology, ISACB, (2014-present)

## PROFESSIONAL ACTIVITIES

#### **Grant Reviewer:**

NIH NIDDK ad hoc grant reviewer

**AHA** – Cardiovascular Development Committee

**French National Research Agency** (ANR) - Translational Research for Applications in Health;

Welcome Trust Grants - Research Career Development Fellowship

#### **Reviewer for Journals:**

Journal of Biomedical Materials Research

Cell Biochemistry and Biophysics

**Tissue Engineering** 

Biomaterials Journal

American Chemical Society-Biomaterials Science & Engineering

#### **Editorial activities**:

**Textbook Co-editor,** "Vasculogenesis and Angiogenesis - from Embryonic Development to Regenerative Medicine", published as an Open Access Textbook by InTech publishing (2011).

**Guest editor** for the special issue: "Patient-Tailored Tissue Regeneration" to be published in the January 2018 issue of the journal *Bioengineering*, ISSN 2306-5354 published by MDPI AG, Basel, Switzerland.

**Textbook Co-editor,** "Physiologic and Pathologic Angiogenesis - Signaling Mechanisms and Targeted Therapy", ISBN 978-953-51-3024-6, published by INTECH as an Open Access resource (2017).

## **CONFERENCE ORGANIZER / CHAIR**

Session Chair / Co-organizer and Abstract Reviewer. Poster Session: "Tissue engineering of models for study of disease and drug discovery" Biomedical Engineering Society Annual Meeting, San Antonio, TX, October 22-25, 2014.

Co-Chair, Plenary Session V: "Translation, Regulatory Science and Commercialization" at the 14th Biennial Meeting of the International Society for Applied Cardiovascular Biology, Cleveland, April 2-5, 2014. Official co-organizer, together with the University of Medicine in Timisoara, of the 5th International Congress and 31th Annual Meeting of the Romanian Society for Cell Biology, Timisoara, Romania, June 5-9, 2013.

**Organizer**, together with the University of Medicine in Targu Mures, of the 6th International Congress and 32nd Annual Meeting of the Romanian **Society for Cell Biology**, Targu Mures, Romania, June 7-10, 2014.

## **PUBLICATIONS**

## **Books and Monographs**

- 1. Simionescu D, **Agneta Simionescu**, Deac R, "Molecular pathology of biomaterials, in "*Cell adhesion and the extracellular matrix*". C. Cruce, **Agneta Simionescu**, D. Simionescu et.al (eds), AIUS Publishers, Craiova, Romania, 1997 (*in Romanian*).
- 2. Dan Simionescu, **Agneta Simionescu**, <u>book editors</u>. InTech Open Access Publisher, Rijeka, Croatia. Title, "*Vasculogenesis and Angiogenesis from Embryonic Development to regenerative Medicine*". ISBN 978-953-307-882 (November <u>2011</u>).
- 3. Dan Simionescu, **Agneta Simionescu**, <u>book editors</u>. InTech Open Access Publisher, Rijeka, Croatia. Second edition of the Angiogenesis textbook: "*Physiologic and Pathologic Angiogenesis Signaling Mechanisms and Targeted Therapy*", ISBN 978-953-51-3024-6, published by INTECH as an Open Access resource (2017).

## **Selected Refereed Journal Publications**

- 1. C Deborde, D Simionescu, J Liao, L Sierad, C Wright, A Simionescu. "Stabilized collagen and elastin-based scaffolds for mitral valve tissue engineering". <u>2016</u>. *Tissue Engineering, Part A.* 22(21-22): 1241-1251.
- 2. J Chow, D Simionescu, AL Carter, A Simionescu. "Immunomodulatory effects of autologous adipose tissue-derived stem cells on vascular scaffold remodeling in diabetes". 2016. *Tissue Engineering and Regenerative Medicine*. 13:701-712.
- 3. M Harpa, I Movileanu, L Sierad, O Cotoi, H Suciu, T Preda, D Nistor, C Sircuta, K Branzaniuc, R Deac, S Gurzu, L Harceaga, P Olah, D Simionescu, M Dandel, A **Simionescu**. "In vivo testing of xenogeneic acellular aortic valves seeded with stem cells". <u>2016</u>. *Rom Rev Lab Medicine*, 24 (3):343-346..
- 4. Chawla V, **Simionescu A**, Langan EM III, LaBerge M. "Influence of clinically relevant mechanical forces on vascular smooth muscle cells under chronic high glucose: An In Vitro Dynamic Disease Model". 2016. *Annals of Vascular Surgery*, 34, 212-226
- 5. L Sierad, EL Shaw, A Bina, B Brazile, N Rierson, S Patnaik, A Kennamer, R Odum, O Cotoi, T Preda, K Branzaniuc, H Smallwood, R Deac, I Egyed, Z Pavai, A Szanto, L Harceaga, H Suciu, V Raicea, P Olah, **A Simionescu**, J Liao, I Movileanu, M Harpa, D. Simionescu. "Functional heart valve scaffolds obtained by complete decellularization of porcine aortic roots in a novel differential pressure gradient perfusion system". <u>2015</u>. *Tissue Engineering, Part C*, 21(12), 1284-1296.
- 6. T Pennel, G Fercana, D Bezuidenhout, A Simionescu, T Chuang, P Zilla, D Simionescu. "The Performance of Cross-linked Acellular Arterial Scaffolds as Vascular Grafts; Preclinical Testing in Direct and Isolation Loop Circulatory Models". 2014. *Biomaterials*. 35(24):6311–6322.
- 7. Mattix BM, Olsen TR, Casco M, Reese L, Poole JT, Zhang J, Visconti R, **Simionescu A,** Simionescu DT, Alexis F. Janus magnetic cellular spheroids for vascular tissue engineering. 2014. *Biomaterials*. 35(3):949-960.
- 8. T Larrew, J Chow, J Schulte, D Simionescu, **A Simionescu**. "The roles of various metabolic enzymes in diabetic cardiomyopathy—in vivo and in vitro approach". *Cardiovascular Pathology*, 2013; 22(3):e48.
- 9. JB Schulte, **A Simionescu**, DT Simionescu. "The Acellular Myocardial Flap; a Novel Extracellular Matrix Scaffold Enriched with Patent Microvascular Networks and

