## BIOGRAPHICAL SKETCH

NAME: **James E. Bear**

eRA COMMONS USER NAME: **James_Bear**

POSITION TITLE: **Professor of Cell Biology and Physiology**

EDUCATION/TRAINING

| INSTITUTION AND LOCATION | DEGREE | Completion Date | FIELD OF STUDY |
|---|---|---|---|
| Davidson College; Davidson, NC | B.S. | 05/1993 | Biology |
| Emory University; Atlanta, GA | Ph.D. | 06/1998 | Cell & Developmental Biology |
| Massachusetts Institute of Technology; Cambridge, MA | Post-doc | 1998-2003 | Cell Motility |

### A. Personal Statement

I have both the expertise and experience to carryout the proposed studies. I am a cell biologist with interests in the regulation of actin dynamics, cell motility and invasive tumor cell behavior. I have expertise in multiple imaging modalities including quantitative live-cell microscopy and intravital imaging of tumors and tumor-associated cells using multiphoton microscopy. Since coming to UNC-Chapel Hill as an assistant professor in 2003, I have risen through the ranks to full professor. In 2014, I became the co-leader of the Cancer Cell Biology Program at the UNC Lineberger Cancer Center. In addition, I serve in several leadership capacities such as being the Director of the UNC-Olympus Imaging Research Center and serving as the founding faculty advisor of the newly created Hooker Imaging Core.

### B. Positions and Honors

**Positions and Employment**

| | |
|---|---|
| 1998-2003 | Postdoctoral Fellow, Lab of Dr. Frank Gertler, Massachusetts Institute of Technology |
| 2003-2009 | Assistant Professor, UNC Lineberger Comprehensive Cancer Center and Dept. of Cell Biology & Physiology, University of North Carolina at Chapel Hill |
| 2009-2013 | Associate Professor, University of North Carolina at Chapel Hill |
| 2009-2015 | HHMI Early Career Scientist |
| 2013-present | Professor, University of North Carolina at Chapel Hill |

**Other Experience and Professional Memberships**

| | |
|---|---|
| 1993 | Phi Beta Kappa, Davidson College chapter |
| 1993-1995 | NIH Biochemistry, Cellular and Molecular Biology Training Grant recipient |
| 1997 | ASCB Predoctoral Travel Award |
| 1999-2000 | Anna Fuller Molecular Oncology Fellow |
| 2000 | NIH NRSA Award |
| 2001-04 | Leukemia and Lymphoma Society Special Fellow |
| 2004-06 | V Scholar Award |
| 2005-07 | Melanoma Research Foundation Junior Faculty Award |
| 2006-09 | Sontag Foundation, Distinguished Scientist Award |
| 2008-12 | Research Scholar Award, American Cancer Society |
| 2008-13 | Jefferson-Pilot Award |
| 2009-12 | Faculty of 1000 |
| 2010 | Director, UNC-Olympus Imaging Research Center |
| 2010 | Ruth and Phillip Hettleman Prize for Artistic and Scholarly Achievement |

2014 Co-leader, Cancer Cell Biology Program, UNC Lineberger Cancer Center
2014 Founding faculty advisor, Hooker Imaging Core
2015 Omicron Delta Kappa, *Honoris Causa*, Davidson College circle

**C. Contributions to Science**

**1. Regulation and function of Arp2/3 complex branched actin:** We have a long-standing interest in the regulation of branched actin networks generated by the Arp2/3 complex. As a graduate student, I discovered the founding member of the SCAR/WAVE family of Arp2/3 complex activators. In my own lab, we have continued to study both the regulation and function of Arp2/3-generated networks. Most recently, we have been focused on the role of the Arp2/3 complex in controlling directional motility in mesenchymal cells. Our lab has developed microfluidic devices to be able to maintain stable gradients of soluble growth factors such as PDGF (chemotaxis) and establish surface-bound gradients of extracellular matrix molecules such as fibronectin (haptotaxis).

