BIOGRAPHICAL SKETCH

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NAME: Sigulinsky, Crystal L.

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

POSITION TITLE: Postdoctoral Research Associate

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
Hillsdale College, Hillsdale, MI	B.S.	05/2004	Biology, Chemistry
University of Utah, Salt Lake City, UT	Ph.D.	12/2012	Neuroscience
University of Utah, Salt Lake City, UT	Postdoctoral	Current	Visual Neuroscience

A. Personal Statement

My long term research goals are to understand the connectivity of visual circuits in the retina, including how these circuits are shaped during development and how disruption of this circuitry in diseases and disorders contributes to blinding conditions. My academic and research training has provided a strong background in neuroscience, with specific training and expertise in the visual circuits of the retina, retinal development, and ultrastructural neuroanatomy. As a PhD candidate at the University of Utah, I received broad academic training in the neurosciences, as well as genetics, molecular and cellular biology, and development. Under the supervision of Dr. Edward M. Levine, I received specific training in developmental neurobiology and retinal biology, studying the integration of intrinsic and extrinsic regulation of the specification, proliferation, and neurogenesis of retinal progenitor cells using the *orJ* mouse model of microphthalmia. Building upon this training in early visual system development, my postdoctoral training under the supervision of Dr. Robert E. Marc has focused on investigating the synaptic connectivity among the retinal components of visual circuits. Dr. Marc is a leading expert in retinal circuitry and connectomics. His team has developed a complete framework for the generation of ultrastructural connectomes using automated transmission electron microscope (ATEM) imaging and a suite of visualization, annotation, and network analysis tools. His team was the first to generate an ultrastructural connectome of mammalian retina, which has expanded to include retinal connectomes for rabbit, mouse, and a rabbit model of retinitis pigmentosa. These connectomes are the highest resolution available, and the only ones capable of visualizing and post hoc confirmation of the gap junctions mediating electrical synapses. My research has focused on characterizing gap junctions in the inner plexiform of the retina and the circuits to which they contribute using these connectomes. I have been instrumental in the design and validation of several new visualization (VikingView) and connectivity analysis tools (Cell Sketches, Graffinity) in collaboration with the University of Utah's Scientific Computing and Imaging Institute and have worked with our internal programmer to advance analysis and visualization functionality of existing tools. I have trained three undergraduates, one high school student, and one technician in the annotation, visualization and analysis of connectomics datasets, and have developed and taught a 9 week course for advanced training in ultrastructural identification in transmission electron microscopy based connectomics for neural tissues. I currently lead the RC1 and RC2 annotation teams, and advise and provide technical assistance for the RPC1 team and all external collaborators. To facilitate these roles, I have completed additional training through the Undergraduate Research Mentor Development Program. Dr. Bryan W. Jones has been an active mentor and collaborator throughout my postdoctoral training. In summary, my accumulated expertise in retinal circuitry, gap junctions, ATEM, ultrastructural neuroanatomy, and connectomics, makes me well suited to successfully contribute to the proposed project.

My undergraduate research in cryobiology with Dr. Robert Miller, Jr. at Hillsdale College resulted in 2 coauthorships published under my maiden name, Crystal Lynn Cornett.

B. Positions and Honors

Positions and Employment:

2002-2004	Lab Assistant, Department of Biology, Hillsdale College, Hillsdale, MI
2004-2012	PhD Candidate, Neuroscience Program, University of Utah, Salt Lake City, UT
2012-current	Postdoctoral Research Associate, Department of Ophthalmology & Visual Sciences, University of Utah, Salt Lake City, UT

Academic and Professional Honors:

2000-2001	Consolidated Electric Cooperative Scholarship, First Place, Girl's Division, OH
2000-2004	Alex and Katherine Nason Foundation Scholarship, Hillsdale College
2000-2004	AAL All College Scholarship
2001	CRC Press Outstanding Freshman Chemistry Achievement Award, Hillsdale College
2002-2003	Frank and Frances McQuiston Science Scholarship, Hillsdale College
2003-2004	Benjamin W. Holmes Endowed Scholarship, Hillsdale College
2003	Marsden Prize for Outstanding Junior Chemistry Research, Hillsdale College
2003	LAUREATES Award, scholarship to conduct independent summer research, Hillsdale College
2004	Edwin T. Koch Award for Outstanding Senior Achievement in the Sciences, Hillsdale College
2004	Outstanding Senior Biology Major Award for academic achievement, Hillsdale College
2004	Marsden Prize for Outstanding Senior Chemistry Research, Hillsdale College
2004	Sigma Zeta Honor Award, Alpha Psi Chapter, Hillsdale College
2004	Pi Beta Phi Scholastic Award, Michigan Alpha Chapter, Hillsdale College
2004	Salutatorian, *summa cum laude*, Hillsdale College
2009-2010	Predoctoral Trainee, Training Program in Genetics, University of Utah, NIH 5T32GM007464
2010	Nominee, Elizabeth Fuhriman Gardner Prize for Outstanding Woman Student in the Health Sciences, School of Medicine, University of Utah
2010-2011	Neuroscience Achievement Award, University of Utah
2013	Best Poster Award, Neuroscience Snowbird Symposium, Intermountain Chapter, Society for Neuroscience, University of Utah
2014-2016	Postdoctoral Trainee, Vision Research Training Program, University of Utah,NIH1T32EY024234
2015	Postdoc Travel Assistance Award; Office of Postdoctoral Affairs, University of Utah

