CURRICULUM VITAE

VENKATESWARAN SUBRAMANIAN, Ph.D.

University of Kentucky
Saha Cardiovascular Research Center
BBSRB, Room B247
741 S Limestone Street
Lexington, KY 40536-0509

PERSONAL DATA

Address	3828 Foleys Trl Lexington KY 40514
Phone:	Office: (859) 323-0598 Lab: (859) 323-3429 Cell: (859) 433-9426
Fax:	(859) 257-3235
E-Mail:	venkat.subramanian@uky.edu

Date of Birth:	October 8, 1972	Place of Birth:	Mayiladuthurai, India
Nationality:	Indian	Immigration Status:	Permanent Resident
Marital Status:	Married		

EDUCATION

Dates	Degree	Subject	Institution
1990-1993	B.Sc.	Chemistry	Bharathidasan University, India
1993-1995	M.Sc.	Biochemistry	Annamalai University, India
1995-1997	M.Phil.	Biochemistry	Annamalai University, India
1999-2003	Ph.D.	Biochemistry	Annamalai University, India
2003-2006	Post-doc	Cardiovascular Physiology	East Tennessee State University, Johnson City, TN (Mentor: Krishna Singh, Ph.D.)
2006-2010	Post-doc	Cardiovascular Pathology	University of Kentucky, Lexington, KY (Mentor: Alan Daugherty, Ph.D.)

APPOINTMENTS/EMPLOYMENT

2015-Present	*Assistant Professor of Research,* Saha Cardiovascular Research Center, Department of Physiology, University of Kentucky
2010-2015:	*Assistant Professor of Research,* Saha Cardiovascular Research Center, Department of Internal Medicine (Cardiology Division), University of Kentucky
2008-2010:	*American Heart Association Post-doctoral Research Fellow,* University of Kentucky
1999-2003:	*Indian Council of Medical Research Pre-doctoral Fellow,* Annamalai University, India
1997-1999:	*Lecturer,* Department of Biochemistry, Vinayaka Mission, School of Medicine, India

1995-1997: *Research Fellow*, Annamalai University, India

PROFESSIONAL AFFILIATIONS

2004- American Heart Association (AHA) – ATVB Council
2011- American Diabetes Association (ADA)
2014- North American Vascular Biology Organization (NAVBO)

AWARDS / HONORS

2000-2003 Indian Council of Medical Research Foundation Fellow
2008-2010 American Heart Association Postdoctoral Fellowship Award (Great Rivers Affiliate)
2009 New Investigator Travel Award, ATVB Council of the American Heart Association - ATVB Annual Scientific Meeting (Spring Session)
2009 Best Poster Presentation Award, 12th Annual Gill Heart Institute Cardiovascular Research Day, University of Kentucky
2009 New Investigator Travel Award, ATVB Council of the American Heart Association - (Fall Session)
2011-2012 Pilot Grant Award from the Center of Research in Obesity and Cardiovascular Disease (COCVD), University of Kentucky
2012-2014 American Heart Association Beginning Grant-in-Aid Award (Great Rivers Affiliate)
2013 Outstanding Research Presentation Award at Barnstable Brown Obesity and Diabetes Research Day, University of Kentucky
2013-2014 Pilot and Feasibility Grant Award from Washington University Diabetes Research Center.
2014-2016 Early Investigator Research Grant from The National Marfan Foundation
2014-2017 American Heart Association Scientist Development Grant (National Center)

RESEARCH SUPPORT

ACTIVE:

Active/Pending/Completed:	**Active**
Project Number/PI/Role	14SDG18740000, Venkat Subramanian, PI
Source:	**American Heart Association**
Title of Project (*and/or Subproject*):	*Role of macrophage-specific calpain-2 in hypercholesterolemia-induced atherosclerosis*
Dates of Approved/Proposed Project:	**01/01/14 – 12/31/17**
The goal of this project is to test the hypothesis that calpain deficiency in macrophages will attenuate hypercholesterolemia-induced atherosclerosis by promoting macrophage reverse cholesterol transport (RCT) and suppressing NF-kB mediated inflammation. The proposed work will test this hypothesis by determining the role of calpain in macrophage cholesterol efflux and inflammation, macrophage RCT in vivo (Aim 1&2), and identifying the role of macrophage specific-calpain-2 in atherosclerosis (Aim 3).	
Annual Direct Costs (Percent Effort)	**$ 70,000 (40%)**