- Biocompatible Cell Niches". Tissue Engineering. 2013; 19(7), 518-530.
- 10. JP Chow, DT Simionescu, H Warner, B Wang, SS Patnaik, J Liao, A Simionescu. "Mitigation of Diabetes-Related Complications in Implanted Collagen and Elastin Scaffolds Using Matrix-Binding Polyphenol". *Biomaterials*. 2013; 34(3): 685-695.
- 11. D Simionescu, M Jaeggli, J Liao, **A Simionescu**. "Translational personalized regenerative medicine; scaffolds and stem cells for patient-tailored aortic heart valve tissue engineering". *Cardiology* 2012, 121;138.
- 12. Tedder ME, Liao J, **Simionescu A**, Simionescu DT, "Assembly and testing of layered collagen constructs for heart valve tissue engineering". *Tissue Engineering, Part A*. 2011.17(1-2):25-36.
- 13. **A Simionescu**, Mary E. Tedder, Ting-Hsien Chuang, D. Simionescu. "Lectin and Antibody-Based Histochemical Techniques For Cardiovascular Tissue Engineering". *Journal of Histotechnology*, April 2011. 34(1):20-28.
- 14. **A. Simionescu**, JB Schulte, G Fercana, DT Simionescu, "Inflammation in Cardiovascular Tissue Engineering: The Challenge to a Promise: A Minireview," *International Journal of Inflammation*, vol. 2011, Article ID 958247, 11 pages, doi:10.4061/2011/958247
- 15. Leslie N. Sierad, Christopher Albers, Jordan Maivelett, Mary E. Tedder, Jun Liao, D. Simionescu, **A Simionescu**, "Endothelialization of decellularized penta- galloyl-glucose treated xenograft scaffolds and dynamic conditioning in a heart valve bioreactor", *Cardiovascular Engineering and Technology*, 2010, 1(2), 138-153
- 16. J Mercuri, A **Simionescu**, D Simionescu. "Xenogenic Cues for Human Mesenchymal Stem Cell Differentiation towards a Nucleus Pulposus Cell-like Phenotype". *Spine Journal*. 2010; 10(9).
- 17. M. E. Plonska-Brzezinska, A. Palkar, K. Winkler, **A. Simionescu**, D. Simionescu, A. Dubis, A. J. Athans, L. Echegoyen, "Small non-cytotoxic carbon nano-onions: investigation of the electrochemical behavior and their potential application", Chemistry, 16(16), 4870-4880. <u>2010</u>.
- 18. Tedder ME, Liao J, Weed B, Stabler C, Zhang H, **Simionescu A**, Simionescu DT. "Stabilized collagen scaffolds for heart valve tissue engineering". *Tissue Engineering Part A*. 2009. 15(6):1257-1268.
- 19. Chuang TH, Stabler C, **Simionescu A**, Simionescu DT. "Polyphenol-stabilize tubular elastin scaffolds for tissue engineered vascular grafts". *Tiss Eng Part A* 2009. 15(10):1257-1268.
- 20. **Simionescu** A, Simionescu D, Vyavahare NR. "Osteogenic responses in fibroblasts activated by elastin degradation products and TGF-β1: role of myofibroblasts in vascular calcification" *American Journal of Pathology*. 2007. 171(1): 116-23.
- 21. Lee JS, Basalyga DM, **Simionescu** A, Isenburg JC, Simionescu D, Vyavahare NR. "Mechanisms of elastin calcification in rat subdermal model: gene expression associated with elastin degeneration and ectopic osteogenesis". *American Journal of Pathology*. 2006.;168(2):490-8
- 22. Lu Q, **Simionescu A**, Vyavahare NR. "Novel capillary channel fiber scaffolds for guided tissue engineering". *Acta Biomater*. 2005;1(6):607-14.
- 23. **Simionescu A**, Philips K, Vyavahare N. Elastin-derived peptides and TGF-beta1 induce osteogenic responses in smooth muscle cells. *Biochem Biophys Res Commun*. 2005;334(2):524-532.