C. Contributions to Science

1. Relationship between spermatozoal membrane composition and cryopreservation success. Artificial reproductive technologies are a critical cornerstone of conservation management for endangered species across the globe. However, these technologies are dependent upon successful cryobanking of spermatozoa. Unfortunately, spermatozoa of many species exhibit poor tolerance for rapid cold shock and/or cryopreservation, resulting in loss of viability. Spermatozoal membrane lipid composition had been proposed as a determinant of cryogenic success through its effects on membrane fluidity. Thus, as an undergraduate student with Dr. Robert Miller, Jr., I investigated the relationship between membrane composition and cryogenic success by comparing the fatty acid and sterol composition of post-cryopreservation spermatozoal membranes from closely related species that differed in cryopreservation tolerance, with the goal of identifying species-specific differences that would direct the development of successful cryogenic protocols. As a part of this research, I developed a novel protocol for the characterization of sterols from spermatozoal membranes. My primary project focused on species-specific differences in membrane fatty acid and sterol composition between the blue and silver fox species. Additionally, I also investigated the impact of common storage buffers on cryopreservation success and discovered species-specific susceptibility to extender-induced changes in membrane composition and that the use of a cryo-specific extender promoted changes that trended toward the membrane composition of species with greater cryopreservation tolerance. As a side project, I analyzed the sterol composition in marsupial spermatozoa. Together, our findings in these various species argue that

cryopreservation tolerance is largely correlated with long–chain polyunsaturated fatty acid (DHA and DPA) and does not support the hypothesis that a high ratio of saturated/unsaturated membrane fatty acids and low membrane sterol composition are predictive of cryopreservation tolerance. Thus, dietary supplements of DHA or DPA may improve future cryogenic success.

a. Miller RR Jr, Sheffer CJ, Cornett CL, McClean R, MacCallum C, Johnston SD. Sperm membrane fatty acid composition in the Eastern grey kangaroo (Macropus giganteus), koala (Phascolarctos cinereus), and common wombat (Vombatus ursinus) and its relationship to cold shock injury and cryopreservation success. Cryobiology. 2004 Oct;49(2):137-48. PubMed PMID: 15351685.
b. Miller RR Jr, Cornett CL, Waterhouse KE, Farstad W. Comparative aspects of sperm membrane fatty acid composition in silver (Vulpes vulpes) and blue (Alopex lagopus) foxes, and their relationship to cell cryopreservation. Cryobiology. 2005 Aug;51(1):66-75. PubMed PMID: 16040024.

2. Development of an optimized method for preparative scale production of (^{15}N)*N*-acetylheparosan. Heparin and heparan sulfate (HS) are clinically important molecules involved in a variety of homeostatic and pathologic biological processes. These functions are mediated by high affinity interactions with specific proteins. However, heparin and HS chain complexity limits structure-function analyses and identification of critical functional groups. Nuclear magnetic resonance (NMR) spectroscopy is used to map microstructure, but extensive variability in the biological forms of heparin and HS prevents unambiguous peak assignments. Due to a low natural abundance of nuclei with net spin, isotope-enrichment is required. During a rotation project as a predoctoral student with Dr. Kuberan Balagurunathan, I sought to overcome this spectral overlap by producing isotope-enriched, sized-defined, and un-modified precursors. I developed and helped characterize an optimized method for preparative-scale production of isotopically-labeled heparin sulfate precursors from E. coli. Characterization of these oligosaccharides revealed extensive isotope enrichment and NMR spectral separation, thereby establishing valuable tools for the study of heparin and HS microstructure-function relationships, including chemoenzymatic synthesis, microstructure mapping, and binding assays.

a. Sigulinsky C, Babu P, Victor XV, Kuberan B. Preparation and characterization of (15)N-enriched, size-defined heparan sulfate precursor oligosaccharides. Carbohydr Res. 2010 Jan 26;345(2):250-6. doi: 10.1016/j.carres.2009.10.024. Epub 2009 Nov 3. PubMed PMID: 19945695; PubMed Central PMCID: PMC2812664

