BIOGRAPHICAL SKETCH

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NAME: Kerschensteiner, Daniel

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

POSITION TITLE: Janet & Bernard Becker Professor of Ophthalmology and Visual Sciences, Neuroscience, and Biomedical Engineering

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
Georg-August University, Göttingen, Germany	MD	12/03	Neurology / Neuroscience
University College London, London, UK	Postdoctoral	02/04 – 02/05	Neuroscience Advisor: M Stocker
University of Washington, Seattle, WA	Postdoctoral	03/05 – 06/09	Neuroscience Advisor: R.O. Wong

A. Personal Statement

My group studies the development and function of neural circuits underlying vision. We combine viral and genetic engineering with imaging, electrophysiology, and computational approaches to identify mechanisms that govern circuit formation and repair, analyze information processing from individual dendrites to pathways of connected cells, and test how neural computations support visual behavior. We aim to translate our insights into strategies to restore visual functions disrupted by degenerative diseases.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022 – Present	Director of the Interdisciplinary Pathway in Vision Science, Washington University School of Medicine, St. Louis, MO
2021 – Present	Vice Chair for Research, Ophthalmology and Visual Sciences, Washington University School of Medicine, St. Louis, MO
2021 – Present	Co-Director of the Neuroscience Ph.D. Program, Washington University School of Medicine, St. Louis, MO
2019 – Present	Professor of Ophthalmology and Visual Sciences, Neuroscience, and Biomedical Engineering, Washington University School of Medicine, St. Louis, MO
2019 – Present	Editorial Board of *Cell Reports*, member
2019	Japanese Society for the Promotion of Science (JSPS), ad hoc reviewer
2021 – Present	NIH Biology and Development of the Eye study section, member
2018 – 2021	NIH Neurotransporters, Receptors, and Calcium Signaling (NTRC) study section, member
2018	Taiwanese Ministry of Science and Technology (MOST), ad hoc reviewer
2018	NIH NEI Special Emphasis Panel (R01 applications), ad hoc member
2017	NIH NEI Special Emphasis Panel (K99 applications), ad hoc member
2017	NIH NIGMS COBRE panel, ad hoc member
2017	NIH NTRC study section, ad hoc member
2017, 2022	European Research Council (ERC), ad hoc reviewer
2016	Fight for Sight Foundation, ad hoc reviewer

2016	NIH NEI Board of Scientific Counselors, ad hoc member
2016	NIH Brain Initiative study section, ad hoc member
2016 – 2021	Chair of Admissions for the Neuroscience Ph.D. Program, Washington University School of Medicine, St. Louis, MO
2015 – 2019	Associate Professor of Ophthalmology and Visual Sciences, Neuroscience, and Biomedical Engineering, Washington University School of Medicine, St. Louis, MO
2015	Editorial Board of *Visual Neuroscience*, member
2015	German Science Foundation (DFG), ad hoc reviewer
2015	NIH Brain Initiative study section, ad hoc member
2014	Human Frontiers Science Program (HFSP), ad hoc reviewer
2014	German Science Foundation (DFG), ad hoc reviewer
2014	NSF grant review committee, Neural Systems, ad hoc member
2009 – 2015	Assistant Professor of Ophthalmology and Visual Sciences, Neuroscience, and Biomedical Engineering, Washington University School of Medicine, St. Louis, MO

Honors

1998 – 2002	Scholar of the German National Merit Foundation (Studienstiftung des deutschen Volkes) Passed all four nationwide medical exams with the highest possible score > 99.5 % rank
2003	*Summa cum laude* for MD Thesis
2004	Otto-Hahn Medal of the Max Planck Society
2007 – 2009	Fellowship of the German Science Foundation (Deutsche Forschungsgemeinschaft, DFG)
2010	Hope for Vision New Investigator Award
2010 – 2012	Alfred P. Sloan Research Fellow
2010	Visiting Fellow at the Institute of Advanced Studies of the Technical University Munich
2010 – 2013	Whitehall Foundation Award
2010 – 2013	Edward Mallinckrodt, Jr. Foundation Award
2012 – 2016	Research to Prevent Blindness Foundation Career Development Award
2016	Distinguished Investigator Award of Washington University, St Louis
2022	Cogan Award from the Association for Research in Ophthalmology and Vision (ARVO)
2022	Janet & Bernard Becker Professor of Ophthalmology and Visual Sciences