Active/Pending/Completed:	**Active**
Project Number/PI/Role	5P20GM103527, Lisa Cassis, Director; Venkat Subramanian, PI-Subproject, Junior Investigator
Source:	**National Institute of General Medical Sciences, P20**
Title of Project (*and/or Subproject*):	*Mechanism of Obesity Accelerated Abdominal Aortic Aneurysms*
Dates of Proposed Project:	**07/01/15 – 08/31/17**
The goal of this project is to test the hypothesis that calpain-2 activation promotes abdominal aortic aneurysms in obese mice by accelerating periaortic adipose tissue mediated aortic adventitial inflammation and medial destruction.	
Annual Direct Costs (Percent Effort)	**$ 175,000 (50%)**

PENDING:

Active/Pending/Completed:	**Pending; Scored 27% The grant was resubmitted in Mar 2016.**
Project Number/PI/Role	1R01HL130086-01, Venkat Subramanian, PI
Source:	**National Heart Lung and Blood Institute, R01**
Title of Project (*and/or Subproject*):	*Calpains and Abdominal Aortic Aneurysms*
The goal of this project is to test the hypothesis that calpain-2 activation promotes AngII-induced abdominal aortic aneurysms by accelerating aortic adventitial inflammation and medial destruction. Our working hypothesis is that calpain-2 promotes aortic adventitial inflammation by stimulating AngII-induced ASK-1/NF-*k*B mediated MCP-1/IL-6 production in AoAFs causing consequent macrophage recruitment. In addition, activated calpain-2 also promotes (myo)fibroblast differentiation and migration to the aortic media via TGF-β and Rho kinase activation, which in turn potentiates cytoskeletal protein- filamin A and talin fragmentation, thereby causing aortic medial destruction.	
Dates of Proposed Project:	**09/01/16 – 08/31/21**

UNFUNDED:

Active/Pending/Completed:	**Unfunded; Scored 24% - Early Stage Investigator (ESI). The funding rank for ESIs-23%. The grant will be resubmitted as a new grant in Oct 2015.**
Project Number/PI/Role	1R01HL121321-01A1, Venkat Subramanian, PI
Source:	**National Heart Lung and Blood Institute, R01**
Title of Project (*and/or Subproject*):	*Role of Calpains in Thoracic Aortic Aneurysm Formation*
The goal of this project is to test the hypothesis that calpain promotes Angiotensin II-induced thoracic aortic aneurysm formation by stimulating aortic adventitial fibroblasts derived-MCP-1 mediated macrophage recruitment, and (myo)fibroblast migration to aortic media, which in turn causes medial destruction by upregulating filamin A fragmentation.	
Dates of Proposed Project:	**07/01/14 – 06/30/19**

COMPLETED:

Active/Pending/Completed:	**Completed**
Project Number/PI/Role	1000401876, Venkat Subramanian, PI
Source:	**National Marfan Foundation**
Title of Project (*and/or Subproject*):	*Role of calpain in ascending aortic aneurysms*
Dates of Approved/Proposed Project:	**01/01/14 – 12/31/15**
The goal of this project is to test the hypothesis that calpain-2 activation promotes AngII-induced ascending aortic aneurysms by upregulating filamin A fragmentation in the aortic media. The proposed work will test this hypothesis by determining the contribution of calpain-2 in AngII-induced filamin A fragmentation in aortic SMCs (Aim 1), and identifying the role of calpain-2 deficiency in the development of AngII-induced ascending aortic aneurysms (Aim 2).	
Annual Direct Costs (Percent Effort)	**$ 37,500 (10%)**

Active/Pending/Completed:	**Completed**
Project Number/PI/Role	13BGIA14560001, Venkat Subramanian, PI
Source:	**American Heart Association – Beginning Grant-in-Aid (Great Rivers Affiliate)**
Title of Project (*and/or Subproject*):	Role of macrophage-specific calpains in hypercholesterolemia-induced atherosclerosis
Dates of Proposed Project:	**01/01/13 – 12/31/14**

Active/Pending/Completed:	**Completed**
Project Number/PI/Role	5 P30 DK020579, P.Kern (PI), Pilot Grant Investigator
Source:	Pilot & Feasibility Award from **University of Kentucky – Washington University Diabetes Research Center** Collaborative Pilot & Feasibility Program
Title of Project (*and/or Subproject*):	*Role of calpain in diabetic atherosclerosis*
Dates of Approved/Proposed Project:	**03/01/13 – 11/30/14**
Annual Direct Costs (Percent Effort)	**$ 43,000 (10%)**