## **Prior to Clemson**

- 1. M. Bracher, D. Simionescu, A Simionescu, N. Davies, P. Human, P. Zilla, "The role of matrix metalloproteinases in tissue valve degeneration a mini-review". *Journal of Long Term Effects of Medical Implants*, 2001;11(3-4), 221-230.
- 2. **A Simionescu**, Simionescu D, Deac R. "Matrix metalloproteinases in the pathology of natural and bioprosthetic cardiac valves". *Cardiovascular Pathology*, 1996, 5, 323-332.
- 3. **A Simionescu**, D. Simionescu, R. Deac, "Biochemical pathways of tissue degeneration in bioprosthetic cardiac valves; the role of matrix metalloproteinases". *ASAIO Journal*, 1996; 42 (5), M561-M567.
- 4. Simionescu D, Deac R, **A Simionescu**. "Inhibition of extracellular-matrix degrading proteases in pericardial-derived cardiovascular bioprostheses". *Journal of Material Science; Materials in Medicine*.1994; 5:748-751.
- 5. D Simionescu, A Simionescu, R. Deac. "Mapping of glutaraldehyde-treated bovine pericardium for use as bioprosthetic cardiac valves", *Journal of Biomedical Materials Research*, 1993; 27, 6, 697-704.
- A Simionescu, Simionescu D, Deac R. "Lysine-enhanced glutaraldehyde crosslinking of collagenous biomaterials". *Journal of Biomedical Materials Research*. 1991; 25(12): 1495-1505.

## **Conference Proceedings (out of 130 total)**

- 1. **A Simionescu**, J Dhulekar, Z Hajdu, D Simionescu. "Vascular tissue engineering in diabetes". *Vascular Research Initiatives Conference, SVS/ATVB, Minneapolis, May 3-6*, **2017.**
- 2. J Dhulekar, E Wright, Z Hajdu, D Simionescu, J Bruch, C Wright, A Simionescu. "Diabetes-Resistant Tissue Engineered Vascular Grafts", TERMIS, San Diego, 2016; selected as a finalist for SYIS Poster Competition
- 3. L McCallum, A Simionescu. "Development of a Tissue Engineered Diabetic Cardiomyopathy Model", TERMIS, San Diego, 2016
- 4. **A Simionescu.** "Stem cells, biomaterials and tissue engineering in diabetes". *International Society for Regenerative Medicine and Surgery International Congress, Bucharest, Romania, June 14-17*, **2017**
- 5. A Simionescu. "Characterization and mitigation of diabetes related complications in tissue engineered aortic valves", "A Universe in the Cell" Symposium, February 23-24, 2017
- 6. J Dhulekar, **A Simionescu**. Cellular and extracellular modifications induced by diabetic conditions in tissue engineered blood vessels". *15<sup>th</sup> Biennial Meeting of the International Society for Applied Cardiovascular Biology (ISACB), Banff, Canada, Sept. 7-10, 2016.*
- 7. J Dhulekar, E Wright, Z Hajdu, D Simionescu, J Bruch, C Wright, A Simionescu. "Diabetes Resistant Tissue Engineered Vascular Grafts", *NISBRE, Washington, DC, June 26-28*, **2016**.
- 8. C Deborde, D Simionescu, C Wright, L Sierad, A Simionescu. "Mitral valve tissue engineering a model for investigating valve degeneration". 9th Biologic Scaffolds for Regenerative Medicine Symposium, Napa Valley, CA, 2016.
- 9. C Deborde, L Sierad, C Wright, J Liao, A Simionescu. Development and Revitalization of a Mitral Valve Scaffold for Tissue-Engineered Regeneration. 2<sup>nd</sup> Annual Scientific Meeting of the Heart Valve Society, New York, March 17-19, 2016. Award for best presentation.
- 10. A Simionescu, "Stabilized collagen and elastin-based scaffolds for mitral valve tissue engineering". 2015 European Meeting of the International Society for Applied Cardiovascular Biology (ISACB), Nuremberg, Germany, December 3-5, 2015.
- 11. C deBorde, Lee Sierad, Sourav Patnaik, A Simionescu. "Acellular mitral valve scaffold

