## BIOGRAPHICAL SKETCH

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NAME: Parekkadan, Biju

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

POSITION TITLE: Associate Professor, Biomedical Engineering

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

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Rutgers University (Piscataway, NJ) | BS | 1999-2003 | Biomedical Engineering |
| Harvard-MIT Division of Health Sciences and Technology (Cambridge, MA) | PhD | 2003-2008 | Chemical and Medical Engineering |
| Harvard-MIT Division of Health Sciences and Technology (Cambridge, MA) | MD Studies | 2005-2008 | Medicine |
| Massachusetts General Hospital, Harvard Medical School (Boston, MA) | Postdoctoral | 2008 | Cell Engineering |

### A. Personal Statement

My lab has core strengths in cell and tissue engineering for regenerative medicine applications, particularly in combining bioengineering technologies with cell therapy. We have recently incorporated new gene constructs into MSCs including suicide switches, biosensors, and therapeutic growth factors to build off this cell platform for more targeted biological studies of MSCs *in vivo* as well as therapeutic applications. This proposal leverages the unique strengths of my lab in cell engineering with organ engineering in Dr. Uygun's lab. With further input from a key leader in the field of transplant tolerance, Dr. Curt Cetrulo, we are very excited to rigorously test this concept of cell biosensors for transplantation with the ability to translate this work to the clinic in the years to come. Along with contributions to science below in engineered biosensors, the following are supportive publications directly towards this project with the co-PIs:

Chin LY, Carroll C, Raigani S, Detelich DM, Tessier SN, Wojtkiewicz GR, Schmidt SP, Weissleder R, Yeh H, Uygun K, Parekkadan B. Ex vivo perfusion-based engraftment of genetically engineered cell sensors into transplantable organs. PLoS One. 2019 Dec 2;14(12):e0225222.

Corentin B. Taveau, MD; Alexandre G. Lellouch, MD, MSc, Ling-Yee Chin, Olivia Mamane, BSc, Philipp Tratnig-Frankl, MD,Laurent A. Lantieri, MD, Mark A. Randolph, MASc, Korkut Uygun, PhD, Curtis L. Cetrulo Jr, MD, FAACS, FAAP, Biju Parekkadan, PhD". In Vivo Activity of Genetically-Modified Cells Pre-Seeded in Vascularized Composite Allografts" *PRS Global Open (under review)*

I am hopeful to leverage my translational experiences to help translate this program. I was the scientific co-founder of Sentien Biotechnologies, Inc., a developer of extracorporeal cell bioreactors for the treatment of ICU patients with critical injuries. This venture-backed company has independently raised >$25M, with independent management, to translate this treatment for patients with severe inflammatory response syndrome in ongoing Phase Ib/IIa human trials (ClinicalTrials.gov Identifier: NCT03015623). I also serve industry as a founding member of CellOne Partners, LLC, a consulting group to the cell and gene therapy industry to strive towards commercialization of these innovative products. My academic lab has continued to expand on other industry-wide challenges in cell therapy, such as the expansion and genetic engineering of new human cell therapies.

**B. Positions and Honors**

**Professional Experience**

2002-2003 Teaching Assistant, Biomedical Engineering, Rutgers University
2004-2008 Research Assistant, Medical Engineering, Harvard-MIT Division of HST
2006-2007 Clinical Clerkship, Department of Medicine, Mount Auburn Hospital
2007-2008 Clinical Observer, Department of Medicine, All-India Institutes of Medicine, Delhi, India
2008-2011 Instructor, Department of Surgery, Massachusetts General Hospital, Harvard Medical School
2009- Affiliated Faculty, Broad Institute
2010- Assistant. Bioengineer, Department of Surgery, Massachusetts General Hospital
2012- Staff Scientist, Shriners Hospitals for Children
2012- Affiliated Faculty, Harvard Stem Cell Institute
2012-2016 Assistant Prof, Surgery (Bioengineering), Harvard Medical School
2017- Associate Prof, Department of Biomedical Engineering/Medicine, Rutgers Univ.

