

BIOGRAPHICAL SKETCH

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NAME Balaji Krishnamachary	POSITION TITLE Research Associate		
eRA COMMONS USER NAME (credential, e.g., agency login) Bkrishn1			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	MM/YY	FIELD OF STUDY
Presidency College, University of Madras, India	B.Sc.	1986	Botany
University of Baroda, India	M.Sc.	1990	Botany
Sardar Patel University, Anand, India	Ph.D.	1995	Botany
Indian Institute of Science, Bangalore, India	Res. Associate	1996	Biochemistry

A. Personal Statement

I have expertise in the delivery of both small interfering RNA (siRNA) and short hairpin (shRNA), and molecular analysis of the transgene. As a postdoctoral fellow in the laboratory of Dr. Gregg L Semenza, I was trained to construct both siRNA and shRNA, establish a retroviral delivery method to silence the transcription factor Hypoxia inducible factor-1 (HIF-1) *in vitro* in renal carcinoma and in various molecular biology techniques to interrogate the transcriptional activity of genes involved in the progression of cancer. Later as a Research associate under mentorship of Dr. Zaver. M. Bhujwalla, Magnetic Resonance Division, Department of Radiology, The Johns Hopkins University, I was involved in the construction of shRNA against choline kinase (Chk) and the successful *in vivo* delivery of lentivirus carrying Chk-shRNA. As a molecular biologist in the Molecular Imaging Program, I have a demonstrated record of successful and productive research experiences in the areas of hypoxia, choline phospholipid metabolites, and delivery of siRNA and shRNA, that will be utilized for this proposed project.

B. Positions and Honors

1992-95 Senior Research Fellowship awarded by the Univ. Grants Commission Government of India
1996-98 Research Associate Department Biochemistry Indian Institute Science, Bangalore, India
1998-2000 Postdoctoral fellow, Department of Pathology, University of California, Los Angeles, CA
2000-2006 Postdoctoral fellow, Department of Pediatrics, Institute of Genetic Medicine, Johns Hopkins University, Baltimore, MD
2006-Present Research Associate, Department of Radiology, Molecular Imaging, Johns Hopkins University, Baltimore, MD

C. Selected Peer-reviewed Publications

Most relevant to the current application

1. Krishnamachary B, Berg-Dixon S, Kelly B, Agani F, Feldser D, Ferreira G, Iyer N, LaRusch J, Pak B, Taghavi P, Semenza GL. Regulation of colon carcinoma cell invasion by hypoxia-inducible factor 1. *Cancer Res.* 2003 Mar 1;63(5):1138-43.
2. Jin Hyen Baek, Patrick C. Mahon, Jane Oh, Brian Kelly, Balaji Krishnamachary, Denise A. Chan, Amato J. Giaccia, and Gregg L. Semenza. OS-9 interacts with hypoxia-inducible factor 1 α and prolyl hydroxylase to negatively regulate HIF-1 activity. *Molecular Cell*, 2005 Feb 18; 17,503-512.
3. David Zagzag, Balaji Krishnamachary, Herman ye, Hiroaki Okuyama, Gregg L. Semenza. SDF-1 α and CXCR-4 expression in Hemangioblastoma and Renal Clear Cell carcinoma: VHL loss of function induces expression of ligand and its receptor. *Cancer Research* 2005 Jul 15; 65(14):6178-88.
4. Krishnamachary B, Zagzag D, Hideko Nagasawa Hiroaki Okuyama, Jin Hyen Baek, Gregg L. Semenza. HIF-1-dependent repression of E-cadherin in VHL-null renal cell carcinoma mediated by TCF3, ZFH1A, and ZFH1B. *Cancer Research* 2006, March 1; 66(5):2725-2731.
5. Hiroaki Okuyama, Balaji Krishnamachary, Yi Fu Zhou, Hideko Nagasawa, Marta Bosch-Marce and Gregg L. Semenza. Expression of vegf receptor 1 in bone marrow-derived mesenchymal cells is dependent on hypoxia-inducible factor 1. *J Biol Chem.* 2006 Jun 2; 281(22):15554-63.

6. Yifu Zhou, Martha Bosch, Hideo Kimura, Hiroaki Okuyama, Krishnamachary Balaji, David L. Huso, Gregg L. Semenza. Spontaneous transformation of cultured bone marrow derived stromal cells. *Cancer Res.* 2006 Nov 15; 66(22):10849-54.
7. Huafeng Zhang, Ping Gao, Ryo Fukuda, Ganesh Kumar, Balaji Krishnamachary, Karen I. Zeller, Chi V. Dang and Gregg L. Semenza. HIF-1 inhibits mitochondrial biogenesis and cellular respiration in VHL-deficient renal cell carcinoma by repression of C-MYC activity. *Cancer Cell* 2007 May; 11(5):407-20.
8. Paul T Winnard Jr., Mahendren Botlagunta, Jessica B Kluth, Sirheen Mukadam, Balaji Krishnamachary, Farhad Vesuna, Venu Raman. Hypoxia induced human endonuclease G expression suppresses tumor growth in xenograft model. *Cancer Gene Therapy* 2008, 15: 645-654.
9. Krishnamachary B, Kristine Glunde, Flonne Wildes, Noriko Mori, Tomoyo Takagi, Venu Raman, Zaver M. Bhujwalla. Noninvasive Detection of Lentiviral-mediated Choline Kinase Targeting in a Human Breast Cancer Xenograft. *Cancer Res.* April 2009, 15; 69(8): 3464-71. PMID2687146.
10. Hypoxia inducible-factor1alpha regulates the metabolic shift of pulmonary hypertensive endothelial cells. Fijalkowska I, Xu W, Comhair SA, Janocha AJ, Mavrakis LA, Krishnamachary B, Zhen L, Mao T, Richter A, Erzurum SC, Tudor RM. *Am. J. Pathol.* 2010 176: 1130-1138. PMID2832136.

D. Research Support

Ongoing Research Support

2P50CA103175-06A2 (Bhujwalla)

09/22/11 - 07/31/16

NCI JHU ICMIC Program

This center grant funds an *in vivo* Cellular and Molecular Imaging Center at Johns Hopkins. The program consists of four research components, four developmental projects, one career development award and four resources.

1R01CA136756-01A1 (Bhujwalla)

07/01/09 – 06/30/14

NIH

Imaging Hypoxia and Cancer Stem Cells

The goal of this project is to understand the role of the tumor microenvironment and choline metabolism in harboring or creating stem-like cancer cells.

Completed Research Within the Last Three Years

R21 CA133600-01A1 (Bhujwalla)

12/01/08 – 11/30/10

NIH

Imaging Permissive Microenvironmental Niches for Cancer Stem Cells

The goal of this application is to use molecular and functional imaging to understand the role of hypoxia and physiological and metabolic characteristics in creating or harboring stem-like cancer cells at primary and metastatic sites.