BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Ernesto Bernal-Mizrachi, M.D.	Assistant Professor of Medicine
eRA COMMONS USER NAME EBERNAL	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Santa Librada School, Cali, Colombia	B.A.	1982	
Universidad del Valle Medical School, Cali, Colombia	M.D.	1989	

NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

2005-present Assistant Professor of Medicine.
1999-2005 Instructor of Medicine, Washington University School of Medicine.
1996-1999 Postdoctoral Fellow in Endocrinology and Metabolism, Barnes Hospital Washington University School of Medicine, St. Louis, MO
1993-1996 Residency, Internal Medicine, Jackson Memorial Hospital, University of Miami, Miami, FL
1991-1993 Residency, Internal Medicine, Universidad del Valle Hospital, Universitario del Valle, Cali, Colombia
1991-1993 Compulsory Social Service, Hospital Universitario del Valle, Cali, Colombia

HONORS

1999-2000 SmithKline Beecham Junior Faculty Award.
1990 National Internal Medicine Award - XI Internal Medicine Congress. Cali, Colombia. Origen Etnico de los Pacientes con Paraparesia Espastica Tropical e Influencia de los Factores Geneticos para la Transmision Perinatal del HTLV-I en la Ciudad de Tumaco, Colombia. (Ethnic Origin of Tropical Spastic Paraparesis Patients and Influence of Genetic Markers in Perinatal Transmission of HTLV-I in Tumaco, Colombia)

B. Selected peer-reviewed publications (in chronological order). Do not include publications submitted or in preparation.

1. Iannotti CA, Inoue H, **Bernal E**, Aoki M, Liu L, Donis-Keller H, German MS, Permutt MA: Identification of a human LMX1-related gene, LMX1B: tissue-specific expression and linkage mapping on chromosome 9. Genomics 46:520-24, 1997.
2. Bernal C, **Bernal E**, Patarca R, Arango C. Evaluation of the cell mediated immunity in asymptomatic Colombian natives with positive or indeterminate serology for HTLV-1 in Tumaco Colombia, Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology. 19(2): 121-3, 1998 Oct 1.
3. Tao T, Wasson J, **Bernal-Mizrachi E**, Behn PS, Chayen S, Duprat L, Meyer J, Glaser B, Permutt MA: Isolation and characterization of the human PAX4 gene. Diabetes 47(10): 1650-3, 1998.
4. Inoue H, Tanizawa Y, Wasson J, Behn P, Kalidas K, **Bernal-Mizrachi E**, Mueckler M, Marshall H, Donis-Keller H, Crock P, Rogers D, Mikuni M, Kumashiro H, Higashi K, Sobue G, Oka Y, Permutt: A novel gene encoding a putative transmembrane protein is mutated in patients with diabetes mellitus and optic atrophy (Wolfram syndrome). Nature Genetics 20(2): 143-8, 1998.

5. Arango C., Maloney E, Rugeles MT, **Bernal E**, Bernal C, Borrero I, Herrera S, Restrepo M, Espinal A, Blattner WA. HTLV-I and HTLV-II coexist among the Embera and Inga Amerindians of Colombia. [Letter] Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology. 20(1):102-103,1999 Jan 1.

6. Arango C, Rugeles MT, Concha M, Borrero I, Lai H, Lai S, Bernal C, **Bernal E**. Risk Factors for HTLV-I Mother to Child Transmission: Influence of Genetic Markers. Braz J Infect Dis. 1998 Jun;2 (3):135-142.

7. **Ernesto Bernal-Mizrachi**, Burton Wice, Hiroshi Inoue, and M. Alan Permutt. Activation of Serum Response Factor in the Depolarization Induction of Egr-1 Transcription in Pancreatic Islet -Cells. J. Biol. Chem. 2000 275: 25681-25689.

8. M. Alan Permutt, **Ernesto Bernal-Mizrachi**, and Hiroshi Inoue. Calpain 10: the first positional cloning of a gene for type 2 diabetes? J Clin Investigat. 2000 106(7) 819-821.