**Other Selected Experience and Professional Memberships**

- Journal Reviewer, *Stem Cells (2008-), Blood (2009-), Tissue Engineering (2009), PLoS One (2010), Journal of Clinical Immunology (2011-), Stem Cells Translational Medicine (2011-), European Journal of Immunology (2012-), Nature Materials (2015-), PNAS (2016-), Nature Biomedical Engineering (2016-), Science Advances (2019-), Nature Regenerative Medicine (2020-), Analytical Chemistry (2020-)*
- Co-Founder, Director, Sentien Biotechnologies, Inc. (2008-); Founding Member, CellONE Partners (2019-)
- Co-Editor, Methods in Stem Cell Bioengineering. Artech House (2009).
- Grant reviewer, Dutch Digestive Disease Foundation (2010), Broad Medical Research Foundation (2010), Medical Research Council of UK (2012), NIH Small Business Innovation Research Awards (2012), Portuguese Foundation for Science and Technology (2012), AAAS Regenerative Medicine Fund (2015-), NIH Diabetes Complications Consortium (DiaComp) (2017)
- Non-Profit Advisory Committees: Associate Scientific Advisor, *Science Translational Medicine (*2014-2016), Member of Executive Council of Mentors, Harvard Medical School (2015- )

**Awards and Honors**

2002 Intramural Research Training Award, NIH/Whitaker Foundation
2003 *Summa Cum Laude*, Rutgers University
2003 James J. Slade Scholar of Engineering, Rutgers University
2003-2006 Graduate Research Fellowship, National Science Foundation
2007 Graduate Research Award, Biomedical Engineering Society
2007 Ford Foundation Fellowship, National Academies of Science, Honorable Mention
2008 Invited Graduation Speaker, Harvard-MIT Division of HST
2008 Presidential Award, American Association for the Study of Liver Disease
2008 Featured Research Article Highlight, Stem Cells Journal
2008-2010 Postdoctoral Research Fellowship, Shriners Hospitals for Children
2009 Keynote Speaker, Biomedical Engineering Senior Design Conference, Rutgers University
2010 Massachusetts General Hospital Scientific Advisory Committee Research Award
2010 Invited Speaker, Keystone Symposia, Advances in Biopharmaceuticals
2010-2015 Mentored Scientist Research Award (K01), National Institutes of Health
2010 Highlight in Cell Biology 2010 Press Book, American Society of Cell Biology 50th Conference
2011 Presidential Early Career Award for Scientists and Engineers (PECASE), National Institutes of Health, Office of the White House
2013 Young Mentor of the Year Award, Harvard Medical School
2015 Top Innovators Under 35, MIT Technology Review, Finalist
2016 Translational Pioneer Award, Cell & Gene Therapy Insights, Finalist
2017 TEDx Invited Speaker
2018 World Cell Therapy Summit, Invited Speaker
2022 Northeast Bioengineering Annual Conference, Keynote Speaker

**C. Contributions to Science**

***1. Engineered Cell Biosensors.*** A major thrust in the lab is to incorporate advanced genetic constructs into transplantable cells to study their fate and therapeutic potential *in vivo.* This includes the use of suicide gene

switches to selectively eliminate fibroblasts *in vivo* as well as overexpression constructs that release cytokines and growth factors for local or systemic therapy. *O*ur lab first incorporated secreted bioluminescent biomarkers into gene vectors and fibroblasts to sensitively track their distribution after transplantation. New genetic constructs driven by transcription factor controls are being explored to sense the *in vivo* environment after transplantation and understand immune clearance of cell and gene therapies.

1. Shen K, Luk S, Elman JS, Murray R, Parekkadan B. Suicide gene-engineered stromal cells reveal a dynamic regulation of cancer metastasis. **Nature Scientific Reports** 2016 Feb 19;6:21239 PMID:26893143 PMCID:PMC4759812
2. Lee J, Heckl D, Parekkadan B. Multiple genetically engineered humanized microenvironments in a single mouse. **Biomater Res.** 2016 Jun 28;20:19. PMID:27354920 PMCID: PMC4924259
3. Singleton A, Khong D, Chin LY, Mukundan S, Li M, Parekkadan B. An Engineered Reporter System to Monitor and Modulate Immune Clearance of Stem Cell Transplants. **Cytotherapy** 2019 Dec (12):1537-1545 PMID:28917628 PMCID:PMC5723229
4. Chin LY, Carroll C, Raigani S, Detelich DM, Tessier SN, Wojtkiewicz GR, Schmidt SP, Weissleder R, Yeh H, Uygun K, Parekkadan B. Ex vivo perfusion-based engraftment of genetically engineered cell sensors into transplantable organs. **PLoS One.** 2019 Dec 2;14(12):e0225222. PMID: 31790444

