BIOGRAPHICAL SKETCH

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NAME: Jeffrey J. Essner

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

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
University of Iowa	B.S.	1983-1987	Biology
University of Minnesota	Ph.D.	1988-1996	Mol. Cell. Dev. Genetics
Scripps Research Institute	Postdoctoral	1996-1997	Neurobiology and Developmental Biology

A. Personal Statement

One of the major focuses of my laboratory is to develop both forward and reverse genetic tools in zebrafish. Currently, we routinely utilize transposon, recombinase, TALEN and CRISPR/Cas9 systems for genome engineering. I have broad training in molecular, cell and developmental biology and more than 25 years of experience working with zebrafish, first as a graduate student and later as a postdoctoral researcher and research associate. Since my initial exposure to zebrafish, I have had a passion for the beauty of the optically clear embryos that allow detailed examination of development and the powerful genetic opportunities of the system. As a research associate at the Huntsman Cancer Institute, I was trained in cardiovascular biology with a focus on understanding the mechanisms of left-right asymmetry in development. Since 2002, I have focused my efforts on identifying novel anti-angiogenesis mechanisms. As the Scientific Director at Discovery Genomics, Inc., I led and conducted morpholino-based screens in zebrafish to identify novel genes required for angiogenesis and innate immunity. As the PI of my laboratory at Iowa State University, I have further examined the identified genes using small molecule screens in zebrafish embryos. My laboratory has developed several transgenic models in zebrafish to follow endothelial tube formation in living embryos. More recently, my laboratory has been a part of developing transformative methodologies to mutate and knockout genes in zebrafish that are broadly applicable to other organisms. I have over the last 12 years to developed methodologies for forward and reverse genetic approaches in zebrafish.

I have had the great pleasure of collaborating with Drs. Ekker and Clark over the last 12 years. Some publications listed below highlight our collaborations, but this is not a complete list.

1. Larson, J.D., Wadman, S.A., Chen, E., Kerley, L., Clark, K.J., Eide, M., Lippert, S., Nasevicius, A., Ekker, S.C., Hackett, P.B., and Essner, J.J., (2004) Expression of *VE-cadherin* in zebrafish embryos: A new tool to evaluate vascular development. *Developmental Dynamics* 231, 204-213. PMID: 15305301
2. Wang Y., Kaiser M.S., Larson J.D., Nasevicius A., Roberg-Perez S., Clark, K.J., Hackett P.B., Ekker S., McGrail M., Essner J.J. (2010) Moesin1 and Ve-cadherin are required in endothelial cells during *in vivo* tubulogenesis. *Development* 137(18): 3119-28. PMID: 20736288
3. Liao, H.K., Wang, Y., Noack-Watt, K.E., Wen, Q., Breitbach, J., Kemmet, C.K., Clark, K.J., Ekker, S.C., Essner, J.J., McGrail, M. (2012) Tol2 gene trap integrations in the zebrafish amyloid precursor protein genes appa and aplp2 reveal accumulation of secreted APP at the embryonic veins. Developmental Dynamics 241(2): 415-25. PMID: 22275008

4. Bedell, V.M., Wang, Y., Campbell, J.M., Poshusta, T.L., Starker, C.G., Krug, R.G., Tan, W., Penheiter, S.G., Ma, A.C., Leung, A.Y., Fahrenkrug, S.C., Carlson, D.F., Voytas, D.F., Clark, K.J., Essner, J.J., Ekker, S.C. (2012) *in vivo* genome editing using a high-efficiency TALEN system. Nature 491(7422): 114-118. PMID: 23000899

As Scientific Director of a small biotech company and as PI of my laboratory at ISU, I have directly supervised and trained 3 PhD and 2 MS graduate students. I currently mentor 4 PhD students on vascular and cancer related projects. I have also served on over 40 Program of Study Committees for graduate students, and was the head of our Genetics and Genomics Graduate Program at ISU.

B. Positions and Honors

Positions and Employment

1985-1987.	Undergraduate Research Assistant, Department of Biochemistry, University of Iowa, Iowa City, IA.
1987-1988.	Research Assistant, Department of Biochemistry, University of Iowa, Iowa City, IA.
1988-1996.	Graduate Student Assistant, Program in Molecular, Cellular, Developmental Biology, and Genetics, University of Minnesota, St. Paul, MN.
1996-1997.	Post Doctoral Training, Scripps Research Institute, La Jolla, CA.
1997-2002.	Research Associate, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT.
2002-2005	Scientific Director, Discovery Genomics, Inc., Minneapolis, MN.
2005-2011	Assistant Professor, Department of Genetics, Development and Cell Biology, Iowa State University, Ames, IA.
2011-	Associate Professor, Department of Genetics, Development and Cell Biology, Iowa State University, Ames, IA.
2014-present	Faculty Leader for HHMI-supported Freshman Research Initiative at Iowa State University
2014-present	Director of Graduate Education for the Genetics and Genomics Program at Iowa State University