9. Wice BM, **Bernal-Mizrachi E**, and Permutt MA. Id proteins, dominant/negative regulators of basic helix loop helix transcription factors, promote the pancreatic islet β cell phenotype.. Diabetologia. 2001 Apr; 44(4):453-63.

10. **Bernal-Mizrachi E,** Wen W, Srinivasan S, Klenk A, Cohen D, and Permutt MA. Activation of Elk-1, an Ets transcription factor, by glucose and EGF treatment of insulinoma cells. Am J Physiol Endocrinol Metab 2001 281: E1286-E1299

11. **Ernesto Bernal-Mizrachi***, Wen W, Stahlhut S, Welling C and M. Alan Permutt. Transgenic Mice Expressing a Constitutively Active Akt1/PKB in Pancreatic Islet β-cells Exhibit Striking Hypertrophy, Hyperplasia, and Hyperinsulinemia. J. Clin. Invest. 2001 108: 1631-1638

12. Srinivasan S, **Bernal-Mizrachi E**, Ohsugi M and Permutt MA. Glucose promotes pancreatic islet beta-cell survival through a PI 3-kinase/Akt-signaling pathway. Am J Physiol Endocrinol Metab. 2002 Oct; 283(4): E784-93

13. **Bernal-Mizrachi E**, Wen W, Shornick M and Permutt MA. Activation of NF-κB by Depolarization and Ca2+ Influx in MIN6 Insulinoma Cells. Diabetes. 2002 51 Suppl 3:S484-8.

14. **Bernal-Mizrachi E**, Cras-Meneur C, Ohsugi M, Permutt MA. Gene Expression Profiling in Islet Biology and Diabetes Research. Diabetes Metab Res Rev. 2003 Jan-Feb;19(1):32-42..

15. Inoue H, Cras-Méneur C, Zhou Y, Ohsugi M, **Bernal-Mizrachi E**, Pape D, Clifton SW, Permutt MA: Comprehensive Analysis of Human Pancreatic Islet Expression Profile by Serial Analysis of Gene Expression (SAGE). Diabetologia 2004; 47(2):284-299.

16. Ohsugi M, Cras-Méneur C, Zhou Y, Warren W, **Bernal-Mizrachi E**, and Permutt MA. Glucose and insulin treatment of insulinoma cells results in transcriptional regulation of a common set of genes. Diabetes. 2004; 53(6):1496-508.

17. **Bernal-Mizrachi E** *, Fatrai S, Johnson JD, Ohsugi M, Otani K, Han Z, Polonsky KS, and Permutt MA. Defective insulin secretion and increased susceptibility to experimental diabetes are induced by reduced Akt activity in pancreatic islet beta cells. J Clin Invest. 2004 Oct;114(7):928-36

18. Ohsugi M, Cras-Meneur C, Zhou Y, **Bernal-Mizrachi E**, Johnson JD, Luciani DS, Polonsky KS, Permutt MA.Reduced expression of the insulin receptor in mouse insulinoma (MIN6) cells reveals multiple roles of insulin signaling in gene expression, proliferation, insulin content and secretion. J Biol Chem. 280(6):4992-5003

19. Srinivasan S, Ohsugi M, Liu Z, 3, Fatrai S, **Bernal-Mizrachi E**, and Permutt MA. Endoplasmic Reticulum Stress Induced Apoptosis is mediated in part by reduced insulin signaling through PI3K/Akt and increased Glycogen Synthase Kinase 3 beta (GSK3β) in Mouse Insulinoma Cells. Diabetes 54(4):968-75.

20. Moynihan KA, Grimm AA, Plueger MM, **Bernal-Mizrachi E**, Ford E, Cras-Meneur C, Permutt MA, Imai S. Increased dosage of mammalian Sir2 in pancreatic beta cells enhances glucose-stimulated insulin secretion in mice. Cell Metab 2005. (2):105-17.