***2. Cell and Gene Transplantation and Pharmacology.*** This thrust is built around cell transplantation and immunotherapy including: (1) biomanufacturing cell and gene therapies; (2) monitoring and modeling the pharmacology of cells *in vivo*; (3) identifying new therapeutic cell populations and testing in disease models; We continue to develop a multi-pronged approach to understanding the limits in delivering cell and gene therapy to the human body and applying engineering tools to enable new delivery methods.

1. Elman JS, Murray R, Wang F, Shen K, Gao S, Conway KE, Yarmush ML, Tannous B, Weissleder R, Parekkadan B. Pharmacokinetics of natural and engineered secreted factors delivered by mesenchymal stromal cells. **PLoS One** 2014 Feb 21;9(2):e89882.
2. Fletcher, AL, Elman J, Astarita J, Murray R, Saeidi N, D'Rozario J, Knoblich K, Brown, FD, Schildberg, F, Nieves, JM, Heng T, Boyd RL, Turley SJ, Parekkadan B. Lymph node fibroblastic reticular cell transplants show robust therapeutic efficacy in models of high-mortality murine sepsis. **Science Translational Medicine**. 2014 Aug 13;6(249):249ra109. PMID:25122637 PMCID: PMC4415170
3. Aijaz A, Li M, Khong D, Fenton OS, Russotti G, Olabisi RM, Libutti S, Tischfield J, Maus MV, Deans R, Barcia R, Anderson DG, Ritz J, Preti R, Parekkadan B. Biomanufacturing of clinically advanced cell therapies. (invited review) **Nature Biomedical Engineering.** 2018 June; 2: 362–376. PMID: 31011198
4. Burr A, Erickson P, Bento R, Shama K, Roth C, Parekkadan B. Allometric-like scaling of AAV gene therapy for systemic protein delivery. **Mol Ther Methods Clin Dev.** 2022 Oct 21;27:368-379. doi: 10.1016/j.omtm.2022.10.011. eCollection 2022 Dec 8. PMID: 36381306

***3. Cellular Macro- and Microfluidic Bioreactors.*** Upon identifying a pharmacological limit to cell therapy by conventional intravenous transplantation, our work evolved into the development of translational bioreactor technology as an alternative form of cell administration. Bioreactors seeded with MSCs were used to concentrate the immunomodulatory effect of MSC secreted factors that could be scaled to human use. I am the scientific co-founder of Sentien Biotechnologies, Inc., a developer of extracorporeal cell bioreactors for the treatment of ICU patients with critical injuries. The venture-backed company is independently managed and is testing its bioreactor product as a continuous treatment for critically-ill acute kidney and liver injury patients in ongoing Phase I human trials. My academic lab has continued to expand on the concept of cellular bioreactors by combining MSCs with other tissue cells as bioartificial organs as well as exploring the ability to condition blood cells *ex vivo* for non-critically ill patients.

1. Li M, Chin LY, Shukor S, Parekkadan B. Closed Loop Bioreactor System for the Ex Vivo Expansion of Human T-Cells. **Cytotherapy 2019 Jan;21(1):76-82.** PMID: 30497956 PMCID: PMC6333522
2. Allen A, Vaninov N, Li M, Nguyen S, Singh M, Igo P, Tilles AW, O'Rourke B, Miller BLK, Parekkadan B, Barcia RN. Mesenchymal Stromal Cell Bioreactor for Ex Vivo Reprogramming of Human Immune Cells. **Nature Sci Rep.** 2020 Jun 23;10(1):10142. PMID: 32576889
3. Swaminathan M, Kopyt N, Atta MG, Radhakrishan J, Umanath K, Nguyen S, , O'Rourke B, Allen A, Vaninov N, Tilles AW, LaPointe E, Blair A, Gemmiti C, Miller BLK, Parekkadan B, Barcia RN.

