BIOGRAPHICAL SKETCH

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NAME: Beningo, Karen A.

eRA COMMONS USER NAME (credential, e.g., agency login): ay5982

POSITION TITLE: Associate 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
Michigan State University, East Lansing, MI	BS	12/1986	Microbiology and Public Health
University of Michigan, Ann Arbor, MI	PHD	12/1998	Cell Biology/Yeast Genetics; Dr. Susan Brown
Marine Biological Laboratory (MBL), WoodsHole, MA	Other training	07/1995	6 week Physiology Summer Course; Dr. Mark Mooseker
University of Massachusetts Medical School, Worcester, MA	NIH training grant	08/2004	Cell Mechanics & Migration; Dr. Yu-li Wang
NCI Cancer Research Imaging Camp, Nashville, TN	NIH training grant	06/2012	In-vivo Imaging; Dr. Bonnie Sloane

A. Personal Statement

My commitment to cell biological research is centered on the question of how mechanical forces dictate cell migration in tissue behavior and organization, and consequently multiple disease states including cancer. This work involves knowledge of migration and the contractile mechanism, biochemical signaling, and microscopy for the measurement of force and compliance at the cellular level. Furthermore, because the tools needed to address the questions of cell mechanics are lacking, a degree of creativity in assay design is necessary. My diverse training and research experience place me in a unique niche to address these questions. I have extensive training from my graduate work in the area of myosins and cytoskeleton in yeast. In my post-doc, this knowledge was expanded to mammalian systems and the study of migration and live-cell imaging. During my post-doc, I was also directly involved in the development and naming of traction force microscopy (TFM) and other assays to measure the miniscule force produced and sensed by cells. Assay design and development was not new to me, prior to graduate training I worked in the pharmaceutical industry in protein purification and the design of screening strategies in a Cancer Biology program. My current interests have expanded to understand how mechanical forces are transduced and what role these mechanical parameters play in the progression of cancer. To this end, over the years I have enhanced my knowledge of cancer biology through multiple avenues. I have taught full courses in cancer biology, joined the Karmanos Cancer Institute, attended regional and national meetings, served on numerous NCI study sections (Physical Science and Oncology), reviewed for cancer journals and I have also been invited to speak at AACR and EMBO meetings. Thus, I am well suited to address the question of cellular forces in the process of metastasis.

1. Jang I and **KA Beningo**. 2019. Integrins, CAF's and Mechanical Forces in the Progression of Cancer. Cancers. 24;11(5). Doi: 10.3390/cancers11050721. *Editor's Choice Award.* **112 citations**

2. Gasparski AN, **Beningo KA**. Mechanoreception at the cell membrane: More than the integrins. Arch Biochem Biophys. 2015 Nov 15;586:20-6. PubMed PMID: 26241498. **59 citations**
3. **Beningo KA**, Lo CM, Wang YL. Flexible polyacrylamide substrata for the analysis of mechanical interactions at cell-substratum adhesions. Methods Cell Biol. 2002;69:325-39. PubMed PMID: 12071003. **233 citations**
4. **Beningo, KA** and Y.-L. Wang. 2002. Flexible substrata for the detection of cellular traction forces. Trends in Cell Biol. 112(2):79-84. PubMed PMID: 11849971**. 334 citations**

B. Positions, Scientific Appointments, and Honors

Positions and Employment

1986 - 1987	Research Assistant, Cancer Biology, Wayne State University, Dr. David Kessel, Detroit, MI
1987 - 1993	Research Associate, Cancer Chemotherapy & Biochemistry, Dr. Judith Sebolt-Leopold, Warner-Lambert/Parke-Davis Pharmaceuticals, Ann Arbor, MI
1993 - 1998	Graduate Research Assistant, Cell Biology, University of Michigan, Ann Arbor, MI
1995 - 1995	Student Teaching Assistant, Medical and Dental Histology, University of Michigan, Ann Arbor, MI
1998 - 2004	Post-doctoral Fellow, Dr. Yu-li Wang, University of Massachusetts Medical School, Worcester, MI
2004 - 2005	Research Assistant Professor, Department of Physiology, University of Massachusetts Medical School, Worcester, MA
2005 - 2012	Assistant Professor, Department of Biological Sciences, Wayne State University, Detroit, MI
2012 -	Associate Professor with tenure, Department of Biological Sciences, Wayne State University, Detroit, MI

