BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES**.

NAME: Klomp, Jeffrey

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

POSITION TITLE: Research Assistant 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
Grand Valley State University, Allendale, MI	BS	12/2003	Biology and Biochemistry
Central Michigan University, Mount Pleasant, MI	MS	06/2007	Population Genetics
Van Andel Institute Graduate School, Grand Rapids, MI	PHD	06/2012	Cellular and Molecular Biology and Genetics
University of Chicago, Chicago, IL	Postdoctoral Scholar	02/2015	Developmental Molecular Biology
University of Illinois, Chicago, IL	Postdoctoral Fellow	10/2017	Molecular and Cellular Biology

A. Personal Statement

I am both an experimental and computational biologist by training and have over 15 years of experience in genetics and cancer biology. My early work focused on the genetic mechanisms leading to metabolic defects in kidney tumors of patients with BHD Syndrome and repurposing genetic modules during development. My current interests relate to characterizing and understanding how different genetic modules are driven by oncogenes in specific cell types, such as the set of genes driven by mutationally activated KRAS in pancreatic cancer cells and precancerous cells. I am also interested in how environmental attributes such as hypoxia drive changes in cell programming and oncogenic mechanisms. I utilize primary and xenograft cell cultures, RNA-sequencing, hypoxic growth conditions, dose-response assays, gene expression modulation, and various other techniques as well as numerous public data sets and bioinformatic tools to experimentally interrogate cellular activities. I have helped supervise numerous trainees from high school students to graduate students.

B. Positions and Honors

Positions and Employment

2004	Analytical Laboratory Technician, Access Business Group, Grand Rapids, MI
2005 – 2007	Graduate Teaching Assistantship, Central Michigan University, Mt. Pleasant, MI
2007 – 2012	Graduate Researcher, VanAndel Research Institute, Grand Rapids, MI
2012 – 2015	Postdoctoral Scholar, University of Chicago, Chicago, IL
2015 (8 mos)	Statistical Modeler, Quicken Loans, Detroit, MI
2015 – 2017	Postdoctoral Fellow, University of Illinois, Chicago, IL
2018 – 2019	Research Associate, University of North Carolina, Chapel Hill, NC
2020 – present	Research Assistant Professor, University of North Carolina, Chapel Hill, NC

<u>Honors</u>

2000	Michigan Competitive Scholars Grant, State of Michigan
------	--

- 2005 Grants-In-Aid of Research Grant, Sigma Xi
- 2005 Student Research and Creative Endeavors Exhibition Grant, Central Michigan University
- 2006 Summer Student Research Assistantship, Central Michigan University
- 2013 Travel Grant, Arthropod Genomics Symposium
- 2014 Platform Presentation, Annual Drosophila Research Conference
- 2014 Award 1355057 \$500,000 to Schmidt-Ott (major contributor), National Science Foundation
- 2015 NIH T32 Fellowship (\$48,000 + travel/research stipend)
- 2016 Chicago Biomedical Consortium Research Award (\$15,000)
- 2016 NIH T32 Fellowship (\$51,000 + travel/research stipend)