Pharmacological effects of ex vivo mesenchymal stem cell immunotherapy in patients with acute kidney injury and underlying systemic inflammation **Stem Cells Transl Med**. 2021 Dec;10(12):1588-1601

4. **Erickson P**, Houwayek T, Burr A, Teryek M, Parekkadan B. A continuous flow cell culture system for precision cell stimulation and time-resolved profiling of cell secretion. **Anal Biochem**. 2021; 625. PMCID: PMC8154734.

***4. Tissue Engineering Microenvironment Models of Stem/Cancer Niches***. Current advancements on this frontier in my lab is focused on generation of high throughput in vitro TB micro-granulomas (μGranulomas) using spheroid formation methods for development of new strategies for disease modelling and therapeutic discovery. Previously, my group has created engineered human tissue systems for modeling healthy and cancerous stem cell microenvironments using biomaterials. I have led an effort to create a synthetic PEG scaffold with the precise structure of decellularized bone marrow. When implanted, this scaffold could attract and capture hematopoietic stem/cancer cells (*PNAS, 2013; Cancer Res 2014)*. We also developed a microengineered tumor-stromal assay (μTSA) to recreate tumor tissue for in vitro validation testing and drug screening. The model controls the spatial organization of multiple cell types with precision using a cell microprinting technique.

1. Lee J, Wang J, Li M, Milwid JM, Dunham J, Vinegoni C, Gorbatov R, Iwamoto Y, Wang F, Shen K, Hatfield K, Enger M, Shafiee S, McCormack E, Ebert B, Weissleder R, Yarmush ML, Parekkadan B. Implantable Microenvironments to Attract Hematopoietic Stem/Cancer Cells. **Proc Natl Acad Sci U S A.** 2012 Nov 27;109(48):19638-43. (Comment in **Nat Methods.** 2013: Stem cells: Blood matters.) PMID: 2315054 PMCID: PMC3511730
2. Bersani F, Lee J, Yu M, Morris R, Desai R, Ramaswamy S, Toner M, Haber DA, Parekkadan B. Bioengineered implantable scaffolds as a tool to study stromal-derived factors in metastatic cancer models. **Cancer Res** 2014 Dec 15;74(24):7229-38. PMID:25339351 PMCID: PMC4267901
3. Shen K, Elman JS, Hicks DF, Bohr S, Luk S, Murray R, Iwamoto Y, Pena K, Milwid JM, Wang F, Seker E, Yarmush ML, Toner M, Sgroi D, Parekkadan B. A Micropatterned Tumor Stromal Assay for Identifying Drugs Targeting Cancer-Stroma Interactions. **Nature Communications** 2014 Dec 9;5:5662. PMID: 25489927 PMCID: PMC4261930
4. Bhatt R, Ravi D, Evens AM, Parekkadan B. Scaffold-mediated switching of lymphoma metabolism in culture. **Cancer Metab.** 2022 Oct 12;10(1):15. doi: 10.1186/s40170-022-00291-y.PMID: 36224623

***5. Genomic and Proteomic Screening Technologies.*** These projects develop functional genomic platforms to resolve complex cell-cell communication pathways and discover new therapeutics from human and microbial cells. We are the first to develop a way to computational approach to cell secretomes in order to find “needles in a haystack” with a genomic enrichment step prior to screening. We have now built a powerful technology for multiplex cloning of protein libraries for discovery of new mediators that are found in novel genomes using antibody-like DNA probes. These screening approaches are designed to be applied to virtually any cell type to dissect and identify exotic/redundant factors that have yet to be explored biologically.