Other Experience and Professional Memberships

Ad-hoc Grant Reviewer

- NCI ZCA1-TCRB-Y Physical Sciences and Oncology Project Grants. Special Emphasis Panel, Bethesda, MD (Feb 2016, Feb 2017, Feb 2018)
- NCI [ZCA1-TCRB-6 (J1)], Special Emphasis Panel, Innovative Molecular Analysis Technologies for Cancer Research, Arlington, VA (Dec 2015)
- CDMRP- DOD, Lung Cancer Research Program (Oct. 2015).
- NCI [ZCA1TCRB-Y] Physical Sciences and Oncology Project Grants. Special Emphasis Panel, Bethesda, MD July 2015).
- NCI [ZCA1 TCRB-Y] Utilizing the PLOC Biospecimens Resources, Special Emphasis Panel (June 2015)
- NCI [ZCA1 TCRB-5 (J1) R] Physical Sciences Oncology Center Grants, Special Emphasis Panel, Bethesda MD (November 2014, June 2015).
- NCI [ZCA1 SRLB-J (J1) R] Validation and Advanced Development of Emerging Technologies for Cancer Research, Special Emphasis Panel, Rockville MD (February, July and November 2013).
- NCI [ZCA1 SRLB-J (J1) R] Validation and Advanced Development of Emerging Technologies for Cancer Research, Special Emphasis Panel, Rockville MD (October 2012).
- NIH. Bioengineering Sciences and Technologies (BST) member conflict Special Emphasis Panel [ZRG1 BST-T (02)] (October 2011).
- NSF/NCI, PESO study section, Bethesda, MD (March 2011).
- NCI, attended IMAT study section, (Bethesda, MD March 2010; October 2010, Rockville, MD).
- French granting agency ANR, CNRS, INSERM, 2009, 2010, 2013, 2017.
- MI (Microscopy and Imaging) Study Section Chicago, IL (Oct 2007, 2008). NIGMS.

Write-in Reviewer

- DFG (Germany) (2022)
- Canadian Cancer Research Council (June 2015).
- Research Grants Council (RGC) of Hong Kong, (March 2016)
- Netherlands Organisation for Scientific Review (NWO),Veni Grant, (Mar 2016)
- Sir Henry Wellcome Trust Post-doctoral Fellowships. (2010,2013)
- Romanian National Research Council and the Biology Commission (August 2012).

Honors

Mountain Memorial Fund Scholarship, 1995
Surdna Foundation Scholarship, 1995
National Research Scholars Award (NRSA), 1998-2000
Keystone Symposium Travel Award, 2003
NSF-ESCALATE Career Development Award 2007, 2008, 2009
NSF- Joint Annual Meeting Invitation and Travel Award 2009
College of Liberal Arts and Sciences Faculty Teaching Award 2011
NCI *in-vivo* Imaging Camp, 2012
Wayne State University Outstanding Graduate Mentor Award, 2018
WSU Academic Leadership Academy, 2019

C. Contributions to Science (Google Scholar 4393 citations 5/2023)

Phagocytosis

My interests in cell dynamics developed in graduate school and an underlying theme of all my work is cellular movements and contractility. Dr. Joel Swanson introduced me to the sophisticated complexity of phagocytosis. At the time it was unknown how such a vital process coordinated its contractile mechanism, more specifically what myosins might be involved or at which stages of the process. I collaborated with Swansons group outside of my own graduate project, both intellectually and at the bench, to make the seminal discovery of how the contractile activity is coordinated to close the phagosome. This paper is now considered a landmark paper in the field and has been cited 329 times. I carried this work into my post-doc with Dr. Yu-li Wang and entered his lab with my own question on the topic of phagocytosis, a topic he had no history studying. It also earned me an NRSA award from NIGMS. I asked, does a macrophage care about the biophysical make-up of what it engulfs? Combining the skills I learned in graduate school I designed a method to create stiff and soft microbeads from polyacrylamide and discovered that indeed a macrophage considers the stiffness or softness of its phagocytic target. This has opened a new paradigm to explore. This paper is also considered landmark in the field and has been cited in 432 articles.

a. **Beningo KA**, Wang YL. Fc-receptor-mediated phagocytosis is regulated by mechanical properties of the target. J Cell Sci. 2002 Feb 15;115(Pt 4):849-56. PubMed PMID: 11865040. **432 citations**

b. Swanson JA, Johnson MT, **Beningo K**, Post P, Mooseker M, Araki N. A contractile activity that closes phagosomes in macrophages. J Cell Sci. 1999 Feb;112 (Pt 3):307-16. PubMed PMID: 9885284. **352 citations**

