Journal of Microbiology and Pathology

Editorial Open Access

Mechanobiology and Mechanics in Cardiovascular Disease

Yongho Bae*

Department of Pathology and Anatomical Sciences, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, USA

Cardiovascular disease is the main cause of death globally. Arterial stiffening significantly contributes to the progression of cardiovascular disease [1-3] including atherosclerosis, coronary heart disease, hypertension and stroke. The molecular mechanisms governing arterial stiffening and the phenotypic changes in vascular smooth muscle cells associated with the stiffening process are critical areas in cardiovascular biology, mechanics and pathology. Evidence suggests that arterial stiffness can drive aberrant vascular smooth muscle cell dedifferentiation, migration, and proliferation within the vessel wall [4-9]. Yet, the underlying mechanisms regulating arterial stiffening and the molecular changes within vascular smooth muscle cells associated with the stiffening process remain unclear.

Vascular smooth muscle cells are highly, but not terminally, differentiated cells and constitute a major component of the biomechanically active cell layer in the media of arteries. In response to vascular injury, vascular smooth muscle cells play a major role in neointima formation when they transition from a contractile state to a synthetic state in which they exhibit increased migration, proliferation, and extracellular matrix protein production (i.e. collagen, fibronectin and lysyl oxidase) [8-11]. Vascular smooth muscle cell dedifferentiation, migration and proliferation occur during vascular development and tissue repair in response to vascular injury. Deregulation of vascular smooth muscle cell phenotype can lead to the progression of cardiovascular disease. The difference between physiological and pathological migration and proliferation has been attributed to a failure to cease migration and proliferation once tissue repair has been completed. Thus, many research laboratories use primary cell culture of vascular smooth muscle cells to study the role of matrix stiffness-mediated mechanosensing in regulating vascular smooth muscle cell behaviours.

To explore how stiffness affects vascular smooth muscle cell function, many laboratories have adapted the use of engineered extracellular matrix protein-coated polyacrylamide hydrogels of biologically relevant stiffness to mimic in vivo patho-physiological microenvironments. The main advantages of this compliant/deformable substrate system are that 1) the polyacrylamide hydrogels are biologically inert as adhesive polymer surfaces and only the extracellular matrix proteins, such as fibronectin and collagen that are covalently bound to their surface, can function as cellular ligands, and 2) the stiffness can be easily controlled by changing the relative ratio of acrylamide to bis-acrylamide to mimic the stiffness levels of most biological tissues. This system has been used in many mechanobiology studies to investigate the role of extracellular matrix stiffness on vascular smooth muscle cell proliferation [4,7,12], migration [13,14], stiffness [7,12,15,16], cell-cell adhesion [12], cyclooxygenase-2 regulation [5,17] and extracellular matrix production (i.e. collagen, fibronectin, and lysyl oxidase) [5,18]. These studies have highlighted the importance of extracellular matrix stiffness and biomechanical signals in regulating key cellular processes in cell/vascular biology, aging [18] and diseases including atherosclerosis [5,19] and fibrosis [20]. Yet, the underlying mechanisms regulating vascular stiffening and the molecular changes within vascular smooth muscle cells associated with the stiffening process remain unclear. Thus, current research themes are to identify signalling pathways by which physiological arterial stiffness controls vascular smooth muscle cell function and to determine how pathological arterial stiffness disrupts that control which contributes to the progression of cardiovascular disease. These research findings will be significantly relevant for clinical revascularization procedures (angioplasty and stenting), where the risk of restenosis attributable to neointimal formation may be mitigated by targeting certain mechano sensitive proteins to maintain lumen diameter, vessel function, and physiological arterial stiffness. Thus, current and future work by researchers may lead to new therapies for treating cardiovascular disease.