Other Experience and Professional Memberships

2006-present	Society for Developmental Biology
2008-present	American Society for Cell Biology
2009-present	Iowa Academy of Science
2008-present	North American Vascular Biology Organization
2009-present	Council for Undergraduate Research
2008	Founder of Recombinetics, Inc. with Drs. Scott Fahrenkrug, Karl Clark, Perry Hackett, and Daniel Voytas
2009	National Science Foundation ad hoc reviewer
2009, 2014	National Institutes of Health (NIH) Peer Review Committee - Special Emphasis Panel on Angiogenesis
2012	NIH Peer Review Committee – Neural Cell Fate Panel
2012, 2013	NIH Peer Review Committee – Zebrafish Tools Panel (co-chair in 2013)
2013	NIH Peer Review Committee – Zebrafish Screens Panel (co-chair), Special Emphasis Panel Complex Phenotypes, Special Emphasis Panel Cardiovascular Sciences
2013	Children's Tumor Foundation Review Committee – Young Investigator Awards Panel
2014, 2015	NIH Peer Review Committee - NCI Exploratory/Developmental Research Grant Program
2014	National Institutes of Health Peer Review Committee – Beyond HAART: Innovative Approaches to Cure HIV-1, U19 applications
2015	National Institutes of Health Peer Review Committee – NIH Special Emphasis Panel to review R15 grant applications- Enhancing Developmental Biology Research at Undergraduate Institutions
2015	National Institutes of Health Peer Review Committee – Cellular and Molecular Biology of Glia (CMBG) Study Section – Transformative Research Award

Honors

1992	Minnesota Sea Grant Fellow
1994-1995	Graduate School Fellow, University of Minnesota
2008	Faculty Escort at Undergraduate Commencement, Recognition for Mentoring
2009	Outstanding Undergraduate Mentor, Biology and Genetics Programs, Iowa State University

Patents

1. Granted GLOF;011US Red, green and yellow recombinant constructs and transgenic fluorescent zebrafish there from. Inventors Blake, A., Crockett, R., Hackett, P.B., Nasevicius, A., S., Essner, J.J.
2. Granted W3021.19US01. Integration-site directed vector systems. Inventors: Hackett, P.B. and Essner, J.J.
3. Granted US 20110059160 A1U.S. Serial No. 61/230,784. METHODS AND COMPOSITIONS FOR TARGETED GENE MODIFICATION. Inventors: Essner, J.J., Liao, H-K., and Fahrenkrug, S.

C. Contribution to Science

29 peer-reviewed, research publications at
http://www.ncbi.nlm.nih.gov/sites/myncbi/12anrvJeywgAr/bibliography/48708972/public/?sort=date&direction=ascending
My contributions to science include the four general areas:

Genome engineering – Since my time as the Scientific Director at Discovery genomics, my research group has focused on the use of recombinases and site-specific nucleases for genome manipulation. Work in this area includes development of novel methods for gene targeting and unique applications of technology to answer questions in vascular and cancer biology. This work has resulted in three patents, the formation of a biotech company with Dr. Scott Fahrenkrug called Recombinetics, Inc. and the following publications:

1. Liao, H.K., Essner, J.J. (2011) Use of RecA fusion proteins to induce genomic modifications in zebrafish. Nucleic Acids Research 39(10): 4166-79. PMID: 21266475
2. Bedell, V.M., Wang, Y., Campbell, J.M., Poshusta, T.L., Starker, C.G., Krug, R.G., Tan, W., Penheiter, S.G., Ma, A.C., Leung, A.Y., Fahrenkrug, S.C., Carlson, D.F., Voytas, D.F., Clark, K.J., Essner, J.J., Ekker, S.C. (2012) *in vivo* genome editing using a high-efficiency TALEN system. Nature 491(7422): 114-118. PMID: 23000899 (cited 421 times)
   Bedell et al. (2012) was featured in Pennisi, E. (2012) News Focus. The tale of the TALEs. *Science* 338: 1408-1411. My laboratory contributed images of zebrafish embryos for this review. This manuscript was also featured on the ISU homepage http://www.news.iastate.edu/news/2012/09/28/zebrafishnature, on the *Nature* homepage, and is associated with a *Nature* News story http://www.nature.com/news/custom-gene-editing-rewrites-zebrafish-dna-1.11463
3. Ma L., Jeffery W.R., Essner J.J., Kowalko J.E. (2015) Genome editing using TALENs in Blind Mexican Cavefish, *Astyanax mexicanus*. PLoS One. 10(3): e0119370. PMID: 25774757
4. Kuo T-H., Kowalko J.E., DiTommaso T., Nyambi M., Montoro D.T., Essner J.J., Whited J.L. (2015) TALEN-mediated gene editing of the *thrombospondin-1* locus in axolotl. Regeneration, 2(1): 37-43. *index in progress*.
5. Solin, S.L., Shive, H.R., Woolard, K.D., Essner, J.J., McGrail, M.A., (2015) Rapid tumor induction in zebrafish by TALEN-mediated somatic inactivation of the *retinoblastoma1* tumor suppressor *rb1*. Scientific Reports 5:13745. PMID: 2634538