Active/Pending/Completed:	**Completed**
Project Number/PI/Role	NIH NCRR P20 RR021954, L Cassis (PI), Pilot Grant Investigator
Source:	Pilot grant award from Center of Research in Obesity and Cardiovascular Disease (COCVD) from NIH NCRR
Title of Project (*and/or Subproject*):	Role of calpain in diet-induced obesity
Dates of Proposed Project:	**11/01/11 – 10/31/12**

Active/Pending/Completed:	**Completed**
Project Number/PI/Role	0825592D, Venkat Subramanian, PI
Source:	**American Heart Association – Post-doctoral Fellowship (Great Rivers Affiliate)**
Title of Project (*and/or Subproject*):	Role of peroxisome proliferator activated receptor gamma in angiotensin II induced abdominal aortic aneurysm
Dates of Proposed Project:	**07/01/08 – 06/31/10**

Active/Pending/Completed:	**Completed**
Project Number/PI/Role	Venkat Subramanian, PI
Source:	**Indian Council of Medical Research – Pre-doctoral Fellowship**
Title of Project (*and/or Subproject*):	Beneficial role of natural plant products on diabetes and insulin secretion in experimental rats
Dates of Proposed Project:	**01/01/00 – 12/31/03**

PUBLICATIONS

1. **Subramanian V,** Pari L, Viswanathan P, Menon VP. Protective effect of Livex, a herbal formulation against Erythromycin Estolate induced hepatotoxicity in rats. ***J Ethnopharmacol*** 1997; 57: 161-167.(PMID: 9292408)
2. **Subramanian V,** Pari L, Viswanathan P. Antiperoxidative effect of Livex, a herbal formulation against Erythromycin Estolate induced lipid peroxidation in rats. ***Phytother Res*** 1998; 12: 465-471.
3. Pari L, Ramakrishnan R, **Subramanian V**. Antihyperglycaemic effect of Diamed, a herbal formulation in alloxan induced experimental diabetes in rats. ***J Pharm Pharmacol*** 2001; 53: 1139 -1143. (PMID:11518024)
4. **Subramanian V,** Pari L. Effect of *Coccinia indica* on blood glucose, insulin and hepatic key enzymes in experimental diabetes. ***Pharm Biol*** 2002; 40: 165-170. (PMID: 2468436)
5. **Subramanian V,** Pari L. Antioxidant effect of *Phaseolus vulgaris* in Streptozotocin-induced diabetic rats. ***Asia Pac J Clin Nutr*** 2002; 11: 206-209. (PMID: 12230234).
6. **Subramanian V,** Pari L, Saravanan G. Effect of *Phaseolus vulgaris* on circulatory antioxidants and lipids in streptozotocin induced diabetic rats. ***J Med Food*** 2002; 5: 97-104. (PMID:12487757)
7. Pari L, **Subramanian V**. Hypoglycemic effect of Scoparia dulcis L (Sweet Broom Weed) in alloxan induced hyperglycemic rats. ***Phytother Res*** 2002; 16: 662-664. (PMID: 12410548)
8. Saravanan G, Pari L, **Subramanian V.** Effect of cogent db, a herbal drug, on plasma insulin and hepatic enzymes of glucose metabolism in experimental diabetes. ***Diab Obes Metab*** 2002; 4: 394-398. (PMID:12406037)

9. **Subramanian V,** Pari L, Suguna L, Chandrakasan G. Modulatory effect of *Coccinia indica* on aortic collagen in streptozotocin-induced diabetic rats. ***Clin Exp Pharmacol Physiol*** 2003; 30: 157-163. (PMID: 12603344)

10. **Subramanian V,** Pari L. Effect of *Coccinia indica* leaves on antioxidant status in streptozotocin-induced diabetic rats. ***J Ethnopharmacol*** 2003; 84: 163-168. (PMID: 12648810)

11. Pari L, **Subramanian V.** Effect of an aqueous extract of *Phaseolus vulgaris* on the properties of tail tendon collagen of rats with streptozotocin-induced diabetes. ***Braz J Med Biol Res*** 2003; 36: 861-870. (PMID:12845372)

12. **Subramanian V,** Pari L. Effect of *Coccinia indica* leaf extract on plasma antioxidants in streptozotocin induced diabetes in rats. ***Phytother Res*** 2003; 17: 605-608. (PMID:12820255)

13. Pari L, **Subramanian V.** Protective effect of *Coccinia indica* on changes in the fatty acid composition in streptozotocin induced diabetic rats. ***Pharmazie*** 2003; 58: 409-412. (PMID: 12857005).

