BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Bar, Eli	Assistant Professor
eRA COMMONS USER NAME EBAR001	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Tel-Aviv University, Tel-Aviv, Israel	B.A.	04/98	Biology
University of Illinois at Chicago, Chicago, IL	Ph.D.	07/03	Molecular Biology

A. Personal Statement

My graduate studies used yeast genetics to dissect signal transduction pathways in the laboratory of Dr. David E. Stone, at the University of Illinois at Chicago. During my postdoctoral training in the laboratory of Dr. Charles G. Eberhart I focused on how to therapeutically target signaling pathways in brain tumors. Many of the pathways I study also play a role in normal brain development, particularly in poorly differentiated stem and progenitor cells, and the parallels between normal stem cells and malignant "cancer stem cells" are numerous. I initially examined the role of the Hedgehog signaling pathway in medulloblastoma and other embryonal tumors. Next, I investigated if Hedgehog was relevant in glioblastomas, which were shown to contain a small sub-population of stem-like cells. We have found that pharmacological inhibition of the Hedgehog pathway in gliomas reduces the percentage of stem-like cells, resulting in a dramatic inhibition of xenotransplantation in immunocompromised mice. We have also found that radiation, the standard-of-care treatment for patients with glioblastoma, resulted in an increase the percentage of these stem-like cells, which may help explain why these tumors almost always recur. When I established my own laboratory in 2008, I began to focus on how hypoxia modulates tumor invasion, stem cell subpopulations, and metabolic reprogramming. We have recently shown that hypoxia increases the percentage of clonogenic, cancer stem cells (GSC), in GBM neurosphere cultures and in primary tumors. Moreover, we have implicated the oxygen-labile transcription factor, HIF-1alpha, in this process, suggesting a novel mechanism by which low oxygen levels may promote tumor aggressiveness. I believe that an improved understanding of how reduced oxygenation modulates the pathobiology of GBM will be necessary if we are to effectively treat these universally fatal neoplasms. In 2012, I relocated my laboratory to Case Western Reserve University.

I feel that my group has contributed to the knowledge of gliomagenesis and therapeutics. Many members of my laboratory including myself have enjoyed honing the experimental technology for glioma research. We have developed several useful tools including clonogenic assays in methyl cellulose, various pathway specific reporter constructs, inducible gene expression systems, as well as integrated imaging reporter system for hypoxia for real-time *in vivo* imaging of malignant gliomas. We have a solid reputation for sharing tools that we develop with the community. I currently serve on graduate committees of several students, and I had a long and enjoyable association with the Pathology for Graduate Students course at the Johns Hopkins University I used to serve as one of the instructors.

B. Positions and Honors

Positions and Employment

1995-1997	Lab Assistant, Tel-Aviv University (Dr. Abraham Hefetz's Lab and the National Laboratory for the Genetics of Israel Populations), Tel-Aviv, Israel
1997-2001	Teaching Assistant (Spring '97, '99, '01 and Fall '97-99, '01), University of Illinois at Chicago, Chicago, IL
2003	Post-Doctoral position, Food and Drug Administration, Bethesda, MD
2004-2007	Post Doctoral Fellow, Johns Hopkins University, School of Medicine, Baltimore, MD
2006-pres	Collaborator with Dr. Angelo Vescovi's group in Milan, Italy on Neural Stem Cell Culture

2008 Research Associate, Johns Hopkins University, School of Medicine, Pathology, Baltimore, MD
2008-2010 Instructor, Johns Hopkins University, School of Medicine, Pathology, Baltimore, MD
2010-2012 Assistant Professor, Johns Hopkins University, School of Medicine, Pathology, Baltimore, MD
2012- Assistant Professor, Case Western Reserve University, School of Medicine, Neurological Surgery, OH

Other experience and Professional Membership

American Association for Cancer Research
Society for Neuro-Oncology

Honors

2006 8th Annual Pathology Young Investigator Award for Excellence in Translational Research
2007 9th Annual Pathology Young Investigator Award for Excellence in Translational Research – First Prize

