BIOGRAPHICAL SKETCH

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NAME: Vijay K. Yechoor

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

POSITION TITLE: Professor

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
All India Institute of Medical Sciences New Delhi, India	M.B.B.S.	1985-1991	Medicine
Michael Reese Medical Center University of Illinois, Chicago, IL	Internship	1992-1993	Internal Medicine
Baylor College of Medicine Houston, TX	Residency	1993-1995	Internal Medicine
Joslin Diabetes Center & Beth Israel Deaconess Medical center, Harvard Medical School Boston, MA	Fellowship	1995-1996 & 2000-2002	Endocrinology, Diabetes and Metabolism
Baylor College of Medicine Houston, TX	Post-Doc	2002-2003	Cell Biology
Center for Molecular Medicine, Baylor College of Medicine, Houston, TX	Fellowship	2003-2004	Molecular Medicine
Board Certification in Internal Medicine by American Board of Internal Medicine	Certification	1996	Internal Medicine
Board Certification in Endocrinology, Diabetes & Metabolism by American Board of Medical Specialties	Certification	2002	Endocrinology, Diabetes and Metabolism

A. Personal Statement

I am a physician-scientist, who has been seeing patients with endocrine disorders and diabetes while engaging in diabetes and metabolism related research for the last 15 years. My work was involved various aspects of diabetes including insulin resistance, islet biology, islet neogenesis, adipogenesis, mitochondrial metabolism and circadian biology as relates to metabolic disease. In my lab, we address various questions

related to islet neogenesis, β-cell compensation and secretory function, circadian control of islet function, mitochondrial control of metabolic processes using various knockout and transgenic mouse models, along with ex vivo and in vitro models to dissect the regulatory molecular mechanisms underlying islet dysfunction in diabetes. We have developed a novel technique of in vivo islet neogenesis coupled with engineering these neo-islets with expression of PD-L1, an inhibitor of co-stimulation to achieve protection of these neo-islets from autoimmune destruction rendering these treated diabetic NOD mice cured of diabetes.
The broad goal of my laboratory is discovering regulatory mechanisms that control β-cell proliferation, function and development and their application to prevention and therapy of diabetes. We are working on understanding the mechanisms underlying regulation of functional β-cell mass in a VA ORD funded project, specifically looking at the mechano-sensing hippo-Tead1 pathway in β-cells. My lab has been working over the last few years on circadian control of islet function. In these NIDDK-R01 and ADA funded projects we have demonstrated that disruption of the molecular clock Bmal1-null islets develops impaired stimulus-secretion coupling and β-cell failure. We demonstrated for the first time that Bmal1 and the β-cell clock regulate β-cell mitochondrial OXPHOS and oxidative stress via regulation of Nrf2.

I moved 2 years ago to the University of Pittsburgh as the Director of the Diabetes and Beta Cell Biology Center and in this capacity, I am building a metabolism oriented integrated physiology program that seeks to decipher the mechanistic basis of diabetes, obesity and metabolic disorders, with a goal to prevent, treat and cure diabetes. In my capacity as a Physician-Scientist who actively takes care of patients with diabetes, I am expanding a collaborative Diabetes Research program with a strong translational component. We have started a program to generate iPS cell-derived islet/beta cells that would physiologically respond to glucose to secrete insulin that are engineered to resist autoimmune destruction. The longer-term goal is to translate these models into patient-specific therapy to cure diabetes, both Type1 and Type 2.

B. Positions and Honors

Positions

1991-92	Internship in Medicine, All India Institute of Medical Sciences, New Delhi, India
1992-93	Internship in Internal Medicine, Michael Reese Medical Center, UIC, Chicago, IL
1993-95	Residency in Internal Medicine, Baylor College of Medicine, Houston, TX
1995-96	Fellowship in Endocrinology, Diabetes & Metabolism, Harvard Medical School, Boston, MA
1997-99	Internal Medicine practice in Medically Underserved Area, El Paso, TX
2000-02	Fellowship in Endocrinology, Diabetes & Metabolism, Joslin Diabetes Center, Harvard Medical School, Boston, MA
2002-03	PostDoc in Cell Biology, Baylor college of Medicine, Houston, TX
2003-04	Fellow in Molecular Medicine, Center for Molecular Medicine, Baylor College of Medicine,
2004-05	Instructor, Division of Diabetes, Endocrinology & Metabolism, Department of Medicine, Baylor College of Medicine, Houston, TX
2005-08	Assistant Professor (non-tenure track), Division of Diabetes, Endocrinology & Metabolism, Department of Medicine, Baylor College of Medicine, Houston, TX
2008-14	Assistant Professor (tenure track), Division of Diabetes, Endocrinology & Metabolism, Department of Medicine and Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX
2015-17	Associate Professor (tenured), Division of Diabetes, Endocrinology & Metabolism, Department of Medicine and Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX
2017-	Staff Endocrinologist, VA Medical Center, VAPHS, Pittsburgh, PA.
2017-	Professor of Medicine and Director of the Diabetes and Beta Cell Biology Center, Division of Diabetes, Endocrinology & Metabolism, Department of Medicine, University of Pittsburgh, Pittsburgh, PA