Transposon-mediated mutagenesis and transgenesis – My laboratory at Iowa State University in collaboration with Dr. McGrail has actively developed and applied transposon tools to the zebrafish genome for forward genetic screens, vascular biology and cancer gene discovery.

1. McGrail, M., Hatler, J.M., Kuang, X., Liao, H.K., Nannapaneni, K., Watt, K.E., Uhl, J.D., Largaespada, D.A., Vollbrecht, E., Scheetz, T.E., Dupuy, A.J., Hostetter, J.M., Essner, J.J. (2011) Somatic mutagenesis with a Sleeping Beauty transposon system leads to solid tumor formation in zebrafish. PLoS One 6(4): e18826. PMID: 21533036
2. Liao, H.K., Wang, Y., Noack-Watt, K.E., Wen, Q., Breitbach, J., Kemmet, C.K., Clark, K.J., Ekker, S.C., Essner, J.J., McGrail, M. (2012) Tol2 gene trap integrations in the zebrafish amyloid precursor protein

genes appa and aplp2 reveal accumulation of secreted APP at the embryonic veins. Developmental Dynamics 241(2): 415-25. PMID: 22275008

Liao et al. (2012) was featured with a cover image for Developmental Dynamics.

3. Solin S.L., Wang Y., Mauldin J., Schultz L.E., Lincow D.E., Brodskiy P.A., Jones C.A., Syrkin-Nikolau J., Linn J.M., Essner J.J., Hostetter J.M., Whitley E.M., Cameron J.D., Chou H-h., Severin A.J., Sakaguchi D.S., McGrail M. (2014) Molecular and cellular characterization of a zebrafish optic pathway tumor line implicates glia-derived progenitors in tumorigenesis. PLOS ONE 9(12): e114888 PMID: 25485542
4. Craig M.P., Grajevskaja V., Liao H.K., Balciuniene J., Ekker S.C., Park J.S., Essner J.J., Balciunas D., Sumanas S. (2015) Etv2 and Fli1b function together as key regulators of vasculogenesis and angiogenesis. Arterioscler Thromb Vasc Biol. 2015 Feb 26. pii: ATVBAHA.114.304768. PMID: 25722433

Developmental vascular biology – My laboratory has extensively used the zebrafish model to assess the cell biology that contributes to endothelial tube formation. We have developed several transgenic lines that are broadly used by the vascular community and have contributed to the understanding of how cellular junctions are involved in generation of vascular tubes.

1. Larson, J.D., Wadman, S.A., Chen, E., Kerley, L., Clark, K.J., Eide, M., Lippert, S., Nasevicius, A., Ekker, S.C., Hackett, P.B., and Essner, J.J., (2004) Expression of *VE-cadherin* in zebrafish embryos: A new tool to evaluate vascular development. *Developmental Dynamics* **231**, 204-213. PMID: 15305301 (cited 67 times)
2. Miao, Z., Luker, K.E., Summers, B.C., Berahovich, R., Bhojani, M.S., Rehemtulla, A., Kleer, C.G., Essner, J.J., Nasevicius, A., Luker, G.D., Howard, M.C., and Schall, T.J. (2007) CXCR7 (RDC1) promotes breast and lung tumor growth in vivo and is expressed on tumor-associated vasculature. *Proc. Natl. Acad. Sci. USA* 104(40), 15735-40. PMID: 17898181 (cited 432 times)
3. Kalén M, Wallgard E, Asker N, Nasevicius A, Athley E, Billgren E, Larson JD, Wadman SA, Norseng E, Clark KJ, He L, Karlsson-Lindahl L, Häger AK, Weber H, Augustin H, Samuelsson T, Kemmet CK, Utesch CM, Essner JJ, Hackett PB, Hellström M. (2009) Combination of reverse and chemical genetic screens reveals angiogenesis inhibitors and targets. *Chem Biol.* 16(4), 432-41. PMID: 19389629 (cited 29 times)
4. Wang, Y., Kaiser, M.S., Larson, J.D., Nasevicius, A., Clark, K.J., Wadman, S.A., Roberg-Perez, S., Ekker, S.C., Hackett, P.B., McGrail, M.A., and Essner, J.J. (2010) Moesin1 and Ve-cadherin are required in endothelial cells during *in vivo* tubulogenesis. *Development* 137(18): 3119-28. PMID: 20736288 (cited 74 times)

