BIOGRAPHICAL SKETCH

NAME: Binata Joddar

eRA COMMONS USER NAME (credential, e.g., agency login):bjoddar

POSITION TITLE: Assistant Professor, Mechanical Engineering & Biomedical Engineering Program

EDUCATION/TRAINING INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Pune University, India	B.S	Aug/99	Pharmaceutics
Jadavpur University, India	M.S	Aug/01	Biomedical Engineering
Clemson University, SC, USA	PhD	Aug/06	Bioengineering
Ohio State University, OH, USA	Post-Doc	June/10	Biomedical Engineering
RIKEN, Japan	Post-Doc	March/ 14	Stem Cells, Biomaterials, Nanotechnology.

A. Personal Statement

The PI has the expertise, leadership, training, expertise and motivation necessary to successfully carry out the proposed research project. **One of the PI's career objectives** is to address the critical issue of post-ischemic cardiac fibrosis by applying novel biomaterials and tissue engineering based strategies. The PI is a bioengineer by way of training, and during her PhD years she worked extensively with biomaterials and hydrogels (e.g. Hyaluronic acid) for cardiovascular elastin regeneration. The PI's first post-doc at Ohio State exposed her to a wider clinical environment (OSU Ross Heart Hospital) where she worked with an interdisciplinary team of CT-surgeons and biomedical engineers trying to elucidate the mechanisms modulating saphenous vein graft disease after CABG. After her post-doc at Ohio State, she received a prestigious fellowship to work in the area of stem cells and tissue engineering in RIKEN, Japan. At UTEP (current institution) the PI is collaborating with Dr. Thomas Boland, who is a pioneer in bio printing. The PI has also recently started collaborating with Dr. Pamela Lucchesi (OSU Nationwide Children's hospital; mentor), who is an expert in translational heart research and transplants. Using her own skills, prior training and collaborative strengths, the PI proposes to develop tissue engineered therapies for replacing injured or dead myocardial tissue.

The PI's publications most relevant to this proposal are:

- Joddar B., Ramamurthi A. Elastogenic effects of exogenous hyaluronan oligosaccharides on vascular smooth muscle cells. Biomaterials 27 (33), 5698-5707, 2006.
- Joddar B., Firstenberg M.S., Reen R.K., Gooch K.J. Arterial levels of oxygen stimulate intimal hyperplasia in human saphenous veins via a ROS-and NOS-dependent mechanism. PloS one 10 (3), e0120301, 2015.
- Joddar B., Chieko Nishioka, Eiki Takahashi, Yoshihiro Ito. Chemically fixed autologous feeder cell-derived niche for human induced pluripotent stem cell culture. Journal of Materials Chemistry B 3 (11), 2301-2307, 2015.
- Joddar B., Kitajima T., and Ito Y. The effects of covalently immobilized hyaluronic acid substrates on the adhesion, expansion, and differentiation of embryonic stem cells for in vitro tissue engineering. Biomaterials 32 (33), 8404-8415, 2011.

Developmental Objectives and Plans

The PI commits 50% effort (6 person months for 3-years) for the entire duration of the project. This will allow the PI to focus on the project and track its progress. Specifically, in this project the PI proposes to bioprint cells within hydrogel sheets to create various stacking configurations of cells that are involved during myocardial development, to elucidate the exact cell types and configurations involved during these processes. Many of the mechanisms that control myocardial development should also be highly involved in myocardial regeneration. To achieve this aim, the first step of this project will be to obtain vascular endothelial cells, smooth muscle cells and cardio myocytes, which will be differentiated from human induced pluripotent stem

cells (iPSC). Using human iPSCs will enable us to devise tissue engineering therapies that are applicable to humans. The PI has expertise in culturing and differentiating human iPSC's. With help from Dr. Boland, cells will be bioprinted within gel structures. Dr. Lucchesi (mentor) will train the PI on performing LAD ligation in rats and monitoring the rats using noninvasive techniques after myocardial infarction. Dr. Lucchesi is excited at the prospect of mentoring the PI, and she hopes to have joint publications with the PI allowing their mutual growth. Dr. Lucchesi's mentorship will continue beyond this project and will be focused on guiding the PI in becoming a world leader in using human iPSCs to mimic tissue-on-a-dish to explore developmental pathways during disease in vitro. The data obtained in the proposed work will support future NIH SC1, R21 and RO1 proposals, allowing a transition from in vitro to in vivo studies. The projected test system using bioprinting has universal applications including cardiac constructs, neural patterns, bone like constructs, pancreatic cell clusters. Therefore the PI has additional interest in using the bioprinted gels for stem cell based therapies in a wide range of tissue repair and regeneration, particularly for tissue repairs for which specialized cells cannot be reproduced and for which stem cells are promising, such as in spinal cord and brain injuries. The PI has maintained a sound publication record so far and hopes to advance it further with NIH support, in order to secure a successful passage through her tenure process at UTEP.