- with intact annulus and chordae tendinae for tissue engineering". 6th Biennal Meeting on Heart Valve Biology and Engineering and Society of Heart Valve Disease (SHVD), London, UK, September 10-12, 2014.
- 12. C deBorde, J Liao, D Simionescu, A Simionescu. "Development of a tissue engineered mitral valve". *Biomedical Engineering Society (BMES) Annual Meeting, San Antonio, TX, Oct 22-25,* **2014.**
- 13. Laura McCallum, Jason Schulte, Katilin McClure, **A Simionescu**. "Tissue Engineering Models for Diabetic Cardiomyopathy". *14th Biannual Meeting of the International Society for Applied Cardiovascular Biology (ISACB), Cleveland, OH, April 2-5*, **2014**.
- 14. Paul A. Human, Helen J. Ilsley, Anel Oosthuysen, Ken Park, Janine de Witt, A Simionescu, Dan Simionescu, Deon Bezuidenhout, Peter Zilla. "Decellularisation Mutes the Differential Response Between Bioprosthetic Porcine and Bovine Pericardial Tissue". 14th Biannual Meeting of the International Society for Applied Cardiovascular Biology (ISACB), Cleveland, OH, April 2-5, 2014.
- 15. Jason B. Schulte, Joshua Biggs, Dan T. Simionescu, **A Simionescu**. "Differentiation of Adipose Stem Cells for Use in Myocardial Tissue Engineering". *14th Biannual Meeting of the International Society for Applied Cardiovascular Biology (ISACB), Cleveland, OH, April* 2-5. **2014**
- 16. Schulte J, Simionescu D, A Simionescu. "Decellularized and Vascularized Scaffolds for Tissue-Engineered Regeneration of Myocardium". *Tissue Engineering and Regenerative Medicine International Society (TERMIS)-AM*, Atlanta, GA, 2013.
- 17. J Chow, H Warner, D Simionescu, J Liao, A Simionescu, "Mitigation of Diabetes-Induced Complications to Constructs for Cardiovascular Tissue Engineering by Matrix-Binding Polyphenols". *Society for Biomaterials (SFB), Boston, MA, April 10-13,* **2013**.
- 18. Chow J, Warner H, Simionescu D, **A Simionescu** "Immunomodulatory Effects of Autologous Adipose-Derived Stem Cells on Scaffold Remodeling in Diabetes." *Tissue Engineering and Regenerative Medicine International Society (TERMIS), Atlanta, GA, November 10-14*, **2013**.
- 19. J Schulte, D Simionescu, A Simionescu. "Decellularized and Vascularized Scaffolds for Tissue-Engineered Regeneration of Myocardium". *Keystone Symposium on Cardiac Remodeling, Signaling, Matrix and Heart Function, Snowbird, UT, April 7-12,* 2013.
- 20. **A Simionescu**, D Simionescu. "Stem cell differentiation and cardiovascular tissue engineering in diabetes". *MSC2013, Adult Stem Cell Therapy and Regenerative Medicine, Cleveland, OH, 19-21 August* **2013**.
- 21. T Pennel, D Bezuidenhout, A Oosthuysen, G Fercana, **A Simionescu**, P Zilla, D Simionescu. "Evaluation of stabilized, decellularized xenografts in a small diameter circulatory animal model. *1st International Symposium in Vascular Tissue Engineering, Leiden, the Netherlands, 28-29 May* **2013**.
- 22. J. Chow, D. Simionescu, H. Warner, B. Wang, J Liao, A Simionescu. "Diabetes-Related Alterations in Collagen Scaffolds used for Cardiovascular Tissue Engineering; Mitigation with Antioxidants". Keystone Symposium on Regenerative Tissue Engineering and Transplantation, Beaver Run Resort, Breckenridge, Colorado, April 1-6, 2012.
- 23. D Simionescu, M Jaeggli, J Liao, A Simionescu. "Translational Patient-Tailored Aortic Heart Valve Tissue Engineering". *Keystone Symposium on Regenerative Tissue Engineering and Transplantation, Beaver Run Resort, Breckenridge, Colorado, April 1-6,* **2012**.
- 24. D. Simionescu, M. Jaeggli, J Liao, A Simionescu. "Translational Personalized Regenerative Medicine: Scaffolds and Stem Cells for Patient-Tailored Aortic Heart Valve

- Tissue Engineering". Fourth Annual Joint Scientific Meeting of the Heart Valve Society of America (HVSA) & Society of Heart Valve Disease (SHVD), New York, April 12-14, 2012.
- 25. J. Chow, D. Simionescu, N. Topoluk, B. Wang, J. Liao, A Simionescu. "Diabetes-Related Alterations in Collagen Scaffolds and Mitigation with Antioxidants". 7th Symposium on Biologic Scaffolds for Regenerative Medicine, Silverado Resort, Napa, CA, April 26-28, 2012.
- 26. James Chow, Harleigh Warner, Dan Simionescu, Jun Liao, **A Simionescu**. "Diabetes-Induced Inflammatory Response in Collagen Scaffolds used for Cardiovascular Tissue Engineering; Mitigation with Antioxidants" *Biomedical Engineering Society (BMES) Annual Meeting, Atlanta, GA, Oct 24-27, 2012*
- 27. Thomas Larrew, James Chow, G. Fercana, Jason Schulte, A **Simionescu**, "Assessment of Biochemical Contributions to Diabetic Cardiomyopathy Pathology and Development of an Appropriate in vitro Model". Biomedical Engineering Society (BMES) Annual Meeting, Atlanta, GA, Oct 24-27, **2012**
- 28. Richard Pascal, Lee Sierad, Dan Simionescu, **A Simionescu**, "Dynamic Endothelialization and Conditioning of Aortic Heart Valve Scaffolds Using Adult Stem Cells". *Biomedical Engineering Society (BMES) Annual Meeting, Atlanta, GA, Oct 24-27, 2012.*
- 29. Thomas Larrew, James Chow, Jason Schulte, **A Simionescu**, "The Roles of Various Metabolic Enzymes in Diabetic Cardiomyopathy In Vivo and In Vitro Approach", *13th Biannual Meeting of the International Society for Applied Cardiovascular Biology (ISACB)*, London, UK, September 12-15,2012.
- 30. Mattix, B., Reese, L., Poole, J., Visconti, R., Simionescu, D., **Simionescu, A.**, Jenkins, L., Bruce, T., Alexis, F. Assembly of Engineered Blood Vessels Using Magnetic Forces. *The South Carolina Project for Organ Biofabrication Scientific Symposium 2012*. Columbia, SC.
- 31. Mattix, B., Poole, J., Casco, M., Visconti, R., Simionescu, D., **Simionescu, A**., Alexis, F. Spatial Control of Magnetic Nanoparticles Integrated with Cellular Spheroids as Tissue Engineered Building Blocks. *Society for Biomaterials* **2012** *Fall Symposium. New Orleans, LA*.
- 32. Moore T, Stoner B, Morrison R, **Simionescu A**, Simionescu D, Recknor C, Alexis F. Targeted, Multifunctional Nanoparticles for Controlled Delivery of Anabolic Bone Therapy Drugs. *Society for Biomaterials Fall Symposium*. **2012**, New Orleans, LA.
- 33. Mattix, B., Poole, J., Casco, M., Visconti, R., Simionescu, D., **Simionescu, A**., Alexis, F. "Spatial Control of Magnetic Nanoparticles Integrated with Cellular Spheroids as Tissue Engineered Building Blocks." *Society for Biomaterials* **2012** *Fall Symposium. New Orleans, LA, October 5*, 2012.
- 34. **A Simionescu**, Chow J, Liao J, Simionescu, D. "Experimental Diabetes Alters Biological Scaffolds used in Cardiovascular Tissue Engineering; Treatment with Polyphenols Protect Scaffolds from Diabetes-related Complications". *4th International Conference on Tissue Engineering, Chania, Crete, Greece, June* **2011**.
- 35. M. Tedder, J. Liao, J. Chen, L. Sierad, R. Stowers, A Simionescu, D. Simionescu, "Patient-tailored aortic heart valve tissue engineering". *Hilton Head Regenerative Medicine Workshop, Hilton Head Island, SC*, 2010
- 36. Zhang, H.S., Maivelett, J., Stowers R., Mary E. Tedder, Simionescu, D., A Simionescu. "Stem Cell Reactivity to Cardiovascular-Specific Differentiation Cues is Altered in Diabetic Conditions". *Society for Biomaterials Annual Meeting, Seattle, WA*, **2010**.
- 37. Mercuri, J, S. Gill, **A Simionescu**, D. Simionescu, "Xenogenic cues for human mesenchymal stem cell differentiation towards a Nucleus Pulposus cell- like phenotype", *North American Spine Society Orlando*, FL, **2010**.