C. Contributions to Science

1. The organization and function of amacrine cells

Amacrine cells are a diverse class (>60 types) of interneurons, which shape feature representations of the retinal output. We discovered that VGluT3-expressing amacrine cells (VG3-ACs) detect object motion (incl. looming) and provide feature-selective excitatory input to W3 retinal ganglion cells (W3-RGCs) *(Kim et al. 2015)*. Using optogenetics and type-specific cell removal, we found that VG3-ACs also provide inhibitory input to transient Suppressed-by-contrast RGCs (tSbc-RGCs) (*Tien et al. 2016*). This identified VG3-ACs as dual transmitter neurons that use their two transmitters (glutamate and glycine) in a target-specific manner. Having shown that VG3-ACs drive responses of W3-RGC responses to local motion, we next discovered that TH2-ACs selectively suppress responses of W3-RGCs to global motion [a]. Unlike VG3-ACs, which distinguish local and global motion in their response polarity (depolarizing and hyperpolarizing, respectively), TH2-ACs distinguish local and global motion in their response timing (slow and fast, respectively). By type-specific neuron silencing, we demonstrated that complementary inputs from VG3-ACs and TH2-ACs give rise to object motion selective responses of W3-RGCs [a]. Type-specific neuron silencing indicated that VG3-ACs send signals with different contrast preferences to different targets. Two-photon calcium imaging revealed that VG3-AC dendrites process input signals locally and differentially organize visual information, including stimulus contrast and location, across their arbors [b]. Recently, we discovered that VG3-ACs respond robustly to looming but not related forms of motion, that looming-selective calcium transients are restricted to a specific layer of the VG3-AC dendrite arbor that provides excitatory input to W3- and OFFα-RGCs, that these projection neurons combine shared excitation with dissimilar inhibition to signal looming onset and speed, respectively, and that W3- and OFFα-RGC responses and innate defensive reactions to looming depend on VG3-ACs [c]. In collaboration with the lab of Dr. Josh Morgan, we developed techniques to combine two-photon calcium imaging and large-scale electron microscopy reconstructions in the same piece of tissue to study the varied subcellular information paths in the dendrites of

amacrine cells. We have first utilized this approach to characterize the local computations and diverse circuit functions of VG3-ACs [d].

a. Kim T, **Kerschensteiner D**. (2017) Inhibitory control of feature selectivity in an object motion selective circuit in the retina. ***Cell Reports***; 19(7):1343-1350 [PMID: 28514655]
b. Hsiang JC, Johnson KP, Madisen L, Zeng H, **Kerschensteiner D**. (2017) Local processing in neurites of VGluT3-expressing amacrine cells differentially organizes visual information. ***eLife***; Oct 12;6 [PMID: 29022876]
c. Kim T, Shen N, Hsiang JC, Johnson KP, **Kerschensteiner D**. (2020) Dendritic and parallel processing of visual threats in the retina control defensive responses. ***Science Advances***; Nov 18;6(47):eabc9920 [PMID: 33208370]
d. Friedrichsen K, Hsiang JC, McCoy L, Valkova K, **Kerschensteiner D.***, Morgan KL*. (2023) Subcellular pathways through VG3 amacrine cells provide regionally tuned object-motion-sensitive signals in the mouse retina. ***bioRxiv***; https://doi.org/10.1101/2023.07.03.547571 * co-corresponding

2. Signals from the retina to the brain

More than 40 RGC types send the results of retinal computations to the brain. RGC spike trains encode a wide variety of features and events and are the sole source of visual information to the brain. What specific information RGCs encode, how presynaptic circuits give rise to their responses, and where the RGCs send their information is, for most cell types, unknown. We genetically identified an RGC type (tSbc-RGCs, which, unlike most others, encodes visual information in the suppression of high baseline firing rates and signals self-generated visual stimuli caused by eye movements and eyelid blinks [a]. We also discovered a pixel-encoder RGC type (Pix_{ON}-RGCs), which responds to contrast and spatial information linearly through spatially offset excitatory and inhibitory receptive fields [b]. We recently pioneered recordings from the human retina. We revealed how midget and parasol RGCs, which account for most signals from our eyes to our brain, efficiently encode our environment [c]. Finally, tracking predator-prey interactions in 3D, we found that mice trace crickets with their binocular visual field and capture them with a stereotypical (bite-and-grab) attack sequence. We discovered that a small fraction of RGC types (9/40+) in mice have ipsilateral projections (ipsi-RGCs) and support binocular vision. Using region- and type-specific cell deletion, we showed that ipsi-RGCs are required for efficient prey capture. Stimuli based on ethological observations suggest that five ipsi-RGC types reliably signal prey [d].