Migration, Adhesion and Cell Mechanics

My work in the area of cell migration, adhesion and cell mechanics began as a post-doc with Dr. Yu-li Wang and has continued since. At the time, a very limited number of groups were interested in how biophysical parameters impact cell behavior. In the late 90's this concept was not well received, however the lab had just conceived the idea of using polyacrylamide hydrogels to explore this phenomenon and the area we came to call "cell mechanics" exploded. I was directly involved in developing these gels, the microbeads

described above, and traction force microscopy (which we named at that time). I continue with these studies to this day, however I have focused on how the cells ability to produce forces is linked to its ability to sense external forces. This remains a major gap in the field as many investigators are not seeking to understand the cellular mechanism of these mechanical interactions.

a. Undyala VV, Dembo M, Cembrola K, Perrin BJ, Huttenlocher A, Elce JS, Greer PA, Wang YL, **Beningo KA.** The calpain small subunit regulates cell-substrate mechanical interactions during fibroblast migration. J Cell Sci. 2008 Nov 1;121(Pt 21):3581-8. PubMed PMID: 18840650; PubMed Central PMCID: PMC3081789. **45 citations**

b. **Beningo KA**, K. Hamao, M, Wang YL, H Hosoya. Traction forces of fibroblasts are regulated by the rho-dependent kinase but not by the myosin light chain kinase. ABB. 2006;456:224-31. PubMed PMID: **151 citations**

c. **Beningo KA,** Dembo M, Wang YL. Responses of fibroblasts to anchorage of dorsal extracellular matrix receptors. Proc Natl Acad Sci U S A. 2004 Dec 28;101(52):18024-9. PubMed PMID: 15601776; PubMed Central PMCID: PMC539758. **328 citations**

d. **Beningo, K.A.,** M. Dembo, I. Kaverina, J.V. Small, and Y.-L. Wang. 2001. Nascent focal adhesions are responsible for the generation of strong propulsive forces in migrating fibroblasts. J. Cell Biol**.** 153(4):881-887. featured cover. (Images from manuscript included in the textbook Cell and Molecular Biology, 4th Edition, by Gerald Karp). **922 citations**.

Cancer and Cell Mechanics

My laboratory focuses on cell mechanics and cancer, an area that remains poorly characterized. The first question I asked was if any correlation between the metastatic state of a cell and mechanical forces existed. My group performed a number of analysis on a panel of metastatic breast cancer cells that were derived from the same tumor but possessing different metastatic abilities, this was the first of such a study and we found that these parameters did change with the metastatic state of the panel (b). We have also focused on a different type of mechanical force than stiffness, that being one of tugging on the extracellular matrix. I reasoned that cells in the microenvironment were remodeling the matrix and migrating through it, both of which would cause the tugging force. The question was whether a tumor cell would use this signal and if so how and when. I designed the assay that is used extensively in this proposal and we found that indeed metastatic cells respond to tugging forces by invading more efficiently, a response unique to highly metastatic cells(a,c). This work attracted much media attention and multiple speaking offers when first published because it is the first to show that this specific form of force can have such a dramatic impact on cancer invasion.

a. Gasparski, AN, Wilson, JT, Banerjee, A., and **KA. Beningo**. The role of PAK1 in the maturation of invadopodia during transient mechanical stimulation. Front Cell Dev Biol. 2019 Nov 6;7:269. doi: 10.3389/fcell.2019.00269. **10 citations**

b. Indra, I., V. Undyala, C.E. Kandow, U. Thirumurthi, M. Dembo and **KA Beningo.** 2011. An In-vitro correlation of mechanical forces and metastatic capacity. Phys Biol. Feb;8(1):015015.Pubmed PMID: 21301068. *Featured cover article. Top 3% of downloads for the suite of journals published by the Institute of Physics (IOP)*. **91 citations**

c. Menon S, **Beningo KA.** Cancer cell invasion is enhanced by applied mechanical stimulation. PLoS One. 2011 Feb 17;6(2):e17277. PubMed PMID: 21359145; PubMed Central PMCID: PMC3040771. **104 citations**

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1VkD-SAnkyekw/bibliography/public/