- 38. D. Simionescu, L. Sierad, C. Albers, J. Maivelett, J. Chen, M. Tedder, J. Liao, A **Simionescu**. "Endothelialization of reversibly stabilized heart valve scaffolds in a pulsatile bioreactor". *12th Biannual Meeting of the International Society for Applied Cardiovascular Biology, Boston, MA*, **2010**.
- 39. **A Simionescu**, D. Simionescu. "Diabetes alters stem cells and scaffolds used in heart valve tissue engineering". *12th Biannual Meeting of the International Society for Applied Cardiovascular Biology*, *Boston*, *MA*, **2010**.
- 40. M.E. Plonska-Brzezinska, J. Luszczyn, A. Dubis, A. Palkar, **A Simionescu**, L. Echegoyen. "Studies of Carbon Nano-Onions based biosensors". *6th International Conf on Nanosci Nanotech, Thessaloniki, Greece*, 13-15, July, **2009**.
- 41. Maivelett, J, Simionescu, D, A Simionescu "Stem Cell Seeding of Heart Valve and Vascular Scaffolds: Tissue Engineering in Diabetes". *Southeast Biomedical Engineering Career Conference (SEBECC)*, Washington, DC, Oct 30, 2009.
- 42. Maivelett, J, Simionescu, D, A Simionescu "Cell Seeding of Heart Valve and Vascular Scaffolds: Tissue Engineering in Diabetes". Biomaterials Day". 2009 Summer Undergraduate Research Programs proceedings. Clemson. July 23, 2009. Oral Presentation. Awarded "Best Undergraduate Presentation".
- 43. **A Simionescu**, Albers C, Stowers R, Sierad LN, Mercuri JJ, Chuang TH, Tedder ME, Simionescu D. "Penta-galloylglucose-Stabilized Acellular Scaffolds for Tissue Engineered Heart Valves". *Tissue Engineering and Regenerative Medicine International Society (TERMIS) NA*, San Diego, CA, **2008**.
- 44. **A Simionescu**, Simionescu D, Vyavahare N. "Molecular mechanisms of elastin-oriented calcification in an aortic injury model". *10th Biennal Meeting of the International Society for Applied Cardiovascular Biology, San Diego, CA*, **2006**
- 45. Lee J, Basalyga D, A Simionescu, Simionescu D, Vyavahare N. "Osteogenic and matrix remodeling gene expression associated with elastin calcification", *Society for Biomaterials Annual Meeting, Memphis, TN,* 2005.

## **Prior to Clemson**

- 1. **A Simionescu**, Simionescu D, Zegrean A, Sin A, Deac R. "Myocardial fibrosis in transplanted human hearts", 9th *Biennal Meeting of the International Society for Applied Cardiovascular Biology, Savannah, GA, USA,* **2004**.
- 2. **A Simionescu**, Simionescu D, Deac R. "Nitric oxide stimulates matrix metalloproteinases and reduces myocardial fibrosis", 8th Biennal Meeting of the International Society for Applied Cardiovascular Biology, St. Gallen, Switzerland, 2002.
- 3. **A Simionescu**, Deac R. Association of HLA compatibility and post-transplant antibody formation with myocardial fibrosis in heart transplantation, *3rd Annual Conference of the National Society for Transplantation, Bucharest, Romania*, **2002**.
- 4. Simionescu D, **A Simionescu**, Girardot N, Girardot JM. "Inhibition of bioprosthetic aortic wall calcification by molecular targeting of calcium binding substrates", 7th Biennal Meeting of the International Society for Applied Cardiovascular Biology, Tucson, AZ, **2000**.
- 5. **Simionescu** A, Simionescu D, Deac R. "Extracellular matrix remodeling in cardiac failure", 3rd Annual Conference of the National Society for Cell Biology, Constanta, Romania, 1999.
- 6. Deac R, Simionescu D, **Simionescu A**. "Evolution of the mitral stentless autologous pericardial valve", *World Symposium on Heart Valve Disease, London, UK,* June 11-14, **1999**.
- 7. Simionescu A, Simionescu D, Deac R. "The effect of glutaraldehyde on the activity of