1. Milwid JM, Elman JS, Li M, Shen K, Manrai A, Gabow A, Jiao Y, Fletcher AJ, Lee J, Cima MJ, Yarmush ML, Parekkadan B. Enriched protein screening of human bone marrow mesenchymal stromal cell secretions reveals MFAP5 and PENK as novel IL-10 modulators. **Mol Therapy** 2014 May;22(5):999-1007. PMID:24496384 PMCID: PMC4017089
2. Tosi L, Yang Y, Sridhara V, Guan D, Segata N, Larmen HB, Parekkadan B. Engineered DNA Capture Probes for Massively Multiplexed Cloning of Kilobase-Sized Genome Regions. **Nature Biomedical Engineering** 2017;1. pii: 0092. PMID:29152409 PMCID: PMC5687285
3. Liu J, Shukor S, Li S, Tamayo A, Tosi L, Larman B, Nanda V, Olson WK, Parekkadan B. Computational Simulation of Adapter Length-Dependent LASSO Probe Capture Efficiency. **Biomolecules**. 2019 May 22;9(5):199.PMID: 31121947
4. Ravi D, Beheshti A, Burgess K, Kritharis A, Chen Y, Evens AM, Parekkadan B. An Analysis of Transcriptomic Burden Identifies Biological Progression Roadmaps for Hematological Malignancies and Solid Tumors. **Biomedicines.** 2022 Oct 27;10(11):2720. doi: 10.3390/biomedicines10112720.PMID: 36359241

**Complete List of Published Work in my Bibliography (>60 publications > 7,000 citations)**:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Parekkadan b

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

***Ongoing Research Support***

"Postdoctoral Training For Translating Research In Regenerative Medicine" (Co-PI)
NIH/NIBIB – 5T32EB005583-18 06/01/20-05/31/23
I am recently charged to serve as a Co-PI for an NIBIB T32 postdoctoral training program, "Training Without Borders: Translational Research in Regenerative Medicine" (2012-2017), has focused on two innovative features: (1) the concept of a geographically dispersed training faculty to harness a unique team of mentors; and (2) a combination of conventional academic training (state-of-the-art science, proposal writing, responsible conduct of research) together with training in translation and commercialization. This has resulted in a geographically dispersed "community of learning".

*"Artificial, Humanized Stem Cell Niches"* (PI)
NIH/NIBIB - R01EB012521 09/15/2018-05/31/2023 NCE
The goal of this renewal is to create disease-mimicking bone marrow environments for the study of bone marrow cancer stem cells.

Genetic-engineered control of the immunogeneic state of vascular composite allografts during preservation (PI)
NIH/NIBIB - R01EB028782 07/01/2021-03/31/2025
The objective of this application is to develop a functional preservation platform that enables creating engineered VCA grafts by exogenous administration of genetically-modified cells, their preservation in a clinically practicable protocol, and testing the efficacy in reducing immunogenicity in rodent models of rejection and tolerance induction.

High subzero preservation of liver for transplantation. (Co-I)
5R01DK114506-05 Uygun, Yarmush, Toner (Contact) 07/17/17 – 12/31/25
NIH/NIDDK
We propose (i) to control ice formation in liver, which our prior studies demonstrated to be a key barrier; (ii) to develop targeted approaches to improve preservation of endothelium, which are at the interface of tissue and ice and are the first point of injury, and (iii) to develop a choreographed metabolic protocol to maximize ATP recovery and improve viability of the grafts for transplant.

***Recently Completed Research Support (last 3 years)***

*"A Functional genomics platform with integrated library cloning and molecular display",* (PI)
NIH/NIGMS - R01GM127353 08/01/2018-07/31/2022
This proposal seeks to develop technologies for high-throughput construction and functional screening of complex protein libraries as a resource for the community.

"Cell Growth Capsules for High-Speed Bioreactor Culture" (PI)
Advanced Regenerative Manufacturing Institute 06/01/2019 – 12/31/2021
The aim of this project is to develop a customized, bioactive, and degradable microcapsule-based cell culture system that overcomes barriers to adherent cell production in stirred tank bioreactor conditions.

*"Engineered cells for Sensitive In Vivo Cell Tracking Using Secreted Bioluminescent Probes"* (PI)
Shriners Hospitals for Children SBI85120 01/01/16-12/31/20
This application develops engineered MSCs as a monitoring strategy that is sensitive enough to detect the fate of an intravenous cell transplant as it distributes across the body *in vivo*.

*"Theranostic approach to transplant rejection using engineered cell biosensors"* (PI)
NIH/NIAID – R21AI134116-01A1 05/14/18-04/30/21 NCE
This application explores a genetically engineered cell biosensor that is pre- engrafted into a transplant in order to report and respond to early warning signals of transplant failure.