Timeline

The project will be broken into several phases and research tasks will be performed in different time periods. The total grant period is 3 years (36 months). Each year is divided into 4 quadrants (Q), 1 Q~3 months. Table 1 summarizes these phases/ tasks and associated schedules.

Phase and task	**Year 1**				**Year 2**				**Year 3**			
	Q1	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**	**Q1**	**Q2**	**Q3**	**Q4**
Aim 1												
Aim 2												
Aim 3												
4. Assess results and modify AIMS as needed												
5. Publication timeframe (estimated at 2/ year)												
6. Application for external funding (other than SCORE)												

Involvement of Students from Underrepresented Groups

- Using funds from her start-up package, the PI will add a PhD student, Beu Primavera Oropeza, a RISE student who has been working in her lab since spring 2015. This individual will also work on the proposed project from fall 2015.
- The PI also co-advises other RISE students such as Luis Solis, PhD candidate in BME program who is trying to cluster β-cells on biomaterial scaffolds for pancreatic islet formation and insulin secretion.

B. Positions and Honors

1. **Positions/Employment**

Since Nov 20, 2014: Assistant Professor of Mechanical/ Biomedical Engineering at the University of Texas at El Paso (UTEP), USA.

2. **Selected Awards/ Honors**

2010 Foreign Post-Doctoral Researcher Fellowship at RIKEN, JAPAN

2009 David & Lindsay Morgenthaler Endowed Fellowship (declined) at the Cleveland Clinic Foundation, Cleveland, OH, USA.
2008 Distinguished Post-Doctoral Fellow Award at the Dorothy.M.Davis Heart and Lung Research Institute of Ohio State University, Columbus, OH, USA
2003 Graduate Research Fellowship at Clemson University Bioengineering Department, USA

3. **Professional Memberships and other affiliations**

PEER REVIEW

- American Heart association: Bioengineering study section for grants (since 2015)

AFFILIATIONS

- The Tissue Engineering and Regenerative Medicine International Society (TERMIS) (Member)
- The International Society for Stem Cell Research (ISSCR) (Member)
- The American Heart Association (AHA) (Member)
- The Biomedical Engineering Society (BMES), the Whitaker Foundation (Member)
- Japanese Society of Regenerative Medicine (Member)

PROFESSIONAL SERVICE: Ad hoc REVIEWER

- Scientific Reports (Nature)
- Biomaterials
- Acta Biomaterialia
- Tissue engineering
- Tissue Engineering and Regenerative Medicine
- International Journal of Nanomedicine
- Annals of Biomedical Engineering
- Atherosclerosis, Thrombosis and Vascular Biology (ATVB-AHA)
- Journal of Pharmacy and Pharmacology

EDITOR

- Managing Editor, Frontiers of Bioscience.
- Member of the Editorial Board of Scientific Reports (Nature Publishing): Stem Cells and Development

C. Contribution to Science

Biomaterials and Tissue Engineering: As part of my doctoral studies at Clemson, I focused my research on the use of biomaterials and scaffolds for reconstructing elastin, which is an essential ECM tissue component. Elastin is a natural tissue component that provides 'elasticity' and binds tissues together like glue, preventing disease invasion and making tissues resistant to enzymatic degradation in the body. Elastin degrades from tissues with age disease. Once it is lost or degraded, it is challenging to regrow. As a result tissues lose elasticity and become more prone to disease. I used biomaterial scaffolds as frames for the regeneration of vascular elastin, which has potential applications in replacing damaged veins or arteries. The most important conclusion from these studies was that scaffolds based on hyaluronan (HA), a glycosaminoglycan, may be useful in regenerating vascular elastin, although these effects appear to be dictated by HA's fragment size and/or dose. Specifically, HA oligomers (shorter fragments of HA) were pro-elastogenic compared to native long chain HA. This finding was novel and resulted in four peer-reviewed publications as well as the filing of a U.S. patent.

- Ibrahim S., Joddar B., Craps M. and Ramamurthi A. A surface-tethered model to assess size-specific effects of hyaluronan (HA) on endothelial cells. Biomaterials 28 (5), 825-835, 2007.
- Joddar B., Ibrahim S, Ramamurthi A. Impact of delivery mode of hyaluronan oligomers on elastogenic responses of adult vascular smooth muscle cells. Biomaterials 28 (27), 3918-3927, 2007.
- Joddar B., Ramamurthi A. Fragment size- and dose-specific effects of hyaluronan on matrix synthesis by vascular smooth muscle cells. Biomaterials 27 (15), 2994-3004, 2006.
- Ramamurthi A., Joddar B., Kothapalli C. Elastogenic cues and methods for using the same. US Patent NO. 8,529,951.