References

1. Mitchell GF, Hwang SJ, Vasan RS, Larson MG, Pencina MJ, et al. (2010) Arterial Stiffness and Cardiovascular Events the Framingham Heart Study. Circulation 121: 505-511.
2. Liao D, Arnett DK, Tyroler HA, Riley WA, Chambless LE, et al. (1993) Arterial Stiffness and the Development of Hypertension. Hypertension 34: 201.
3. Mattace-Raso FUS, Van der Cammen TJM, Hofman A, Van Popele NM, Bos ML, et al. (2006) Arterial Stiffness and Risk of Coronary Heart Disease and Stroke the Rotterdam Study. Circulation 113: 657-663.
4. Klein EA, Yin L, Kothapalli D, Castagnino P, Byfield FJ, et al. (2009) Cell-Cycle Control by Physiological Matrix Elasticity and In Vivo Tissue Stiffening. Current Biology 19: 1511-1518.
5. Kothapalli D, Liu SL, Bae YH, Monslow J, Xu T, et al. (2012) Cardiovascular Protection by Apo E and Apo E-HDL Linked to Suppression of ECM Gene Expression and Arterial Stiffening. Cell Reports 2: 1259-71.
6. Hahn C, Schwartz MA (2009) Mechanotransduction in vascular physiology and atherogenesis. Nature reviews Molecular cell biology 10: 53-62.
7. Bae YH, Mui KL, Hsu BY, Liu SL, Cretu A (2014) A FAK-Cas-Rac-lamellipodin signaling module transduces extracellular matrix stiffness into mechano sensitive cell cycling. Science signaling 7: 57.
8. Thyberg J, Hedin U, Sjölund M, Palmberg L, Bottger BA (1990) Regulation of differentiated properties and proliferation of arterial smooth muscle cells. Arteriosclerosis Thrombosis and Vascular Biology 10: 966-990.
9. Owens GK, Kumar MS, Wamhoff BR (2004) Molecular Regulation of Vascular Smooth Muscle Cell Differentiation in Development and Disease. Physiological Reviews 84: 767-801.
10. Owens GK (1995) Regulation of differentiation of vascular smooth muscle cells. Physiological Reviews 75: 487-517.
11. Thyberg J, Blomgren K, Roy J, Tran PK, Hedin U (1997) Phenotypic Modulation of Smooth Muscle Cells after Arterial Injury Is Associated with Changes in the Distribution of Laminin and Fibronectin. Journal of Histochemistry & Cytochemistry 45: 837-46.

***Corresponding author:** Yongho Bae, Department of Pathology and Anatomical Sciences, Jacobs School of Medicine and Biomedical Sciences, University at Buffalo, State University of New York, USA, Tel: 716-829-3523; E-mail: yonghoba@buffalo.edu

Received December 27, 2017; **Accepted** December 28, 2017; **Published** January 12, 2018

Citation: Bae Y (2018) Mechanobiology and Mechanics in Cardiovascular Disease. J Microbiol Pathol 2: e109.

12. Mui KL, Bae YH, Gao L, Liu SL, Xu T, et al. (2015) N-Cadherin Induction by ECM Stiffness and FAK Overrides the Spreading Requirement for Proliferation of Vascular Smooth Muscle Cells. Cell Reports 10: 1477-86.

13. Liu F, Mih JD, Shea BS, Kho AT, Sharif AS, et al. (2010) Feedback amplification of fibrosis through matrix stiffening and COX-2 suppression. The Journal of Cell Biology 190: 693-706.

14. Peyton SR, Putnam AJ (2005) Extracellular matrix rigidity governs smooth muscle cell motility in a biphasic fashion. Journal of Cellular Physiology 204: 198-209.

15. Yeung T, Georges PC, Flanagan LA, Marg B, Ortiz M, et al (2005) Effects of substrate stiffness on cell morphology, cytoskeletal structure, and adhesion. Cell motility and the cytoskeleton 60: 24-34.

16. Solon J, Levental I, Sengupta K, Georges PC, Janmey PA (2007) Fibroblast Adaptation and Stiffness Matching to Soft Elastic Substrates. Biophysical Journal 93: 4453-4461.

17. Hsu BY, Bae YH, Mui KL, Liu S-L, Assoian RK (2015) Apo lipoprotein E3 Inhibits Rho to Regulate the Mechanosensitive Expression of Cox2. PLoS ONE 10: 128974.

18. Liu S-L, Bae YH, Yu C, Monslow J, Hawthorne EA, et al. (2015) Matrix metalloproteinase-12 is an essential mediator of acute and chronic arterial stiffening. Scientific Reports 5: 17189.

19. Davies PF (2009) Hemodynamic shear stress and the endothelium in cardiovascular pathophysiology. Nat Clin Pract Cardiovasc Med.

20. Huang X, Yang N, Fiore VF, Barker TH, Sun Y, et al. (2012) Matrix Stiffness–Induced Myofibroblast Differentiation Is Mediated by Intrinsic Mechanotransduction. American Journal of Respiratory Cell and Molecular Biology 47: 340-348.