Other Experience and Professional Memberships

Member	American Diabetes Association
Member	Endocrine Society
2013-18	American Diabetes Association Research Grant Review Committee.

2013- Grant reviewer for Health and Medical Research Fund (HMRF), Hong Kong
2015 Grant Reviewer for Swiss National Science Foundation, Berne
2013 American Diabetes Association 73rd Scientific Sessions - abstract reviewer
2013 American Diabetes Association 73rd Scientific Sessions - Session Chair for “Phenotyping the Engineered Beta Cell”
2017-21 Standing Member, CADO study Section, NIH.

Honors

1. V. Ramalingaswami prize for the "BEST INTERN" at the comprehensive health services project at Ballabgarh in 1990 during the compulsory rotating internship (All India Institute of Medical Sciences, New Delhi, India)
2. Sorel Catherine Freyman prize for the "BEST UNDERGRADUATE IN PEDIATRICS" in 1989 (All India Institute of Medical Sciences, New Delhi, India)
3. "BEST HOUSE OFFICER" during the first-year residency in Internal Medicine in 1991 at the All India Institute of Medical Sciences New Delhi, India.
4. Elected (by peers) to be “BEST INTERN” 1992-93 at Michael Reese Hospital and Medical Center, Chicago, IL
5. McIntosh award for 'OUTSTANDING RESIDENT' 1994-95 at Baylor College of Medicine, Houston, TX
6. FIRST in clinical research for "Tuberculous Meningitis in an urban teaching hospital" in 1995 research poster symposium at Baylor College of Medicine, Houston, TX
7. Young Investigator award for “Thymic Hyperplasia is a cause of an Anterior Mediastinal Mass in Patients of Thyroid Carcinoma at the annual meeting of the American Association for Clinical Endocrinologists, Chicago, May 2002
8. Awarded the Institutional National Research Service Award for research fellowship in Molecular Medicine at the Center for Molecular Medicine at Baylor College of Medicine, Houston, TX, June 2003
9. Ira Rosenthal award for 2004 for the best abstract in Genetics awarded by the Endocrine Society
10. Michael E. DeBakey, M.D., Excellence in Research Award, Baylor College of Medicine, 2009
11. Best Teacher Award – Division of Diabetes, Endocrinology, & Metabolism, Baylor College of Medicine

1) **C. Contributions to Science**

My early work as an Endocrine fellow focused on understanding insulin signaling in the context of the global transcriptome using diabetic and insulin receptor knockout models. These studies paved the way to understand the significant differences between transcriptional changes due to loss of insulin signaling and those stemming from hyperglycemia in diabetes. These two are usually inseparable but important to distinguish to full understand the molecular mechanisms if diabetes and glucotoxicity. Using the muscle specific insulin receptor knockout mice with or without insulin deficient diabetes induced by STZ that were untreated or treated with insulin, I was able to fully separate the transcriptional signatures of insulin signaling that is distinguishable from that from glucotoxicity.

   a) **Yechoor VK**, Patti ME, Saccone R, Kahn CR. Coordinated patterns of gene expression for substrate and energy metabolism in skeletal muscle of diabetic mice. Proceedings of the National Academy of Sciences of the United States of America 2002; 99(16):10587-10592. PMCID: PMC124982
   b) **Yechoor VK**, Patti ME, Ueki K, Laustsen PG, Saccone R, Rauniyar R, Kahn CR. Distinct pathways of insulin-regulated versus diabetes-regulated gene expression: an in vivo analysis in MIRKO mice. Proceedings of the National Academy of Sciences of the United States of America. 2004 Nov 23;101(47):16525-30. Epub 2004 Nov 16 PMCID: PMC534529