C. Selected peer-reviewed publications

Most relevant to the current application

1) **Bar EE**, Chaudhry A, Lin A, Fan X, Schreck K, Matsui W, Piccirillo S, Vescovi AL, DiMeco F, Olivi A, Eberhart CG. Cyclopamine-mediated hedgehog pathway inhibition depletes stem-like cancer cells in glioblastoma. Stem Cells. 2007;25(10):2524-33.
2) Nasonkin I, Mahairaki V, Xu L, Hatfield G, Cummings B, Eberhart C, Ryugo DK Maric D, **Bar EE** and Koliatsos VE: Long-Term stable differentiation of human embryonic stem cell-derived neural precursors grafted into the adult mammalian neostriatum, Stem Cell 2009, p. pp. 2414-2426 PMCID:PMC2906132
3) Schreck KC, Taylor P, Marchionni L, Gopalakrishnan V, **Bar EE**, Gaiano N, Eberhart CG. The Notch target Hes1 directly modulates Gli1 expression and Hedgehog signaling: a potential mechanism of therapeutic resistance. Clin Cancer Res. 2010;16(24):6060-70.
4) **Bar EE**, Lin A, Mahairaki V, Matsui W, Eberhart CG. Hypoxia Increases the Expression of Stem-Cell Markers and Promotes Clonogenicity in Glioblastoma Neurospheres. Am J Pathol. 2010;177(3):1491-502
5) **Bar EE**. Glioblastoma, cancer stem cells and hypoxia. Brain Pathol. 2011;21(2):119-29.
6) Kahlert UD, Bender NO, Maciaczyk D, Bogiel T, **Bar EE**, Eberhart CG, et al. CD133/CD15 defines distinct cell subpopulations with differential *in vitro* clonogenic activity and stem cell-related gene expression profile in *in vitro* propagated glioblastoma multiforme-derived cell line with a PNET-like component. Folia Neuropathol. 2012;50(4):357-68
7) Kah Suan Lim , Kah Jing Lim, Antoinette C. Price, Brent Orr, Charles G. Eberhart and **Eli E. Bar**. Inhibition of Monocarboxylate Transporter-4 Depletes Stem-Like Glioblastoma Cells in a Lactate Independent Fashion. Oncogene 2013 (Accepted with revisions).

Additional recent publications of importance to the field (in chronological order)

1) **Bar EE**, Ellicott AT, Stone DE. Gbetagamma recruits Rho1 to the site of polarized growth during mating in budding yeast. J Biol Chem. 2003;278(24):21798-804.
2) **Bar EE**, Chaudhry A, Farah MH, Eberhart CG. Hedgehog signaling promotes medulloblastoma survival via Bcl2. Am J Pathol. 2007;170(1):347-55.
3) **Bar, E.E.**, Chaudhry, A., Lin, A., Fan, X., Schreck, K., Matsui, W., Piccirillo, S., Vescovi, A.L., DiMeco, F., Olivi, A., and Eberhart, C.G. Cyclopamine-mediated hedgehog pathway inhibition depletes stem-like cancer cells in glioblastoma. Stem Cells 25(10), 2524-2533, 2007.
4) **Bar EE**, Stearns D. New developments in medulloblastoma treatment: the potential of a cyclopamine-lovastatin combination. Expert Opin Investig Drugs. 2008;17(2):185-95.
5) **Bar EE**, Lin A, Tihan T, Burger PC, Eberhart CG. Frequent gains at chromosome 7q34 involving BRAF in pilocytic astrocytoma. J Neuropathol Exp Neurol. 2008;67(9):878-87.
6) **Bar EE**, Lin A, Mahairaki V, Matsui W, Eberhart CG.. Hypoxia Increases the Expression of Stem-Cell Markers and Promotes Clonogenicity in Glioblastoma Neurospheres. Am J Pathol 2010 Sep; 177(3):1491-502 PMCID: PMC2928980

7) Raabe EH, Lim KS, Kim JM, Meeker A, Mao XG, Nikkhah G, Maciaczyk J, Kahlert U, Jain D, **Bar EE**, Cohen KJ, Eberhart CG. BRAF activation induces transformation and then senescence in human neural stem cells: a pilocytic astrocytoma model. Clin Cancer Res. 2011;17(11):3590-9.
8) Asnaghi L, Ebrahimi KB, Schreck KC, **Bar EE**, Coonfield ML, Bell WR, Handa J, Merbs SL, Harbour JW, Eberhart CG. Notch signaling promotes growth and invasion in uveal melanoma. Clin Cancer Res. 2012.
9) Lim KJ, Bisht S, **Bar EE**, Maitra A, Eberhart CG. A polymeric nanoparticle formulation of curcumin inhibits growth, clonogenicity and stem-like fraction in malignant brain tumors. Cancer Biol Ther. 2011 Mar 1;11(5):464-73. Epub 2011 Mar 1. PMCID:PMC 3087900
10) Lin A, Rodriguez FJ, Karajannis MA, Williams SC, Legault G, Zagzag D, Burger PC, Allen JC, Eberhart CG, **Bar EE.** BRAF alterations in primary glial and glioneuronal neoplasms of the central nervous system with identification of 2 novel KIAA1549:BRAF fusion variants, J Neuropathool Exp Neurol. 2012 Jan;71(1):66-72
11) Raffaella Spina, Gessica Filocamo, Enrico Iaccino, Stefania Scicchitano, Michela Lupia, Emanuela Chiarella, Tiziana Mega, Francesca Bernaudo, Daniela Pelaggi, Maria Mesuraca, Simonetta Pazzaglia, Samantha Semenkow, **Eli E. Bar**, Marcel Kool, Stefan Pfister, Heather M. Bond, Charles G. Eberhart, Christian Steinkühler, Giovanni Morrone. Critical role of zinc finger protein 521 in the control of growth, clonogenicity and tumorigenic potential of medulloblastoma cells. Oncotargets. 2013 July, 1-13.