BIOGRAPHICAL SKETCH

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NAME: Minna Roh-Johnson

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POSITION TITLE: Assistant Professor, University of Utah

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
Simon Fraser University	B.S.	08/2002	Biology
Simon Fraser University	M.S.	07/2004	Molecular Biology and Biochemistry
University of North Carolina – Chapel Hill	Ph.D.	05/2010	Molecular, Cell and Developmental Biology
Albert Einstein College of Medicine		10/2013	Cancer Cell Biology
Fred Hutchinson Cancer Research Center		12/2017	Cancer Cell Biology

A. Personal Statement

I am an Assistant Professor, and an advocate for enhanced research and career development for trainees in science. I also have a track record of being in involved in initiatives aimed at increasing diversity in STEM, beginning as a graduate student involved in URM undergraduate research opportunities and now as a Faculty Co-Mentor of the University of Utah SACNAS Chapter. Scientifically, my lab studies metastasis. Metastasis is still the main cause of cancer-related deaths. Our inability to combat the disease is largely due to our inability to identify which cells will metastasize. In addition to genetic changes in tumor cells, local interactions within the microenvironment modulate tumor cell behavior. With the initial successes of immunotherapies, a wealth of studies has defined roles for many of the tumor microenvironmental immune components. However, intercellular communication strongly underlies therapeutic failure and tumor relapse. Future immunotherapies should be developed with a clear understanding of how immune cells function and under which contexts. There still remains paradoxical roles for certain cells in the microenvironment, even for those that densely populate the tumor microenvironment such as tumor-associated macrophages. Tumor-associated macrophages can both promote and block tumorigenesis. By visualizing and manipulating highly migratory tumor cells and their microenvironment in vivo, we found that tumor-associated macrophages transfer their cytoplasmic contents to melanoma cells in a cell contact-dependent manner. Remarkably, there is a striking correlation between tumor cells that have received macrophage cytoplasm and tumor cell dissemination in vivo. Remarkably, 70% of tumor cells that received macrophage cytoplasm disseminated from the primary tumor in zebrafish models. We found the same results in a murine model of melanoma in which there was an equally striking correlation (80%) between macrophage cytoplasmic transfer to tumor cells and subsequent tumor cell metastasis. We hypothesize that this unique mode of cell-to-cell communication allows for target cell specificity, and could represent a mechanism by which tumor cells obtain the necessary components for metastasis from its environment. A key question that arises from these studies is what are the components transferred from macrophages to tumor cells for metastasis, cell biologically, how are these components transferred, and what is the result of this transfer on metastatic potential? We propose to address these questions to generate a strong foundational knowledge of the diverse functions of immune cells in the tumor microenvironment to develop more effective immunotherapies.

B. Positions and Honors

Positions and Employment

2010 – 2013 Postdoctoral Fellow with John Condeelis, AECOM, NY, USA
2013 – 2017 Postdoctoral Fellow with Cecilia Moens, FHCRC, WA, USA
2018 – Present Assistant Professor, University of Utah, UT, USA

Other Experience and Professional Memberships

2005 – Present American Society for Cell Biology, Member
2020 – Present American Society for Cell Biology, Ambassador
2019 – 2020 Mary Kay Foundation Innovative/Translation Research Award, Reviewer

Honors

2003 Frank A. Linville Scholarship in Sensory Science
2003 British Columbia Medical Services Foundation Summer Scholarship
2004 Simon Fraser University Graduate Fellowship
2006 UNC Cell and Molecular Biology Travel Grant
2007 First Prize for Best Student Talk, 2007 Southeast Reg. Mtg of Society for Dev. Biol
2008 UNC Dissertation Completion Fellowship
2011 American Society for Cell Biology Childcare Award
2011 NCI NRSA F32 Award
2012 American Society for Cell Biology Travel Grant
2015 NCI K99/R00 Transition to Independence Award
2019 Mary Kay Foundation Cancer Research Project Award