a. **Bear JE**, Rawls J and Saxe CL. 1998. SCAR, a WASP-related protein, isolated as a suppressor of receptor defects in late *Dictyostelium* development. (*Journal of Cell Biology*, 142(5): 1325-1335) PMC2149354
b. Wu C, Asokan SB, Berginski ME, Haynes EM, Sharpless NE, Griffith JD, Gomez SM and **Bear JE**. 2012. Arp2/3 is critical for lamellipodia and response to extracellular matrix cues, but is dispensable for chemotaxis. (*Cell*, 148(5):973-87). PMC3707508
c. Wu C, Haynes EM, Asokan SB, Simon JM, Sharpless NE, Baldwin AS, Davis IJ, Johnson GL and **Bear JE.** 2013. Loss of Arp2/3 induces an NF-κB-dependent, non-autonomous effect on chemotactic signaling. (*Journal of Cell Biology,* 203(6):907-16). PMC3871425
d. Haynes EM, Asokan SB, King SJ, Johnson HE, Haugh JM and **Bear JE**. 2015. GMFβ controls branched actin content and lamellipodial retraction in fibroblasts. (*Journal of Cell Biology*, 209(6):803-12) PMC4477851

**2. Ena/VASP proteins:** As a postdoc, I elucidated the anti-capping mechanism of Ena/VASP function. The two papers describing this mechanism have been collectively cited >800 times. Recently, we have returned to Ena/VASP proteins after having discovered their key role in compensating for the loss of Arp2/3 complex.

a. **Bear JE**, Loureiro JJ, Libova I, Fässler R, Wehland J and Gertler FB. 2000. Negative regulation of Fibroblast Motility by Ena/VASP Proteins. (*Cell*, 101: 717-728)
b. **Bear JE***, Svitkina TM*, Krause M, Schafer DA, Loureiro JJ, Strasser GA, Maly IV, Chaga O, Cooper JA, Borisy GG and Gertler FB. 2002. Antagonism between Ena/VASP Proteins and Actin Filament Capping regulates Fibroblast Motility. (*Cell*, 109: 509-521) [Cover] *equal contributors
c. **Bear JE** and Gertler FB. 2009. Ena/VASP: towards resolving a pointed controversy at the barbed end. (*J Cell Sci,* 122(Pt 12): 1947-53) PMC2723151
d. Rotty JD, Wu C, Haynes EM, Suarez C, Winkelman JD, Johnson HE, Haugh JM, Kovar DR, **Bear JE**. 2015. Profilin-1 serves as a gatekeeper for actin assembly by Arp2/3-dependent and -independent pathways. (*Dev Cell* 32(1):54-67) PMC4296256

**3. Coronins:** In my own lab, we have been studying the Coronins, a highly conserved family of F-actin binding proteins that are poorly understood. We discovered that these proteins serve as coordinators of Arp2/3 and cofilin activity, two major pathways that control the birth and death of actin filaments. We identified the first phosphorylation site on a coronin and definitively identified the F-actin binding site.

a. Cai L, Holoweckyj N, Schaller MD and **Bear JE**. 2005. Phosphorylation of Coronin 1B by PKC regulates interactions with Arp2/3 and Cell Motility. (*Journal of Biological Chemistry*, 280(36): 31913-23)
b. Cai L, Marshall TW, Uetrecht AC, Schafer DA and **Bear JE**. 2007. Coronin 1B coordinates Arp2/3 and Cofilin activity at the leading edge. (*Cell,* 128(5): 915-29) PMC2630706 [Featured as a Research Highlight in *Nature*]
c. Cai L, Makhov AM, Schafer DA and **Bear JE**. 2008. Coronin 1B antagonizes Cortactin and remodels Arp2/3-containing actin branches in lamellipodia. (*Cell,* 134: 828-42). PMC2570342 [Cover]

**d.** Chan KT, Creed SJ and **Bear JE**. 2011. Unraveling the enigma: Progress towards understanding the Coronin family of actin regulators. (*Trends in Cell Biology*, 21(8):481-8) PMC3163407

**4. Nanoparticle clearance:** As part of our work with the Carolina Cancer Nanotechnology Center of Excellence, we have developed an interest in the clearance of nanoparticles from circulation. This is a critical problem for the delivery of nanoparticle-based therapeutics. We developed an intravital imaging based clearance assay that allows the pharmaco-kinetic profile of micro- and nanaparitcle to be quantitatively determined.