21. Elghazi L, Balcazar N, **Bernal-Mizrachi E***. Emerging role of protein kinase B/Akt signaling in pancreatic beta-cell mass and function. Int J Biochem Cell Biol. 2005 Sep 23; [Epub ahead of print].
22. Riggs AC, **Bernal-Mizrachi E**, Ohsugi M, Wasson J, Fatrai S, Welling C, Murray J, Schmidt RE, Herrera PL, Permutt MA. Mice conditionally lacking the Wolfram gene in pancreatic islet beta cells exhibit diabetes as a result of enhanced endoplasmic reticulum stress and apoptosis. Diabetologia. 2005;48(11):2313-21.
23. Fatrai S, Elghazi L, Balcazar N, Cras-Méneur C, Kiyokawa H and **Bernal-Mizrachi E***: Akt induces β-cell proliferation by regulating cyclin D1, cyclin D2, p21 levels and cdk4 activity. Diabetes. 2006;55(2):318-25.
24. Martinez SC, Cras-Meneur C, **Bernal-Mizrachi E**, Permutt MA. Glucose Regulates Foxo1 Through Insulin Receptor Signaling in the Pancreatic Islet beta-cell. Diabetes. 2006 Jun;55(6):1581-91.
25. Johnson JD, Ford EL, **Bernal-Mizrachi E**, Kusser KL, Luciani DS, Han Z, Tran H, Randall TD, Lund FE, Polonsky KS: Suppressed insulin signaling and increased apoptosis in CD38-null islets. Diabetes. 2006 Oct;55(10):2737-46.
26. Rachdi L, Balcazar N, Elghazi L, BarkerDJ, Krits I, Kiyokawa H and **Bernal-Mizrachi E***: Differential effects of p27 in regulation of beta cell mass during development, neonatal period and adult life. Diabetes Diabetes. 2006 Dec;55(12):3520-8.
27. Johnson JD, **Bernal-Mizrachi E**, Alejandro EU, Han Z, Kalynyak TB, Li H, Beith JL, Gross J, Warnock GL, Townsend RR, Permutt MA, Polonsky KS. Insulin protects islets from apoptosis via Pdx1 and specific changes in the human islet proteome. Proc Natl Acad Sci U S A. 2006 Dec 19;103(51):19575-80.
28. McDunn JE, Muenzer JT, Rachdi L, Chang KC, Davis CG, Dunne WM, Piwnica-Worms D, **Bernal-Mizrachi E**, Hotchkiss RS. Peptide-mediated activation of Akt and extracellular regulated kinase signaling prevents lymphocyte apoptosis. FASEB J. 2008 Feb;22(2):561-8.
29. Elghazi L, Rachdi L, Weiss A.J, Cras-Méneur C and **Bernal-Mizrachi E***. Regulation of β-cell mass and function by the Akt/protein kinase B signaling pathway. Diabetes, Obesity and Metabolism 2007 Nov;9 Suppl 2:147-57.
30. Hegedus B, Dasgupta B, Shin JE, Emnett RJ, Hart-Mahon EK, Elghazi L, Bernal-Mizrachi E, Gutmann D. Neurofibromatosis-1 regulates neuronal and glial cell differentiation from neuroglial progenitors in vivo by both cAMP- and Ras-dependent mechanisms. Cell Stem Cell, 2007; 443-457.
31. Martinez SC, Tanabe K, Cras-Meneur C, Abumrad NA, **Bernal-Mizrachi E**, Permutt MA. Inhibition of Foxo1 Protects Pancreatic Islet β-Cells Against Fatty Acid and ER-Stress Induced Apoptosis. Diabetes. 2008 Jan 9; [Epub ahead of print]
32. Liu Z, Tanabe K, **Bernal-Mizrachi E**, Permutt MA. Mice with beta cell overexpression of glycogen synthase kinase-3beta have reduced beta cell mass and proliferation. Diabetologia. 2008 Jan 25;
33. Tanabe K, Liu Z, Patel S, Doble BW, Cras-Meneur C, Martinez SC, Welling C, White MF, **Bernal-Mizrachi E**, Woodgett JR, Permutt MA. Genetic deficiency of glycogen synthase kinase-3beta corrects diabetes in mouse models of insulin resistance. PLoS Biol. 2008 Feb;6(2):e37.
34. Elghazi L, Weiss AJ, Gould A, Callaghan J, Hegedus B, Gutmann D and **Bernal-Mizrachi E***. Generation of a reporter mouse line expressing Akt and EGFP upon Cre-mediated recombination. Genesis in press.