14. Pari L, **Subramanian V.** Effect of an aqueous extract of *Phaseolus vulgaris* on plasma insulin and hepatic key enzymes of glucose metabolism in experimental diabetes. ***Pharmazie*** 2003; 58: 916-919. (PMID: 14703973)

15. Pari L, **Subramanian V.** Protective role of *Phaseolus vulgaris* on changes in the fatty acid composition in experimental diabetes. ***J Med Food*** 2004; 7: 204-209. (PMID: 15298769).

16. Krishnamurthy P, **Subramanian V**, Singh M, Singh K. Deficiency of β1 integrins results in increased myocardial dysfunction after myocardial infarction. ***Heart*** 2006; 92: 1309- 1315. (PMID:16547211)

17. Southerland EM, Milhorn DM, Foreman RD, Lineroth B, DeJongste MLJ, Armour JA, **Subramanian V**, Singh K, Singh M, Ardell JL. Pre-emptive, but not reactive, spinal cord stimulation mitigates transient ischemia-induced myocardial infarction via cardiac adrenergic neurons. ***Am J Physiol Heart Circ Physiol*** 2007; 292: H311-317. (PMID: 16920800)

18. Ding X, Mountain DJ, **Subramanian V**, Singh K, Williams CA. The effect of high cervical spinal cord stimulation on the expression of SP, NK-1 and TRPV1 mRNAs during cardiac ischemia in rat. ***Neurosci Lett*** 2007; 424(2):139-144. (PMID:17714867)

19. Krishnamurthy P, **Subramanian V,** Singh M, Singh K. β1 integrins modulate β-adrenergic receptor stimulated apoptosis and myocardial remodeling. ***Hypertension*** 2007; 49: 865-872. (PMID: 17283249)

20. **Subramanian V**, Krishnamurthy P, Singh K, Singh M. Lack of Osteopontin improves cardiac function in streptozotocin induced diabetic mice. ***Am J Physiol Heart Circ Physiol*** 2007; 293: H673-683. (PMID: 16980342)

21. Krishnamurthy P, Peterson JT, **Subramanian V**, Singh M, Singh K. Inhibition of matrix metalloproteinases improves left ventricular function in mice lacking osteopontin after myocardial infarction. ***Mol Cell Biochem*** 2009; 322: 53-62. (PMID: 1879185)

22. Owens AP 3rd, **Subramanian V**, Moorleghen JJ, Guo Z, McNamara CA, Cassis LA, Daugherty A. Angiotensin II Induces a Region-Specific Hyperplasia of the Ascending Aorta Through Regulation of Inhibitor of Differentiation 3. ***Circ Res*** 2010; 106: 611-619. (PMID: 20019328)

23. **Subramanian V**, Golledge J, Ijaz T, Bruemmer D, Daugherty A. Pioglitazone-Induced Reductions in Atherosclerosis Occur via Smooth Muscle Cell–Specific Interaction With PPARγ. ***Circ Res*** 2010; 107: 953-958. (PMID: 20798360)

24. Rateri D, Moorleghen J, Balakrishnan A, Owens AP, Howatt DA, **Subramanian V,** Poduri A, Charnigo R, Cassis LA, Daugherty A. Endothelial Cell-specific Deficiency of AngII Type 1a Receptors Attenuates AngII-induced Ascending Aortic Aneurysms in LDL Receptor -/- Mice. ***Circ Res*** 2011; 108: 574-581. (PMID: 21252156)

25. Foster CR, Singh M, **Subramanian V,** Singh K. Ataxia telangiectasis mutated kinase plays a protective role in β-adrenergic receptor stimulated cardiac myocyte apoptosis and myocardial remodelling. ***Mol Cell Biochem*** 2011; 353: 13-22. (PMID: 21404020).