- matrix degrading proteases", 44rd Annual Conference of the American Society for Artificial Internal Organs (ASAIO), New York, NY, USA, April 23-25 1998.
- 8. **Simionescu** A, Simionescu D, Deac R. "The role of metalloproteinases in bioprosthetic valve degeneration", 6th Biannual Meeting of the International Society for Applied CV Biology (ISACB), Munich, Germany, March 3-5, **1998**.
- 9. **Simionescu** A, Simionescu D, Deac R. "Modulation of collagenases and the biocompatibility of pericardial derived heart valves", *43rd Annual Conference of the American Society for Artificial Internal Organs (ASAIO)*, *Atlanta, GA, USA*, May 1-3, **1997**.
- 10. **Simionescu A**, Simionescu D, Deac R. "Matrix metalloproteinases in the pathology of natural and bioprosthetic cardiac valves". *42nd Annual Cardiovascular Science and Technology Conference of the American Society for Artificial Internal Organs (ASAIO), Washington, DC, USA*, May 2-4, **1996**.
- 11. Simionescu D, Deac R, **Simionescu A**. "Inhibition of extracellular matrix degrading proteases in pericardial derived cardiovascular bioprostheses", *11th European Conference on Biomaterials, Pisa, Italy,* Sept. 10-14, **1994**.
- 12. Simionescu D, **Simionescu A**, Deac R. "Proteolytic activities in glutaraldehyde crosslinked bovine pericardium and explanted bioprosthetic heart valves", *10th European Conference on Biomaterials, Davos, Switzerland,* Sept. 8-11, **1993**.
- 13. Deac R, **Agneta Simionescu**, Simionescu D. "Gamma-carboxyglutamic acid a putative indicator of the evolution of calcification in heterologous pericardium", *14th Annual Meeting of the Medical Research Center, Targu Mures, Romania*, **1988**.
- 14. Simionescu D, **Simionescu A**, Deac R. "Calcium Deposition in Bioprosthetic Heart Valves. Attempted Mechanisms & Experimental Models", *Fourth International Conference on Water and Ions in Biological Systems, Bucharest, Romania*, **1987**.
- 15. Simionescu D, Simionescu A, Deac R. "Surface Charge Characterization of Bioprosthetic Heart Valves", *The 17th National Symposium of Biophysics, Targu Mures, Romania*, **1986**.
- 16. **Simionescu A**, Simionescu D, Deac R. "Cellular biology and pathology of normal and artificial heart valves", *3rd Annual Conference of the National Society for Cell Biology, Targu Mures, Romania*, **1985**.
- 17. Deac R, Bradisteanu S, Simionescu D, Fagarasanu E, **Simionescu A**. "Recent developments in basic research of heart valve replacement with artificial bioprostheses", *Symposium "Progress in medical sciences"*, *Cluj Napoca, Romania*, **1982**.

#### PRESENTATIONS as INVITED SPEAKER

- 1. **Agneta Simionescu**, "Vascular tissue engineering in diabetes". *International Workshop on Biomedical Engineering, Osaka Institute of Technology,* Osaka, Japan, November 16<sup>th</sup>, **2014**.
- 2. **Agneta Simionescu**, "Vascular tissue engineering in diabetes" *Institute for Cell Biology and Pathology*, Bucharest, Romania. July 3, **2013**.
- 3. **Agneta Simionescu**, "The Role of Matrix Metallo-Proteinases in Bioprosthetic Valve Degeneration". *International Society for Applied Cardiovascular Biology*, Munich, Germany. **1998**.
- 4. **Agneta Simionescu**, "Extracellular Matrix Degrading Metallo-Proteinases in Cardiovascular Pathology". *Connective Tissue Research Institute*, **University of Pennsylvania** Medical School, Philadelphia, PA, **1996**.

## **PATENTS**

- 1. "Self-adjusting tissue holder". **Provisional patent application** 14/807,407 **(2017).** With Chris deBorde, D. Simionescu and Leslie Sierad.
- 2. "Treatment to Render Implants Resistant to Diabetes". US Patent # 9,283,241 (2016) with James Chow and D. Simionescu.
- 3. "Method and kit for rapid preparation of autologous tissue medical devices". US/World, **Patent** #6,214,055/USPTO, (2001) with D. Simionescu, R. Deac

#### **Disclosures to CURF:**

- CURF ID 2011-107: "Perfusion Tissue Processor/Bioreactor for Preparing Myocardial Scaffolds"
- 2. CURF ID 2011-093: "Pre-vascularized Scaffold for Muscle Tissue Regeneration and Method to Obtain Such Biomaterial"
- 3. Magnetic Printing of Viable Cell Spheroids." Disclosure (2012).