C. Contributions to Science

- 1. Characterization of gene expression modules in cancer. A major continuing challenge in cancer diagnoses and treatments is understanding variations in individual patients and across tumor types that lead to differences in progression or efficacy of therapeutics. While working with kidney oncologists Dr. Bin Teh and Dr. Kyle Furge, I investigated the molecular underpinnings of a unique class of renal tumors found in patients with a rare hereditary disease, known as Birt-Hogg-Dubé Syndrome. We showed these tumors exhibited deregulation of a gene expression module for mitochondrial oxidative phosphorylation metabolism that was attributed to mutations in the gene *FLCN*. This discovery strengthened support for the role of FLCN in the AMPK PGC-1α signaling axis (Klomp *et al.* 2010a). In additional work, I summarized gene expression modules and approaches in kidney cancer (Klomp *et al.* 2010b, Klomp *et al.* 2013).
 - a. **Klomp, J.A.**, *et al.* (2010a). Birt-Hogg-Dube renal tumors are genetically distinct from other renal neoplasias and are associated with up-regulation of mitochondrial gene expression. <u>BMC Med.</u> <u>Genomics</u> 3, 59.
 - b. Klomp, J., Teh, B., and Furge, K. (2010b). An Integrated Oncogenomic Approach: From Genes to Pathway Analyses. In <u>An Omics Perspective on Cancer Research</u>, W.C.S. Cho, ed. (Springer New York), pp. 31–50.
 - c. **Klomp, J.**, Dykema, K., Teh, B.T., and Furge, K. (2013). Molecular Biology and Genetics. In <u>Renal</u> <u>Cancer</u>, J.A. Libertino, ed. (Springer New York), pp. 19–37
- 2. Identification of transcriptional controls of vascular endothelial cells under hypoxic stress. Our understanding of the diverse role that endothelial cells play in vascular biology has increased greatly in the past couple of decades. We have found their functions to be as diverse as that of non-professional antigen presenting cells for the immune response, to driving developmental and tumorigenic growth, to their classical functions for detecting oxygen stress and control of vasodilation. However, the precise gene expression programs and controls have not been elucidated fully using current high throughput technologies. Working with Dr. Asrar Malik (UIC), I have comprehensively evaluated expression modules of endothelial cells with oxygen-controlled time series experiments. Surprisingly, we found that nearly one third of the endothelial cell transcriptome is regulated by hypoxia and most changes begin within five or six hours of hypoxic exposure. We also discovered that a transient increase in the expression of a development gene, *SOX7*, controls angiogenic expression programs during hypoxia.
 - a. **Klomp, J.**, *et al.* (2020). Comprehensive transcriptomic profiling reveals SOX7 as an early regulator of angiogenesis in hypoxic human endothelial cells. <u>*J. Biol. Chem.*</u> doi: 10.1074.
- 3. Understanding how novel developmental gene expression modules and controls evolve. While at the University of Chicago I worked with a pioneer in fly model systems, Dr. Urs. Schmidt-Ott. Using carefully selected phylogenetic representatives and *de novo* approaches with high-throughput sequencing data, we identified a novel anterior morphogen gene (Klomp *et al.* 2015). This was the first gene discovered to perform a role in primary body axis formation in flies since Christiane Nüsslein-Volhard's pivotal discoveries in *Drosophila* that led to earning a Nobel Prize nearly 30 years prior. My subsequent work has identified numerous other anterior morphogen genes and led to the identification of alternative transcriptional start sites for gene expression control of primary body axis formation in embryogenesis (Yoon *et al.* 2019).

In separate research to understand the gene expression modules and controls for appendage formation, I worked with Dr. Neil Shubin (U. of Chicago). We identified reengagement of classical gene expression

modules in the posterior fins of skates and novel apical ectodermal ridge-like structures without Gli3 repressor gene expression that enable anterior growth and expansion of fins, ultimately resulting in the unique broad shape of the ray fin (Nakamura *et al.* 2015). In further collaborative work with Dr. Karen Crow (SFSU), we evaluated the transcriptional controls that enable formation of a unique appendage of cownose rays, the cephalic lobe. This is one of the only known examples of a tissue that becomes detached from an appendage and reattached to the head during development. We showed that this appendage shares expression modules with anterior fin development as well as development of another paired fin found in males, the claspers (Swenson *et al.* 2018). These results suggested the cephalic lobe was derived from expansion of anterior fin domains rather than *de novo* limb formation, deepening our understanding of the complexity in how gene expression modules are combined to derive novel appendages and is under further exploration by the group.

- a. **Klomp, J.**, *et al.* (2015). A cysteine-clamp gene drives embryo polarity in the midge Chironomus. <u>Science</u> 348, 1040–1042.
- b. Yoon, Y., **Klomp, J.**, *et al.* (2019). Embryo polarity in moth flies and mosquitoes relies on distinct old genes with localized transcript isoforms. <u>eLife</u> 8, (e46711).
- c. Nakamura, T., **Klomp, J.**, *et al.* (2015). Molecular mechanisms underlying the exceptional adaptations of batoid fins. *Proc. Natl. Acad. Sci.* 112 (52), 15940-15945.
- d. Swenson, J., **Klomp, J.**, Fisher, R.A., Crow, K.D. (2018). How the devil ray got its horns. <u>*Front. Eco. And*</u> <u>*Evol.*</u> 6, 181.

D. Additional Information: Research Support and/or Scholastic Performance

Completed Research Support

T32 HL007829-23 (PI: Malik)10/2015 – 10/2017Training Program in Lung Biology and PathobiologyUniversity of Illinois, Chicago, ILRole: Postdoctoral Research Fellow10/2015 – 10/2017