26. Uchida HA, Poduri A, **Subramanian V,** Cassis LA, Daugherty A. Urokinase-Type Plasminogen Activator Deficiency in Bone Marrow-Derived Cells Augments Rupture of Angiotensin II-Induced Abdominal Aortic Aneurysms. ***Arterioscler Thromb Vasc Biol*** 2011; 31: 2845-2852. (PMID: 21868698)

27. Wang S, **Subramanian V,** Lu H, Howatt DA, Moorleghen JJ, Charnigo R, Cassis LA, Daugherty A. Deficiency of receptor-associated protein attenuates angiotensin II-induced atherosclerosis in hypercholesterolemic mice without influencing abdominal aortic aneurysms. ***Atherosclerosis*** 2012; 220: 375-380. (PMID: 22153700)

28. **Subramanian V***, Golledge J, Heywood EB, Bruemmer D, Daugherty A. Regulation of Peroxisome Proliferator-Activated Receptor-γ by Angiotensin II Via Transforming Growth Factor-β1-Activated p38 Mitogen-Activated Protein Kinase in Aortic Smooth Muscle Cells. ***Arterioscler Thromb Vasc Biol*** 2012; 32: 397-405. (PMID: 22095985) ***- Author for Correspondence**.

29. **Subramanian V***, Uchida HA, Ijaz T, Moorleghen JJ, Howatt DA, Balakrishnan A. Calpain Inhibition Attenuates Angiotensin II-induced Abdominal Aortic Aneurysms and Atherosclerosis in LDL Receptor Deficient Mice. ***J Cardiovasc Pharmacol*** 2012; 59: 66-76. (PMID: 21964156) ***- Author for Correspondence**.

30. **Subramanian V*,** Moorleghen JJ, Balakrishnan A, Howatt DA, Chishti AH, Uchida HA. Calpain-2 Compensation Promotes Angiotensin II-induced Ascending and 1 Abdominal Aortic Aneurysms in Calpain-1 Deficient Mice. ***PLoS One*** 2013**;** 19: e72214. (PMCID: PMC3747148) ***- Author for Correspondence.**

31. Howatt DA, Balakrishnan A, Moorleghen JJ, Muniappan L, Rateri DL, Uchida HA, Takano, J, Saido TC, Chishti AH, Baud L, **Subramanian V***. Leukocyte Calpain Deficiency Reduces Angiotensin II-induced Inflammation and Atherosclerosis but not Abdominal Aortic Aneurysms in Mice. ***Arterioscler Thromb Vasc Biol*** 2016, In Press. (PMID:26966280) ***- Author for Correspondence**.

Under revision/Submitted/In Preparation

32. Muniappan L, Balakrishnan A, Howatt DA, Katz, WS, Moorleghen JJ, **Subramanian V***. Pharmacological and Genetic Inhibition of Calpain Attenuates Adipose Tissue Apoptosis, Macrophage Accumulation and Inflammation in Diet-induced Obese Mice. (***In Preparation for Am J Physiol***) ***- Author for Correspondence.**

PUBLISHED ABSTRACTS

1. **Subramanian V**, Prasanna K, Singh K, Singh M. Lack of Osteopontin improves cardiac function in streptozotocin induced diabetic mice. *American Heart Scientific Sessions 2005* Dallas, TX. *Circulation 2005; 112(17) (suppl): II-100 (Abstract No. 566).*
2. Prasanna K, **Subramanian V**, Singh M, Singh K. β1 integrins play a pivotal role in Myocardial Infarction-induced cardiac myocyte apoptosis and left ventricular remodeling. *American Heart Scientific Sessions 2005* Dallas,TX. *Circulation 2005; 112(17) (suppl): II-145 (Abstract No. 778).*
3. **Subramanian V**, Prasanna K, Singh K, Singh M. Differential activation of protein kinse C isoforms and mitogen-activated protein kinases in diabetic heart lacking osteopontin. *American Heart Scientific Sessions 2006* Chicago, IL. *Circulation 2006; 114(18) (suppl): II-273 (Abstract No. 1427).*
4. Prasanna K, **Subramanian V,** Singh M, Singh K. β1 integrins play a critical role in pivotal role in β-adrenergic receptor stimulated cardiac myocyte apoptosis and myocardial remodeling. *American Heart Scientific Sessions 2006* Chicago, IL. *Circulation 2006; 114(18) (suppl): II-242 (Abstract No.1282).*
5. **Subramanian V**, Golledge J, Daugherty A. Angiotensin II reduces abundance of Peroxisome Proliferator Activated Receptor γ in aortic smooth muscle cells via the TGF-β1 activated-P38 MAP Kinase in a Smad-2 independent manner. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2008* Atlanta, GA. ATVB 2008; (Abstract No.447).
6. **Subramanian V**, Bruemmer D, Golledge J, Daugherty A. Smooth Muscle Specific PPARγ Deficiency Augments Angiotensin II-induced Atherosclerosis But Does Not Affect Abdominal Aortic Aneurysms in Male LDL Receptor Deficient Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2009* Washington, DC. ATVB 2009 (Abstract No.605).
7. **Subramanian V,** Bruemmer D, Golledge J, Daugherty A. Pioglitazone Attenuates AngII-induced Atherosclerosis via a Smooth Muscle Cell-Specific PPARγ Mechanism but Has No Effect on Abdominal Aortic Aneurysms. *American Heart Scientific Sessions 2009* Orlando, FL. Circulation 2009 (suppl) (Abstract No.5194).
8. **Subramanian V**, Ijaz T, Uchida HA. Pharmacological Inhibition of Calpain Attenuates Angiotensin II-induced Atherosclerosis and Abdominal Aortic Aneurysms in Male LDL Receptor Deficient Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2010* San Francisco, CA. ATVB 2010 (Abstract No.722).
9. **Subramanian V**, Jessica J. Moorleghen JJ, Howatt DA, Balakrishnan A. Calpain-1 Deficiency Attenuates Angiotensin II-induced Atherosclerosis and Abdominal Aortic