C. Contributions to Science

1. My early publications describe how cytoskeletal networks drive cellular movements. Using *C. elegans* as a model to dissect the molecular basis of morphogenesis, I found that actomyosin contractions on the apical surface of gastrulating cells preceded cell shape changes. Through high-resolution live imaging, genetics, and measurements in cortical tension, I found that constriction of the apical surface appears to be triggered not by a change in cortical tension, but by dynamic linking of apical junctions to an already contractile apical cortex. These experiments addressed force generation and cytoskeletal regulation of epithelial morphogenesis, which are central issues in developmental biology. I designed and performed the experiments related to this work.
    a) **Roh-Johnson, M**. and Goldstein B. (2009) *in vivo* roles for Arp2/3 in cortical actin organization during C. elegans gastrulation. J. Cell Sci. Nov 1; 122: 3983-93. PMCID: PMC2773197.
    b) Sawyer, J.M., Harrell, J.R., Shemer, G., Sullivan-Brown, J., **Roh-Johnson, M**., and Goldstein, B. (2010) Apical constriction: A cell shape change that can drive morphogenesis. Dev Bio. May 1; 341(1):5-19. PMCID: PMC2875788.
    c) Werts AD, **Roh-Johnson M**, Goldstein B (2011). Dynamic localization of C. elegans TPR-GoLoco proteins mediates mitotic spindle orientation by extrinsic signaling. *Development*, *138*(20), 4411-22. PMCID: PMC3177311.
    d) **Roh-Johnson, M**.*, Shemer, G.*, Higgins, C.D., McClellan, J., Werts, A.D., Tulu, U.S., Gao, L., Betzig, E., Kiehart, D.P., and Goldstein, B. (2012). Triggering a cell shape change by exploiting pre-existing actomyosin contractions. Science 9;335(6073): 1232-5. *equal contributing authors. PMCID: PMC3298882.

2. I subsequently sought to understand how developmental paradigms regulating cell motility are recapitulated in disease cells *in vivo*. Cells in the environment were known to influence tumor cell behavior, but the mechanisms underlying these dynamic processes were unknown. We took advantage of *in vitro* approaches to understand signaling mechanisms that regulate this process. I designed and performed the experiments related to this work.
    a. Bravo-Cordero JJ, Sharma VP, **Roh-Johnson M**, Chen X, Eddy R, Condeelis J, Hodgson L (2013). Spatial regulation of RhoC activity defines protrusion formation in migrating cells. *J Cell Sci*, *126*(Pt 15), 3356-69

b. Zhou ZN, Sharma VP, Beaty BT, **Roh-Johnson M**, Peterson EA, Van Rooijen N, Kenny PA, Wiley HS, Condeelis JS, Segall JE (2014). Autocrine HBEGF expression promotes breast cancer intravasation, metastasis and macrophage-independent invasion in vivo. *Oncogene*, *33*(29), 3784-93
c. **Roh-Johnson M.**, Bravo-Cordero J.J., Pastialou A., Sharma V.P., Liu H., Hodgson L., Condeelis J. Macrophage contact induces RhoA GTPase signaling to trigger tumor cell intravasation. (2014). Oncogene. Aug 14;33(33):4203-12. PMCID: PMC3962803.
d. Pignatelli J, Bravo-Cordero JJ, **Roh-Johnson M,** Gandhi SJ, Wang Y, Chen X, Eddy RJ, Xue A, Singer RH, Hodgson L, Oktay MH, Condeelis JS (2016). Macrophage-dependent tumor cell transendothelial migration is mediated by Notch1/MenaINV-initiated invadopodium formation. Sci Rep. 2016. Nov 30;6:37874.

3. To understand the role of macrophages in cancer cell invasion *in vivo*, I developed a reliable novel zebrafish assay. I worked in collaboration with colleagues to use this approach to understand intrinsic regulation of cell invasion. I designed and performed the experiments related to this work.
    a. Anderson, S., Poudel, K.R., **Roh-Johnson, M.**, Brabletz T., Yu M., Borenstein-Auerbach, N., Grady, W.N., Bai, J., Moens, C.B., Eisenman, R.N., Conacci-Sorrell, M. (2016). MYC-nick promotes cell migration by inducing fascin expression and Cdc42 activation. PNAS, 113(37):E5481-90 PMCID 27566402.
    b. Poudel K.R., **Roh-Johnson M**., Su A., Ho T., Mathsyaraja H., Anderson S., Grady W.M., Moens C.B., Conacci-Sorrell M., Eisenman R.N., Bai J. (2018). Developmental Cell. Jun 18;45(6):738-752. PMCID: PMC29920278.