3. Defining the relationship between the transcription factor Vsx2 and extrinsic signaling in the regulation of retinal progenitor cell properties. The homeobox gene Vsx2 is expressed in RPCs and required for proper execution of the retinal program. In the absence of Vsx2 function, maintenance of retinal identity, RPC proliferation, and retinal neurogenesis are disrupted, with serious consequences on overall ocular development and visual function. How Vsx2 integrates with other known regulators was only beginning to be unraveled and few direct targets had been identified. In particular, an understanding of how Vsx2-mediated regulation integrated with that of extrinsic signals was lacking. Thus, in my doctoral research with Dr. Edward M Levine, I addressed this question by examining the relationships between Vsx2 and the extracellular signals and signaling pathways regulating RPC properties, using the *ocular retardation J* mouse model, which is functionally Vsx2 null, a variety of culture techniques, and the generation of genetic chimeras. In addition to defining the autonomy requirements for Vsx2 in these processes, I was able to tease apart the interdependency of the different phenotypes. I also demonstrated the requirement for Vsx2 in promoting both the reception and availability of the extrinsic signals necessary for the regulation of RPC properties, thereby ensuring the proper growth and differentiation of this important sensory tissue.

a. Sigulinsky CL, Green ES, Clark AM, Levine EM. Vsx2/Chx10 ensures the correct timing and magnitude of Hedgehog signaling in the mouse retina. Dev Biol. 2008 May 15;317(2):560-75. doi: 10.1016/j.ydbio.2008.02.055. Epub 2008 Mar 14. PubMed PMID: 18417110; PubMed Central PMCID: PMC2671289.
b. Sigulinsky CL, German ML, Leung AM, Clark AM, Yun S, Levine EM. Genetic chimeras reveal the autonomy requirements for Vsx2 in embryonic retinal progenitor cells. Neural Dev. 2015 Apr 27;10:12. doi: 10.1186/s13064-015-0039-5. PubMed PMID: 25927996; PubMed Central PMCID: PMC4450477.

4. Connectomics-based discovery of retinal circuits in the mammalian inner plexiform layer. The retina has long served as a valuable model of the central nervous system. Although the large-scale architecture of information flow is well established and the census cell classes is considered largely complete, few specific circuits had been fully identified and lack connectivity weights. Connectomics allows complete, unbiased identification of networks, including topology and connectivity attributes. Although pervasive and powerful, the role of electrical synapses in many neural circuits are poorly defined due to the small size of the gap junctions that mediate them. Thus, the primary focus of my postdoctoral research under Dr. Robert E. Marc has been to investigate the contribution of gap junctions to mammalian retinal circuitry using TEM-based ultrastructural connectomics. Examination of ganglion cell coupling revealed differential feedforward and feedback roles for partner amacrine cells and reveal complex function of ganglion cell circuitry. Examination of gap junctions formed by ON cone bipolar cells revealed a previously unappreciated contribution by gap junctions in their circuitry, particularly the prominence of within- and cross-class coupling with other ON cone bipolar cells. This investigation revealed class-specific coupling patterns and novel partnerships, and facilitated a unified classification of ON CBCs. The latter project, in particular, has proved instrumental in flushing out additional circuits, including the rod-cone cross suppression motifs that mediate the rapid, winner-take-all switch between the rod-driven dim light vision and cone-driven day vision pathways and the surprising complexity of the AII amacrine cell circuitry.

a. Sigulinsky, CL, Lauritzen, JS, Hoang, JV, Watt, CB, Jones, BW, Anderson, JR, Mohammed, S, Marc, RE. Sparse network principles of GABAergic amacrine cell heterocellular coupling. (conference abstract). The Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting 2013.
b. Marc RE, Anderson JR, Jones BW, Sigulinsky CL, Lauritzen JS. The AII amacrine cell connectome: a dense network hub. Front Neural Circuits. 2014 Sep 4;8:104. doi: 10.3389/fncir.2014.00104. eCollection 2014. PubMed PMID: 25237297; PubMed Central PMCID: PMC4154443.
c. Sigulinsky, CL, Lauritzen, JS, Emrich, DP, Rapp, CN, Sessions, AM, Pfeiffer, RL, Rapp, KD, Anderson, JR, Marc, RE. Class-specific coupling patterns among ON cone bipolar cells in the mammalian retina. (conference abstract). Society for Neuroscience 2015.
d. Lauritzen JS, Sigulinsky CL, Anderson JR, Kalloniatis M, Nelson NT, Emrich DP, Rapp C, McCarthy N, Kerzner E, Meyer M, Jones BW, Marc RE. Rod-cone crossover connectome of mammalian bipolar cells. J Comp Neurol. 2016 Jul 22. doi: 10.1002/cne.24084. [Epub ahead of print] PubMed PMID: 27447117.
e. Kerzner E, Lex A, Sigulinsky CL, Urness T, Jones BW, Marc RE, Meyer M. Graffinity: Visualizing Connectivity in Large Graphs. arXiv preprint arXiv:1703.07729. 2017 Mar 22.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/41960894

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

Ongoing Research Support
N/A

Completed Research Support
N/A