2) Currently there is no long-lasting cure for diabetes. I have addressed this problem using mouse models and demonstrated that a cure of insulin deficient diabetes is possible with the induction of islet neogenesis ectopically in the liver, using gene delivery of Neurogenin 3 - the islet-lineage defining factor. I demonstrated that the new β-cells arise not by transdifferentiation of hepatocytes but by transdetermination of hepatic oval cells. I was able to conclusively demonstrate that these newly induced β-cells attained

mature functions. In another series of experiments, we were able to demonstrate that we could coax these β-cells to evade autoimmune destruction by engineering them to over express PD-L1, an inhibitor of co-stimulation. In this report, we demonstrate that, without any peripheral immunosuppression, this approach leads to a lasting cure of autoimmune diabetes in mice.

a) **V. Yechoor**, V. Liu, A. Paul, J. Lee, E. Buras, K. Ozer, S. Samson, L. Chan. Gene Therapy with Neurogenin3 and Betacellulin Reverses Major Metabolic Problems in Insulin-deficient Diabetic Mice. Endocrinology 2009 Nov; 150(11):4863-73. Epub 2009 Oct 9. PMCID: PMC2775983
b) Li R, Lee J, Kim MS, Liu V, Moulik M, Li H, Yi Q, Xie A, Chen W, Yang L, Li Y, Tsai T, Oka K, Chan L, **Yechoor V**. PD-L1 driven Tolerance Protects Neurogenin3-induced Islet Neogenesis to Reverse Established Type 1 Diabetes in NOD Mice. Diabetes. 2015 Feb;64(2):529-40. Epub 2014 Oct 20. PMCID: PMC4303975
c) Li R, Buras E, Lee J, Liu R, Liu V, Espiritu C, Ozer K, Thompson B, Nally L, Yuan G, Oka K, Chang B, Samson S, **Yechoor V***, Chan L. Gene therapy with Neurogenin3, Betacellulin and SOCS-1 Reverses Diabetes in NOD Mice. Gene Ther. 2015 Nov;22(11):876-82. Epub 2015 Jul 14. PMCID: PMC4636470
***Co-**corresponding senior author.

3) My current work has also provided novel insight into the regulatory mechanisms that underlie the circadian control of β-cell function. In a series of papers, we demonstrated for the first time how the molecular clock regulates mitochondrial function by controlling uncoupling protein 2 and that diabetes results from the loss of the β-cell antioxidant response with circadian disruption. We demonstrated that the β-cell clock regulates the circadian expression of antioxidant genes, by direct transcriptional regulation of Nfe2l2 (Nrf2), the master antioxidant response gene. This seminal finding has since been shown by other groups to be operative in other tissues including the brain, in neurodegenerative disorders, an indication of the impact of this discovery.
   a) Lee J, Moulik M, Fang Z, Saha P, Zou F, Xu Y, Nelson DL, Ma K, Moore DD, **Yechoor VK**. "Bmal1 and β-Cell Clock Are Required for Adaptation to Circadian Disruption, and Their Loss of Function Leads to Oxidative Stress-Induced β-Cell Failure in Mice". Mol Cell Biol. 2013 Jun;33(11):2327-38. Epub 2013 Apr 1. PMCID: PMC3648066.
   b) Lee J, Kim M, Li R, Liu V, Fu L, Moore DD, Ma K, **Yechoor V**. Loss of Bmal1 leads to Uncoupling and Impaired Glucose-stimulated Insulin Secretion in β-cells. Islets 2011 Nov 1;3(6) (epub). PMCID: PMC3329519
   c) Chatterjee S, Yin H, Li W, Lee J, **Yechoor VK**, Ma K. The Nuclear Receptor and Clock Repressor Rev-erbα Suppresses Myogenesis. Scientific Reports. 2019. 9(1): 4585