4. Using *in vivo* zebrafish and mouse models, I discovered a novel mode of cell-contact based communication between macrophages and cancer cells. Macrophages physically contact cancer cells to directly transfer cytoplasmic contents or facilitate cell-cell fusion. These findings will aid in the identification of novel molecules to inhibit in the clinic, and may reveal processes to modify to specifically deliver drugs to cancer cells. I designed and performed the experiments related to this work.
    a. **Roh-Johnson M,** Shah AN, Stonick JA, Poudel KR, Kargl, J, Yang, GH, di Martino J, Hernandez RE, Gast CE, Zarour LR, Antoku S, Houghton, AM, Bravo-Cordero JJ, Wong MH, Condeelis J, Moens CB. Macrophage-dependent cytoplasmic transfer drives melanoma invasion *in vivo*. (2017). Developmental Cell. Dec4;43(5):549-562. PMCID: PMC5728704.
    b. Gast CE, Silk AD, Zarour L, Riegler L, Burkhart JG, Gustafson KT, Parappilly MS, **Roh-Johnson** M, Goodman JR, Olson B, Schmidt M, Swain JR, Davies PS, Shasthri V, Iizuka S, Flynn P, Watson S, Korkola J, Courtneidge SA, Fischer JM, Jaboin J, Billingsley KG, Lopez CD, Burchard J, Gray J, Coussens LM, Sheppard BC, Wong MH. (2018). Cell fusion potentiates tumor heterogeneity and reveals circulating hybrid cells that correlate with stage and survival. Science Advances. Sep 12;4(9):eaat7828. PMCID: PMC6135550

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/minna.roh.1/bibliography/public/

D. Research Support

Ongoing Research Support

R00 CA190836 (w/ NCE) Roh (PI) 01/01/2018 – 12/31/2021
Cell Biological Mechanisms of Melanoma Cell Motility in Vivo
The goal of this proposal is to identify markers that will aid doctors in detecting harmful melanoma and also be potentially used as a target for treatment of melanoma
Role: PI

Mary Kay Foundation Roh (PI) 10/01/2019 – 09/31/2021
Immune cell contributions to breast cancer cell metabolism during metastasis
The goal of this proposal is to design future drugs targeting mitochondria, and to generate a strong foundational knowledge of the diverse functions of immune cells in breast cancer.
Role: PI

Department of Defense Roh (PI) 07/01/2020 – 06/30/2023
Mitochondrial Horizontal Transfer in Triple-Negative Breast Cancer
The goal of this proposal is to determine whether transferred mitochondria acts as a signal to regulate tumor growth in triple negative breast cancer.

American Cancer Society Roh (PI) 09/01/2020 – 08/31/2024
Macrophage mitochondrial transfer during metastasis
The goal of this proposal is to identify key molecular players underlying macrophage mitochondrial transfer to melanoma and breast cancer cells.

Completed Research Support

F32 CA159663 Roh (PI) 09/01/2011 – 05/24/2014
Identifying the Mechanisms Governing Mena-Induced Tumor Cell Dissemination
The goal of this project is to understand the molecular basis of tumor cell spread, with the goal of uncovering new markers to identify high-risk patients and ultimately develop new anti-metastatic therapies
Role: PI

Cooperative Center of Excellence in Hematology Award Roh (PI) 05/31/2014 – 06/01/2015
An In Vivo CRISPR/Cas9 Screen for Genes Controlling Macrophage and Neuron Migration
The goal of this project is to identify genes required for macrophage infiltration to tumor cells and neuronal migration in the tumor microenvironment
Role: PI

R21 CA195126 Moens (PI) 02/01/2015 – 01/31/2017
In Vivo Cell-Cell Interactions Regulating Melanoma Metastatic Cell Behaviors
The goal of this proposal is to identify biomarkers to aid in the treatment of melanoma
Role: Key Personnel

K99 CA190836 Roh (PI) 09/01/2015 – 12/31/2017
Cell Biological Mechanisms of Melanoma Cell Motility in Vivo
The goal of this proposal is to identify markers that will aid doctors in detecting harmful melanoma and also be potentially used as a target for treatment of melanoma
Role: PI