Aneurysms in Male LDL Receptor Deficient Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2011* Chicago, IL. ATVB 2011 (Abstract No.512).

10. **Subramanian V**, Jessica J. Moorleghen JJ, Howatt DA, Balakrishnan A. Calpain-1 Deficiency Does Not Effect Angiotensin II-induced Atherosclerosis or Abdominal Aortic Aneurysms in Male LDL Receptor Deficient Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2012* Chicago, IL. ATVB 2012 (Abstract No.402).
11. **Subramanian V**, Moorleghen JJ, Howatt DA, Balakrishnan A, Chishti AH, Uchida HA. Calpain-2 Compensation Promotes Angiotensin II-induced Ascending and Abdominal Aortic Aneurysms in Calpain-1 Deficient Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2013* Lake Buena Vista, FL. ATVB 2013 (Abstract No.655).
12. **Subramanian V**, Balakrishnan A, Howatt DA, Moorleghen JJ, Katz, WS. Pharmacological Inhibition of Calpain Attenuates Adipose Tissue Apoptosis, Macrophage Accumulation and Inflammation in Diet-induced Obese Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2013* Lake Buena Vista, FL. ATVB 2013 (Abstract No.661).
13. **Subramanian V**, Howatt DA, Balakrishnan A, Moorleghen JJ, Rateri DL, Baud L. Calpain Inhibition in Bone Marrow-Derived Cells Attenuates Atherosclerosis But Not Aortic Aneurysms in Hypercholesterolemic Mice Infused with Angiotensin II. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology 2014* Toronto, Ontario, Canada. ATVB 2014 (Abstract No.495).
14. Balakrishnan A, Howatt DA, Moorleghen JJ, Uchida HA, Takano, J, Saido TC, **Subramanian V.** Inducible Depletion of Calpain-2 Attenuates Angiotensin II-induced Abdominal Aortic Aneurysms in Male LDL Receptor Deficient Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology May 8 2015 San Francisco*, CA. ATVB 2015 (Abstract No.223).
15. Howatt DA, Balakrishnan A, Moorleghen JJ, Rateri DL, Uchida HA, Takano, J, Saido TC, Chishti AH, Baud L, **Subramanian V**. Leukocyte Calpain Deficiency Reduces Angiotensin II-induced Inflammation and Atherosclerosis in Hypercholesterolemic Mice. *Annual Conference of Arteriosclerosis Thrombosis and Vascular Biology, May 9 2015 San Francisco*, CA. ATVB 2015 (Abstract No.299).

SEMINARS

Date	Title, Meeting, Location
2/99	9th Annual Scientific Meeting of Society of Biological Chemists (INDIA) Annamalainagar Chapter, Annamalai University, India. “Hypoglycemic effect of *Musa sapientum* (Banana) in alloxan induced diabetic rats”.
2/02	34th Annual conference of The Indian Pharmacological Society, Nagpur, India. “Antidiabetic and Antioxidant activity of ethanolic extract of *Coccinia indica* leaves in experimental diabetes”.

2/04 13th Annual Scientific Meeting of Society of Biological Chemists (INDIA) Annamalainagar Chapter, Annamalai University, India. “Antioxidant effect of *Phaseolus vulgaris* in streptozotocin induced diabetic rats”.