4) My lab has been interrogating the mammalian-Hippo-Tead organ size control pathway to study its regulatory role in various tissues, including the β-cell, heart, liver, adipocyte, skeletal muscle and other metabolically active tissues. We have generated tissues specific, inducible deletions of this pathway, including that of Tead1, the downstream transcriptional effector for this pathway. We have demonstrated that Tead1 is critical for the maintenance of adult cardiomyocyte function and its loss of function only in adult cardiomyocytes leads to rapid-onset heart failure.
   a) Liu R, Lee J, Kim BS, Wang Q, Buxton SK, Balasubramanyam N, Kim JJ, Dong J, Zhang A, Li S, Gupte AA, Hamilton DJ, Martin JF, Rodney GG, Coarfa C, Wehrens XH, **Yechoor VK***, Moulik M. Tead1 is required for maintaining adult cardiomyocyte function, and its loss results in lethal dilated cardiomyopathy. JCI Insight. 2017 Sep 7;2(17). *Corresponding and co-senior author
   b) Liu R, Jagannathan R, Li F, Lee J, Balasubramanyam N, Kim BS, Yang P, **Yechoor VK***, Moulik M. Tead1 is required for perinatal cardiomyocyte proliferation. PLOS One. 2019 Feb 27;14(2). *Corresponding and co-senior author.
   c) Liu H, Zhang CH, Ammanamanchi N, Suresh S, Lewarchik C, Rao K, Uys GM, Han L, Abrial M, Yimlamai D, Ganapathy B, Guillermier C, Chen N, Khaladkar M, Spaethling J, Eberwine J, Kim J, Walsh S, Choudhury S Little K, Francis K, Sharma M, Viegas M, Bais A, Kostka D, Ding J, Bar-Joseph Z, Wu Y, **Yechoor V**, Moulik M, Johnson J, Weinberg J, Reyes-Múgica M, Steinhauser ML, Kühn B. Control of cytokinesis by β-adrenergic receptors indicates an approach for regulating cardiomyocyte endowment. Sci Transl Med. 2019 Oct 9;11(513).

Complete List of Published Work in My Bibliography

http://www.ncbi.nlm.nih.gov/sites/myncbi/vijay.yechoor.1/bibliography/40361395/public/?sort=date&direction=ascending.

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

Ongoing Research Support

1. 1I01BX002678 (Yechoor-PI) 01/01/2016 – 05/31/2020
VAORD
"Tead1 - A Regulator of Quiescence and Proliferation in Pancreatic Beta Cells"
The major goal of this project is to identify the regulatory role of Tead1 in β-cell proliferation and regulation of the decision between cell cycle entry and quiescence in adult β-cells.
Role: PI

2. R01DK097160 (Yechoor -PI) 02/01/2014 - 03/01/2021
NIH/NIDDK
"Circadian Clock and β-cell stress adaptation"
The major goal of this project is to identify the regulation of β-cell stress adaptive pathways involving regulation of ER stress, by Bmal1, Rev-erbα and the intrinsic molecular clock.
Role: PI

3. 1UG3DK119973-01 (Taylor – PI) 09/20/2018 – 07/31/2020
NIH/NIDDK
"Human Microphysiology Systems Disease Model of Type 2 Diabetes Starting with Liver and pancreatic Islets"
The goal of this project is to develop a combined liver and islet organ-on-a-chip, microphysiological system technology to elucidate the crosstalk between the liver and islet in physiologic and insulin resistant states.
Role: Co-Investigator

4. The Pittsburgh Foundation (Kershaw and Yechoor- Co-PIs) 09/2018 – 08/31/2019
"Engineered Patient-specific β-cells to Cure Diabetes"
The goal of this project is to engineer patient-specific islets, ex vivo, that resist immune destruction.
Role: Co-Principal Investigator

Completed Research Support (only grants where I was the PI are listed)

1. 5R01AG041782 (Sekhar-PI) 09/01/2012 - 05/31/2017
   NIH/NIA "Correcting Glutathione Deficiency to Restore Mitochondrial Fat Oxidation in Aging"
2. 7-12-BS-210 (Yechoor -PI) 07/1/2012 - 06/30/2015
   American Diabetes Association "Mechanisms underlying circadian control of beta-cell function"
3. 5R56DK089061 (Yechoor -PI) 07/01/2010 – 06/30/2012
   NIH/NIDDK "Circadian Control of Islet Function"
4. RO3DK078716 (Yechoor -PI) 12/1/2008 - 11/30/2010
   NIH/NIDDK Reversing Autoimmune Diabetes with Gene Therapy Induced Islet Neogenesis
5. K08DK068391 (Yechoor -PI) 7/1/2004 – 6/30/2009
   NIH/NIDDK "Islet Neogenesis with Ngn3 Therapy Reverses Diabetes"
6. DERC – P&F project (Yechoor - PI) 11/1/2009 – 10/31/2010
   NIH/NIDDK "Circadian Control of Islet Function"
7. DERC – P&F project (Yechoor - PI) 9/1/2008 – 8/31/2009
   NIH/NIDDK "Engineering Autoimmune-resistant Islet Neogenesis to Cure Type1 Diabetes in NOD Mice"
8. JDRF Innovative Award (Yechoor - PI) 02/01/2006 - 1/31/2007
   JDRF "Gene Therapy Induced Autoimmunity-evading Islet Neogenesis Reverses Diabetes"