#### **HONORS AND AWARDS**

- 1. "Enabling Technologies to Replace Each Valve" Section Poster Award for the paper "Development and Revitalization of a Mitral Valve Scaffold for Tissue-Engineered Regeneration" by Chris deBorde, Leslie Sierad, Christopher Wright, Jun Liao and Agneta Simionescu. Annual Scientific Meeting of the Heart Valve Society, New York March 17-19, (2016).
- The Journal of Histotechnology Diamond Cover Award (2011) from the *National Society for Histotechnology*, for the manuscript: "Lectin and Antibody-Based Histochemical Techniques for Cardiovascular Tissue Engineering". Agneta Simionescu, Mary E. Tedder, Ting-Hsien Chuang, D. Simionescu. *Journal of Histotechnology*, April 2011\_34(1):20-28.
- 3. **Dr. C. Velican Award** for "Outstanding Research in atherosclerosis and cardiovascular diseases". Romania (1996).
- 4. **Romanian Academy Award** for "Research on Collagenous Biomaterials". Romanian Academy of Sciences. Romania (1995).

## SPONSORED RESEARCH: TOTAL OF > \$2.5 M (\$\$ available to A Simionescu)

- 1. "Mitral valve tissue engineering". American Heart Association (AHA) AIREA Award. \$144,000 / 2 years. Role: PI. July 2017- July 2019.
- "Diabetic-Resistant Vascular Grafts"; NIH COBRE Grant P20. "SC BIOCRAFT".
  \$11 million total awarded / 5 years; (\$500,000). Role: PI for Target Project #5. 2014-2019.
- 3. "Targeted therapy for aortic valve disease in diabetes". Romanian Ministry of Research and the EU (R01-equivalent): **Role: PI**; \$2,400,000 (\$500,000) / 4 years. July 2016-July 2020.
- 4. "Cardiovascular Tissue Engineering in Diabetes", **NIH R21 grant. Role: PI**. \$400,000 (\$400,000), 04/01/2010-12/31/2013.
- 5. "Tissue engineering aortic heart valves; scaffolds and cells". **NIH RO1 grant. Role: Co-PI,** \$1,450,000 (\$290,000), 03/01/2010-02/28/2014.

- 6. "Elastin-derived scaffolds for tissue engineered small diameter vascular grafts". **NIH FIRCA grant. Role: Co-PI,** \$150,000 (\$30,000), 04/01/2011-03/30/2014.
- 7. "Stem cell differentiation and cardiovascular tissue engineering in diabetes", **NIH COBRE P20; Role: Target Project PI.** \$10,000,000 (\$200,000); 06/01/2012-05/31/2014.
- 8. "Stem cell seeded collagen scaffolds for heart valve tissue engineering". Romanian Ministry of Research and the EU (**R01-equivalent**): **Co-PI**; \$1,600,000 (\$450,000). July 2012-July 2015.
- 9. "Bioactive scaffolds for vascular surgery" **NIH R21; Co-PI**: \$400,000 (\$50,000). 1/15/2007-12/31/2009
- i. "Efficacy of rotator cuff regeneration using scaffolds and stem cells"; **Co-PI. The Hawkins Foundation of the Carolinas**. \$25000 (\$10,000). 1/12/2011 4/30/2013.

#### **CONTRIBUTIONS TO SCIENCE**

## Natural, bioprosthetic, and tissue-engineered cardiac valves

Since the beginning of my career I worked on heart valves. I was among the first to show that degenerative dysfunction of cardiac valves may be accounted for extracellular matrix degradation processes in which matrix metalloproteinases (MMPs) could play a major role (*ASAIO Journal 1996*). I showed that tissue crosslinking for bioprosthetic heart valves became more stable if a diamine, such as lysine was used in addition to glutaraldehyde (JBMR 1991). Tissue-engineered heart valves were developed in my lab based on decellularized porcine valves as scaffolds (CVET, 2010; Tissue Eng. 2015, 2016)

## Vascular calcification

As a postdoc, I worked on calcification of the arterial media, which is frequently associated with chronic kidney disease, diabetes, and aging. Intense calcium deposition on the elastic lamellae is accompanied by proteolysis and elastic fiber degradation. My results support the idea that elastin-related calcification involves dynamic remodeling events, as elastin degradation products and TGF- $\beta$ 1 promote osteogenic differentiation in fibroblasts and smooth muscle cells (American Journal of Pathology, 2007, 2006; Biochem Biophys Res Commun. 2005).

## **Cardiovascular Tissue Engineering in Diabetes**

My goals are to understand the diabetes-related alterations in native blood vessels and in implanted tissue engineered blood vessels and to develop vascular grafts resistant to these changes, by treating them with a polyphenol antioxidant and stabilizing agent. In recent years I published on mitigation of diabetes-related complications in implanted collagen and elastin scaffolds using matrix-binding polyphenols (Biomaterials, 2013) and the immunomodulatory effects of adipose tissue-derived stem cells on elastin scaffold remodeling in diabetes (Tissue Eng. Regen Med, 2016).