11/06 American Heart Association, AHA 2006 Annual meeting in Chicago, Illinois. “Differential activation of protein kinase C isoforms and mitogen-activated protein kinases in diabetic heart lacking osteopontin”.

4/13 Saha Cardiovascular Research Center Seminar Series (April 12, 2013), University of Kentucky, Lexington, KY. “Role of Calpain in Aortic Aneurysms”.

5/13 Arteriosclerosis, Thrombosis & Vascular Biology, ATVB 2013 Annual meeting in Orlando, FL. “Pharmacological Inhibition of Calpain Attenuates Adipose Tissue Apoptosis, Macrophage Accumulation and Inflammation in Diet-induced Obese Mice”.

7/13 FASEB Summer Research Conference on Biology of Calpains in Health and Disease, Saxtons River, VT. “Calpain-2 Compensation Promotes Angiotensin II-induced Ascending and Abdominal Aortic Aneurysms in Calpain-1 Deficient Mice”.

8/14 Texas Tech University Health Sciences Center, School of Medicine, Department of Anesthesiology., Lubbock, TX. Invited Seminar (August 14th 2014). “Role of Calpain in Aortic Aneurysms”.

10/14 University of Iowa, School of Medicine, Department of Cardiovascular Medicine, Iowa City, IA. Invited Seminar (October 13th 2014). “Role of Calpain in Aortic Aneurysms”.

STUDENTS

Date	Student	Degree	Department	My Role	Current
2005	Brandon Johnson	MD	Physiology	Rotation Research Supervisor	Residency Emory University
2008-2010	Talha Ijaz	BS	CVRC	Rotation Research Advisor	MD/PhD, University of Texas, Galveston
2011	Qing Jing	BS	CVRC	Rotation Research Advisor	MD, University of Virginia
2013	Kruti Patel	DO	CVRC	Rotation Research Advisor	DO, University of Tennessee

TEACHING

Date	Role	Course	Total lectures
Vinayaka Mission, School of Medicine, India			
1997,1998	Lecturer	Biochemistry – Lipid Metabolism in Diseases	6 lectures
Annamalai University, India			
2001	Lecturer	Nutritional Biochemistry – Vitamin Disorders	4 lectures

EXTRACURRICULAR ACTIVITIES

Participation on Review Panels

Grant Reviewer:

2016: Adhoc Member, NIH Kidney Molecular Biology and Genitourinary Organ Development Study Section.

Manuscript Reviewer:

Atherosclerosis
Arteriosclerosis, Thrombosis and Vascular Biology (ATVB)
Biochemie
Biomed Central Journals
Circulation Research
Heart and Vessels
Histology and Histopathology
Journal of Vascular Research
PLoS One
PPAR Research

SERVICE

Oct, 2010 – Present: Judge for Student Posters at Cardiovascular Research Day, University of Kentucky.

May, 2011- Present: Judge for Student Posters at Barnstable Diabetes Research Day, University of Kentucky.

RESEARCH PLAN

My overall research goal is to identify efficient therapeutic targets for the complex cardiovascular disease mainly aortic aneurysms and atherosclerosis. To fulfil this goal requires broad research training and will be aided by my education and training experience in biochemistry, molecular biology, physiology and pathology. The primary focus of my research is to identify the functional role of calpain, a cysteine protease in these vascular diseases. To delineate the functional contribution of calpain in vascular pathologies, I have used an animal model of Angiotensin II (AngII) -induced aortic aneurysms and atherosclerosis developed by Dr. Daugherty and Dr. Cassis, at University of Kentucky. Using this animal model, recently, I have demonstrated that pharmacological inhibition of calpains completely attenuate the development of AngII-induced aortic aneurysm in mice. To further explore the molecular mechanisms by which calpain activation contributes to these vascular diseases, recently I have developed unique reagents including transgenic, whole body or conditional cell-specific calpain (1 or 2 isoform specific) deficient mice. Using these novel reagents, the work that I hope to accomplish over the next several years are summarized below.

PROJECT A: Role of calpains in thoracic and abdominal aortic aneurysms.