* *Corresponding author*

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

Ongoing:

Z1R03DK068028-01 (E. Bernal-Mizrachi PI) 7/01/04-6/30/08
NIH.

Regulation of pancreas development by PI3K/Akt signaling
The overall goal of this proposal is to extend previous observations in the adult pancreas by studying the role of Akt signaling in the differentiation program of the pancreas. In these studies the hypothesis that Akt regulates b-cell mass by controlling the relative balance between self-renewal and differentiation of pancreatic and endocrine progenitors will be tested.

1R01DK073716-01 (E. Bernal-Mizrachi PI) 7/01/06-06/30/11
NIH/NIDDK
AKT/mTOR signaling and regulation of cell cycle in β-cells
The objective of this proposal is to delineate the molecular mechanisms that link AKT to activation of the cyclin D/cdk4 complex.

7-06-CD-02 (E. Bernal-Mizrachi PI) 7/1/06-6/30/11
Career Development Award
American Diabetes Association
AKT signaling and regulation of cell cycle in β cells.
This project has two major goals. One of the goals of this project is to study transcriptional regulation of cell cycle components by Akt/pdx1 signaling. Another goal of this project is the study of Akt/mTOR signaling in regulation of β-cell proliferation by modulating protein levels and activity of cyclin D/cdk4 complex components.

Research Grant (E. Bernal-Mizrachi PI) 04/01/08-03/31/11
JDRF
"Akt and regulation of pancreas development and cell plasticity"
The objective of this proposal is to extend our observations by examining the role of Akt signaling activation in proliferation and differentiation of pancreatic progenitors during development and plasticity of mature cells.

1R03DK068028-01 (E. Bernal-Mizrachi PI) 6/01/04-6/30/08
NIH.
Regulation of pancreas development by PI3K/Akt signaling
The overall goal of this proposal is to extend previous observations in the adult pancreas by studying the role of Akt signaling in the differentiation program of the pancreas. In these studies the hypothesis that Akt regulates b-cell mass by controlling the relative balance between self-renewal and differentiation of pancreatic and endocrine progenitors will be tested.

P60 DK20579 (Permutt, PD) 12/1/02-11/30/07
NIH/NIDDK
Diabetes Research and Training Center
Morphology Core Director
The overall goal of the DRTC is to bring together and support clinical and basic science investigators and health care professionals from varied disciplines to join in an effort that increases the effectiveness of diabetes research and health care delivery.

Completed:

Pilot and Feasibility grant from the Diabetes Research and Training Center at Washington University School of Medicine (E. Bernal-Mizrachi PI). 12/01/03-7/01/04

Regulation of pancreas development by PI3K/Akt signaling
The overall goal of this proposal is to extend previous observations in the adult pancreas by studying the role of Akt signaling in the differentiation program of the pancreas.

Research Grant (E. Bernal-Mizrachi, co-investigator) 01/01/02-12/31/04
Pharmacia
Transgenic Models for Growth and Preservation of Islet Beta Cell Mass.
The goal of this studies is to test the hypothesis that control of islet β-cell size and number occurs predominantly through Akt activation of the nutrient/growth factor.

Junior Faculty Award (E. Bernal-Mizrachi, PI) 7/1/03-6/30/06
American Diabetes Association

Role of Akt in the Regulation of Pancreatic Beta-Cell Mass and Function
The overall goal of this project is to test the hypothesis that Akt regulates Beta-Cell growth by controlling the rate of replication, differentiation and survival under conditions that require expansion of Beta-Cell mass.

Innovative Grant (E. Bernal-Mizrachi PI) 11/01/06-10/31/07
JDRF
AKT Activating Compounds in Islets: Design and Characterization
The major goal of this project is to develop small peptides that can freely cross cell membranes and activate Akt signaling.