Cardiovascular Biology (Saphenous Vein graft disease): By reason of my achievements as a Ph.D. student, in September 2006 I was offered a post-doctoral position at Ohio State University in Columbus, Ohio. At OSU I collaborated with a group of cardiothoracic surgeons to do research in vascular biology and the use of

therapeutic interventions to prevent or treat blood vessel remodeling in vivo. Specifically, my research focused on vascular remodeling, which occurs when veins are grafted into arterial circulation after coronary artery bypass graft surgery in patients. As an indication of the importance of this research to the medical community, this work was accepted for presentation at the American Heart Association annual scientific meeting in 2008, following which an abstract was published in Circulation. I also received the Distinguished Post-Doctoral Fellow Award at OSU's Davis Heart and Lung Research Institute. In addition, this research has been the basis of a number of articles in peer-reviewed and refereed journals as well as presentations and articles for international conferences in the field of Biomaterials and Biomedical Engineering.

- Joddar B., Reen R.K, Firstenberg Michael.F, Varadharaj Saradhadevi, McCord Joe.M, Zweier Jay.L, Gooch Keith.J. Protandim inhibits the development of intimal hyperplasia in human saphenous veins ex vivo via a catalase dependant pathway. Free Radical Biology and Medicine 50 (6), 700-709, 2011.
- Joddar B., Shaffer RJG, Reen RK, Gooch KJ. Arterial pO2 stimulates intimal hyperplasia and serum stimulates inward eutrophic remodeling in porcine saphenous veins cultured ex vivo. Biomechanics and modeling in mechanobiology 10 (2), 161-175, 2011.
- Joddar B., Reen.R.K, Firstenberg.M.F, Gooch.K.J. Role of oxygen tension and oxidative stress in modulating the development of neointimal hyperplasia in human saphenous veins. Circulation 118 (18 Supplement), S_1017, 2008.

Stem cell based approaches for tissue engineering: In 2010 I received a prestigious 'Foreign Post-Doctoral Fellowship' (FPR) from the renowned research institute RIKEN in Japan to work with stem cells and regenerative medicine. While working in Tokyo, I collaborated with many scientists in (RIKEN Brain Science Institute) and outside RIKEN (USA, Germany, UK, and Turkey). One of the most productive collaborations was with the Center for Induced Pluripotent stem cells research and application (CiRA) in Kyoto, Japan. At this center, which was founded by Shinya Yamanaka (Nobel Prize 2012, Physiology and Medicine), I received training in working with induced pluripotent stem cells (iPSC), which may be a game changer for the field of regenerative medicine. They can be differentiated into any kind of body component cells, making them an attractive tool to regenerate organs or tissues lost due to injury or disease in vivo. Integrating the ability to culture human iPSCs and with bioprinting of cells in hydrogels (collaboration), I would like to mimic healthy or diseased tissue-on-a-dish allowing unique avenues for in vitro investigation into complex 3D tissues, which is not possible in vivo.

- Zhou Y., Joddar B., et al. (Accepted: in press). Moderate membrane fluidity of feeder cells is sufficient for mouse-induced pluripotent stem cell culture. Scientific Reports, Nature 2015.
- Joddar B., Takashi Hoshiba, Guoping Chen, Yoshihiro Ito. Stem cell culture using cell-derived substrates. Biomaterials Science 2014.
- Joddar B., Adam T. Guy, Hiroyuki Kamiguchi, Yoshihiro Ito. Biomaterials 2013. Spatial gradients of chemotropic factors from immobilized patterns to guide axonal growth and regeneration.
- Joddar B., Aydin Albayrak, Jeonghwa Kang, Mizuki Nishihara, Hiroshi Abe and Yoshihiro Ito. Acta Biomaterialia 2013. Sustained release of siRNA from dopamine coated stainless steel surfaces for siRNA-mediated gene silencing.

Updated List of Published Work in Google Scholar (total 20):
http://scholar.google.com/citations?hl=en&user=AQo7YOEAAAAJ

D. Research Support (Current)

Active

- University of Texas at El Paso Start Up Grant (Goals: Use gradients of varying growth factor concentration and substrate stiffness to differentiate iPS cells into neurons, and cardiovascular cell types)
  Role: PI, Period: Jan 2015-Jan 2018
- UTEP COE Interdisciplinary Research funds (~6000$) (Goals: To use bioprinting as a tool for transfection of Yamanaka factors into adult fibroblasts to make iPS cells).
  Role: PI, Co-PI: Thomas Boland, PhD. Period: May 15- Aug 31, 2015.