**a.** Merkel TJ, Jones SW, Herlihy KP, Kersey FR, Shields AR, Napier M, Luft JC, Wu H, Zamboni WC, Wang AZ, **Bear JE**, and DeSimone JM. 2011. Using mechanobiological mimicry of red blood cells to extend circulation times of hydrogel microparticles. (*Proc Natl Acad Sci U S A,* 108(2):586-91) PMC3021010
**b.** Perry JL, Reuter KG, Kai MP, Herlihy KP, Jones SW, Luft JC, Napier M, **Bear JE**, and DeSimone JM. 2012. PEGylated PRINT Nanoparticles: The Impact of PEG Density on Protein Binding, Macrophage Association, Biodistribution, and Pharmacokinetics. (*Nano Lett.* 12(10):5304-10) PMC4157665
**c.** Jones SW, Jillian PL, Kai KP, Chen K, Bo T, Napier M, DeSimone JM and **Bear JE**. 2013. Th1/Th2 Immune Status Controls the Circulation Time of Nanoparticles *in vivo*. (*Journal of Clinical Investigation*, 123(7):3061-73) PMC3696555
**d.** Yang Q, Jones SW, Parker CL, Zamboni WC, **Bear JE**, Lai SK. 2014. Evading immune cell uptake and clearance requires PEG grafting at densities substantially exceeding the minimum for brush conformation. (*Mol Pharm*,11(4):1250-8) PMC in progress

**5. Melanoma:** We have a long-standing interest in translating our understanding of cell motility to the context of tumor cell invasion of malignant melanoma. In collaboration with Ned Sharpless at UNC, we have developed several unique approaches to studying melanoma including intravital multiphoton imaging and molecular profiling of tumor heterogeneity. We are particularly interested in the tumor suppressor LKB1 that we recently discovered has a critical role in directional motility of tumor cells towards ECM cues.

**a.** Shields JM, Thomas NE, Cregger M, Berger AJ, Leslie M, Torrice C, Hao H, Penland S, Arbiser J, Scott G, Zhou T, Bar-Eli M, **Bear JE**, Der CJ, Kaufmann W, Rimm DL and Sharpless NE. 2007. Lack of ERK mitogen-activated protein kinase signaling demonstrates a new type of melanoma. (*Cancer Research,* 67(4): 1502-12)
**b.** Liu W, Monahan KB, Pfefferle AD, Shimamura T, Sorrentino J, Chan KT, Roadcap DW, Ollila DW, Thomas NE, Castrillon DH, Miller CR, Perou CM, Wong K-K, **Bear JE**, Sharpless NE. 2012. LKB1/STK11 Inactivation Leads to Expansion of A Pro-Metastatic Tumor Sub-Population in Melanoma. (*Cancer Cell*, 21(6):751-64). PMC3660964
**c.** Chan KT, Jones SW, Brighton HE, Bo T, Cochran SD, Sharpless NE and **Bear JE**. 2013. Intravital imaging of a spheroid-based orthotopic model of melanoma in the mouse ear skin. (*IntraVital*, 2:2, e25805) PMC in progress
**d.** Chan KT, Asokan SB, King SJ, Bo T, Dubose ES, Liu W, Berginski ME, Simon JM, Davis IJ, Gomez SM, Sharpless NE and **Bear JE**. 2014. LKB1 loss in melanoma disrupts directional migration toward extracellular matrix cues. (*Journal of Cell Biology,* 207(2):299-315) PMC4210439

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