## GRADUATE STUDENT ADVISING

## **Current Graduate Advising – major advisor**

- 1. Laura Mccallum. (PhD) "Pathogenesis of diabetic cardiomyopathy". (May 2018). Past proposal status.
- 2. Jhilmil Dhulekar (PhD) "Diabetes Resistant Vascular Graft Remodeling" (May 2018) Past qualifier exam.
- 3. Spencer Marsh (PhD) "Cardiac remodeling in tissue engineering" (May 2020).
- 4. Anna Lu Carter (MS) "
- 5. Co-advisor for Varun Chawla (PhD) "Influence of low shear and cyclic strain on hyperglycemic rat aortic smooth muscle cells: An *In Vitro* dynamic disease model" (December 2017)

# Past Graduate Advising – major advisor

- 1. Christopher Deborde. (PhD) "Development of a Novel Tissue engineered mitral valve". (May 2017).
- 2. Jason B Schulte (PhD) "Vascularized Scaffold for Tissue-Engineered Regeneration of Human Myocardium" (December 2014). Co-inventor.
- 3. Chow James P. (PhD) "Cardiovascular Tissue Engineering in Diabetes" Received the best presentation award at the departmental seminar. Co-inventor. (May 2014).
- 4. James McManus (MS) "Whole organ regeneration" (December 2017)
- 5. Maria Portilla (MS) "Immunomodulatory properties of stem cells" (December 2017).
- 6. Robert Marti (MS) "Electrophysiology of stem cells in cardiac tissue engineering" (August 2016).
- 7. Joshua Biggs (MS) "Stem cells in cardiac tissue engineering" (August 2016).
- 8. Josh Rodriguez (MS) "Vascular bioreactor" (August 2016).
- 9. Lisa Larrew (MS) "Vascular cell modifications in diabetes" (May 2016).
- 10. Eric Wright (MS) "Endothelial progenitor cells as a source of endothelialization of cardiovascular tissue engineered tissues" (May 2016)
- 11. Elizabeth Fontaine (MS) "Tissue surface modification to improve endothelial cell adhesion" (May 2015).
- 12. Satyem Patel (MS) "Heart valve endothelialization imaging" (August 2014)

#### UNDERGRADUATE STUDENT ADVISING

**Current Undergraduate Advising** – 5 students (2 Honors)

Past Undergraduate Advising in my lab – 38 students

## **TEACHING**

# **Courses Taught**

BIO E 1010 - Biology for Bioengineers

BIO E 4480 - Tissue Engineering with Lab

BIO E 4510 (026) - Creative Inquiry - Cardiovascular microtissues

BIO E 4510 (027) - Creative Inquiry - Insulin-secreting microtissues

BIO E 4910 (H) - Undergraduate Research (Honors)

BIOE 8730 - Translational Cellular Therapy and Regenerative Medicine

BIOE 8910 - MS Research

BIOE 9910 - PhD Research

## **New Course Development**

BIO E 1010, Biology for Bioengineers, started 2009

BIO E 4480 Tissue Engineering with Lab, started 2009

BIO E 8730 Translational Cellular Therapy and Regenerative Medicine, started 2016

## UNIVERSITY AND PUBLIC SERVICE

# **Department Committees**

ABET Committee, member. (2008-2017)

Graduate Affairs Committee, member (20014-2016), chair (2016-present).

## Other service

## **Thesis Committees**

58 graduate students: Lee Sierad (MS and PhD), Elisabeth M Tedder (PhD), Ting Hsien Chuang (PhD), Bradley Winn (PhD), Richard Pascal, (MS), Duong Nguyen (PhD), George Fercana (PhD), Fuad Mefleh (PhD), Sarah Rollinson (PhD), Ariel Nissan (MS), Ryan Waddell (MS), Tara Briton (MS), Grace Dion (MS), Katy Jaeggli (MS), Michael Jaeggli (PhD), Brandon Mattix (PhD), James Chow (PhD), Jason Schulte (PhD), Allison Kennamer (MS), Mellissa Gaillard (MS), Ian Hale (PhD), Huaxiao Yang (PhD), Yunkai Dai (PhD), Saketh Karamched (PhD), Megan Casco (PhD), Aesha Desai (PhD), Jayesh Betala (PhD), Astha Kanna (PhD), Chris Ferreira (MS), Jessica Canavan (MS), Alison Welch (PhD), Dan Odenwelder (PhD), Kayla Gainey (PhD), Chris Deborde (PhD), Laura McCallum (PhD), Jhilmil Dhulekar (PhD), Varun Chawla (PhD), Spencer Marsh (PhD), Eric Wright (MS), Josh Rodriguez (MS), Joshua Biggs (MS), Robert Marti (MS), Maria Portilla (MS), Lisa Larrew (MS), James MCManus (MS), Margarita Portilla (MS), Andrew DeMaria (MS), Anna Lu Carter (MS), Brady Cullbreth (MS), Harrison Smallwood (MS), Megan Casco (PhD), Nicholas Rierson (MS), Clayton Compton (MS), Andrew DeMaria (PhD), Erik Schatzer (MS), Alison Welch (MS), Kayla Wilson (PhD), Yunkai Dai (PhD), Zachary Reinhardt (PhD).

#### **MISCELLANEOUS**

# **Translational Study Coordinator**

<u>2012-present</u> Official **Clinical Study Coordinator** for the IRB-approved translational study **Pro0007510** entitled "*Personalized Regenerative Medicine with Human Stem Cells and Scaffolds*" performed in collaboration with GHS and the Patewood clinics of Orthopedics and Vascular Surgery.

<u>2013-present</u> Official **Clinical Study Coordinator**; Clinical Study "*Factors involved in progression of valvular heart disease*"; IRB/IBC approved; project goals are collection of pathological valve tissues from patients and evaluation of mechanisms of pathogenesis by biochemical, molecular and histological techniques.

## Clinical applications of biomaterials - Research and Development

- 1. The first Romanian cardiac bioprosthetic heart valve made from bovine pericardium (1981). Almost 1000 valves created and implanted between 1985 1990.
- 2. The mitral valve autologous free graft, original procedure for valvular reconstruction (about 175 grafts implanted since 1990).

Updated August 14, 2017