Aortic aneurysm (AA) is an asymptomatic, life-threatening disorder that mainly occurs in the ascending and abdominal aorta. AAs often cause death by aortic rupture in patients with genetically determined connective tissue disorders, e.g. Marfan's syndrome. The current available therapy is restricted to surgical repair, highlighting the need to explore mechanistic insights into AA to develop effective, non-surgical therapeutics. In AA patients, structural integrity of the aortic wall is disrupted due to dissociation of smooth muscle cell (SMC) contractile filaments from myofibrils of extracellular matrix (ECM) by proteases. However, the mechanism underlying ECM degradation in AA formation is not completely understood. Calpains are the only known proteolytic enzymes targeting an array of cytoskeletal and membrane proteins that maintain structural integrity of the aorta.

Calpains are calcium dependent cysteine proteases that are uniquely different from other intracellular proteolytic enzymes in substrate recognition. Calpains directly bind to their substrates and promote proteolysis. In this project, our hypothesis is that activated calpain promotes aortic aneurysms by stimulating adventitial fibroblast-derived MCP-1 mediated macrophage recruitment, and (myo)fibroblasts migration to aortic media, which in turn causes medial destruction by upregulating cytoskeletal filament fragmentation. Our working hypothesis is that calpain promotes aortic adventitial inflammation by stimulating AngII-induced ASK-1/NF-*k*B mediated MCP-1 production in aortic adventitial fibroblasts (AoAFs) and consequent macrophage recruitment. In addition, activated calpain also promotes (myo)fibroblast differentiation and migration to the aortic media, which in turn potentiates filamin A fragmentation and thereby causes aortic medial destruction. I will address this hypothesis using genetically modified transgenic, whole body or cell-specific calpain deficient mice, and lenti or adenoviral mediated calpain overexpressing or knockdown cell systems. These studies will establish how proteolytic activity of the calpain pathway contributes to AA propagation and thereby provides new insight for development of diagnostic and therapeutic strategies for this insidious and clinically devastating disease.

PROJECT B: Role of calpains in atherosclerosis and macrophage reverse cholesterol transport.

Development of atherosclerosis is associated with hypercholesterolemia, intracellular lipid accumulation, macrophage foam cell formation, and inflammation. Reverse cholesterol transport (RCT) is a pathway that transports excess cholesterol from macrophage-derived foam cells in the arterial wall to liver for excretion in bile. A critical process in RCT is cholesterol efflux from macrophage-derived foam cells to HDL and lipid-poor apoA-I, which removes accumulated cholesterol and consequently prevents atherosclerosis progression. The ATP binding cassette transporters, ABCA1 and ABCG1, play a key role in RCT by mediating cholesterol efflux from macrophages and protects against atherosclerosis. Interestingly, both ABCA1 and ABCG1 are negatively regulated and cleaved by calpains, which consequently reduce expression and cholesterol efflux function. Human atherosclerosis is associated with prolonged activation of calpains, however, surprisingly few calpain substrates have been identified. Recently, I published novel evidence that pharmacological inhibition of calpains attenuates angiotensin II-induced atherosclerosis and NF-*k*B mediated inflammation in LDLr-/- mice. In this project, our hypothesis is that calpain deficiency in macrophages will attenuate hypercholesterolemia-induced atherosclerosis by promoting macrophage RCT and suppressing NF-kB mediated inflammation. We will address this hypothesis using the newly developed tamoxifen-inducible whole body and macrophage-specific calpain deficient mice. These studies will provide novel insights on regulation of macrophage RCT by calpains and will define the role of enzymatic inactivation of calpain in the formation and progression of atherosclerosis. This may lead to defining a powerful target for the development of anti-atherogenic drugs

In addition to these above mentioned 2 major projects, I have an additional project focusing on the role of calpain on adipose tissue inflammation and insulin resistance.

PROJECT C: Role of calpains in adipose tissue inflammation and insulin resistance.

Adipose tissue undergoes extensive modifications during the development of obesity which includes adipocyte hypertrophy, apoptosis, fibrosis and macrophage accumulation. This in turn leads to adipose tissue inflammation and insulin resistance. Interestingly, activated calpain promotes cellular apoptosis, fibrosis and inflammation in various tissues. Here our interest is to understand whether activated calpain plays any critical role in adipose tissue inflammation. In this project, our hypothesis is that calpain deficiency in macrophages will attenuate adipose tissue macrophage accumulation and insulin resistance. We will address this hypothesis using the newly developed tamoxifen-inducible whole body and macrophage-specific calpain deficient mice. These studies will provide novel insights on regulation of adipose tissue macrophage accumulation by calpains and will define the role of enzymatic inactivation of calpain in the development of insulin resistance during obesity.