   Wang et al., 2010 was selected by the Faculty of 1000 Biology by Andrew Kowalczyk, Emory University. "This article provides novel insights into the process of endothelial tubulogenesis by revealing interdependent and essential roles for the adherens junction protein VE-cadherin and the ERM family protein moesin1. The results of the study indicate that both proteins are important in establishing endothelial cell polarity. A central observation in this study is that intersegmental vessel development in the zebrafish occurs by a cord hollowing mechanism rather than a cell hollowing mechanism. The authors suggest that distinct mechanisms of lumen formation are used during the formation of different vessels."
5. Craig M.P., Grajevskaja V., Liao H.K., Balciuniene J., Ekker S.C., Park J.S., Essner J.J., Balciunas D., Sumanas S. (2015) Etv2 and Fli1b function together as key regulators of vasculogenesis and angiogenesis. Arterioscler Thromb Vasc Biol. 2015 Feb 26. pii: ATVBAHA.114.304768. PMID: 25722433

Left/right development – Since my time as a Research Associate in Dr. H. Joseph Yost's laboratory, I have actively contributed to our understanding of how the left/right axis is initiated. My work in this area has resulted in several important contributions that have defined the field. My contributions include defining pathways for left/right development, establishing evolutionarily conserved mechanisms and contributing to the understanding of the morphogenesis of a ciliated organ of asymmetry.

1. Essner, J.J., Branford, W.W., Zhang, J., and Yost, H.J. (1999). Mesendoderm and left-right brain, heart, and gut development are differentially regulated by *pitx2* isoforms. *Development* **127,**1081-1093. PMID: 10662647 (cited 176 times)
2. Bisgrove, B.W., Essner, J.J., and Yost, H.J. (2000). Multiple pathways in the midline regulate concordant brain, heart and gut left-right asymmetry. *Development* **127**, 3567-3579. (cited 169 times)
3. Essner, J.J., Vogan, K.J., Wagner, M.K., Tabin, C.J., Yost, H.J., and Brueckner, T. (2002). Conserved Function for Embryonic Nodal Cilia. *Nature* **418**(6893), 37-38. PMID: 12097899 (cited 288 times)
   Essner et al., 2002 was selected by the Faculty of 1000 three times by George Witman, University of Massachusetts Medical School, Alejandro Sanchez-Alvarado, HHMI, University of Utah School of Medicine and Patrick Tam, Childrens Medical Research Institute, Australia. Dr. Sanchez-Alvarado commented "This brief communication reports that left-right dynein heavy chain gene (Lrdr) expression precedes the appearance of conserved asymmetries in the early embryos of chicks, Xenopus and zebrafish. This observation suggests that ciliary mechanism underlying the establishment of left/right handedness in vertebrates may be evolutionarily conserved." Scott Gilbert features Essner et al., 2002 in the textbook "Developmental Biology".
4. Essner, J.J., Amack, J.D., Nyholm, M.K., Harris, E.H., and Yost, H.J. (2005) Kupffer's Vesicle is a Ciliated Organ of Asymmetry in the Zebrafish Tail that Initiates Left-Right Development of the Brain, Heart and Gut. *Development* **132**(6), 1247-1260. PMID: 15716348
   Essner et al., 2005 was selected by the Faculty of 1000 by Sebastian Shimeld, University of Oxford, UK. "This reports the interesting finding that cilial activity in Kupffer's vesicle, a small transient organ of embryonic fish, influences subsequent development of left-right asymmetry." Scott Gilbert features Essner et al., 2002 in the textbook "Developmental Biology".
5. Hatler J.M., Essner J.J., and Johnson R.G. (2009) A gap junction connexin is required in the vertebrate left-right organizer. *Dev. Biol.* 336(2): 183-91. PMID: 19799895
   Hatler et al., 2009 was selected by the Faculty of 1000 Biology by Eric Beyer, University of Chicago. "This is the best paper relating gap junctions and development in several years."

D. Research Support

Ongoing Research Support

5R01GM088424 NIH NIGMS Essner (PI) 09/01/2011-08/31/2016
in vitro and *in vivo* mechanisms of endothelial tube formation
The goal of this application is to develop *in vitro* and *in vivo* models for endothelial tubulogenesis.
Role: PI

R03CA182061 NIH NCI McGrail (PI) 12/01/2013-11/30/2015
Sleeping Beauty transposon system for mutagenesis in zebrafish
The goal of this grant is to utilize the Sleeping Beauty transposon system for somatic mutagenesis to study metastasis.
Role: Co-PI

Howard Hughes Medical Institute Oglive (PI) 09/01/2014-08/31/2019
Engage to Excel at Iowa State University
The goal of this application is to increase authentic research experiences for undergraduates at the freshmen level.
Role: Co-P.I.