a. Tien NW, Pearson JT, Heller CR, Demas J, **Kerschensteiner D**. (2015) Genetically identified Suppressed-by-Contrast retinal ganglion cells reliably signal self-generated visual stimuli. ***Journal of Neuroscience***; 35(30):10815-10820 [PMID 26224863]
b. Johnson KP, Zhao L, **Kerschensteiner D**. (2018) A pixel-encoder retinal ganglion cell with spatially offset excitatory and inhibitory receptive fields. ***Cell Reports***; 22(6):1462-1472 [PMID 2945502]
c. Soto F, Hsiang JC, Rajagopal R, Piggott K, Harocopos GJ, Couch SM, Custer P, Morgan JL, **Kerschensteiner D**. (2020) Efficient coding by midget and parasol ganglion cells in the human retina. ***Neuron***; Jun 3:S:0896-6273 [PMID 32533915]
d. Johnson KP, Fitzpatrick MJ, Zhao L, Wang B, McCracken S, Williams PR, **Kerschensteiner D**. (2021) Cell-type-specific binocular vision guides predation in mice. ***Neuron***; Mar 19 [PMID 33784498]

3. Homeostatic plasticity of retinal circuits

How plasticity shapes the development of circuits and their responses to neurodegeneration are central questions of neuroscience. Studying connections between bipolar cells and RGCs, we found that different excitatory inputs converging onto the same target use different strategies to establish specific patterns of connections. The influence of neurotransmission varies between converging input cell types [a]. We showed that developing RGCs adjust inputs from converging bipolar cell types to establish and preserve specific light responses (i.e., homeostatic plasticity) [b]. Similarly, we found that homeostatic plasticity shapes the configuration of the visual system's first synapse between photoreceptors and bipolar cells [c]. Recently, we showed that homeostatic plasticity shapes retinal circuits' response to photoreceptor degeneration, that homeostatic plasticity is cell type-specific, that it declines steeply with age, and that this decline determines the functional deficits incurred from photoreceptor degeneration [d].

a. Morgan JL, Soto F, Wong RO, **Kerschensteiner D**. (2011) Development of cell-type-specific connectivity patterns of converging excitatory axons in the retina. ***Neuron***; 71(6):1014-1021 [PMID 21943599]

b. Tien NW, Soto F, **Kerschensteiner D**. (2017) Homeostatic plasticity shapes cell-type-specific wiring in the retina. ***Neuron***; 94(3):656-665 [PMID 28334599]

c. Johnson RE, Tien NW, Shen N, Pearson JT, Soto F, **Kerschensteiner D**. (2017) Homeostatic plasticity shapes the visual system's first synapse. ***Nature Communications***; 8(1):1220 [PMID 29089553]

d. Shen N, Wang B, Soto F, **Kerschensteiner D**. (2020) Homeostatic plasticity shapes the retinal response to photoreceptor degeneration. ***Current Biology***; 39(10):1916-1926 [PMID 32243858]

4. Molecular mechanisms of circuit development and maintenance

To identify molecular cues that guide the formation of specific retinal circuits, we performed expression screens. In one, we identified netrin-G ligand 2 (NGL2), a leucine-rich cell adhesion molecule expressed selectively by horizontal cells. We found that NGL2 localizes to axons of horizontal cells and regulates their size, targeting, and the formation and function of synapses between horizontal cell axons and rod photoreceptors [a]. Compared to circuit development, we know little about the molecular mechanisms of circuit maintenance. We developed an AAV-mediated CRISPR/Cas9 strategy to remove NGL2 from individual horizontal cells with temporal control. In addition, we used AAVs to restore the expression of NGL2 to individual horizontal cells in knockout mice. Thus, we found that NGL2 promotes the formation, maintenance, and restoration of synapses in the developing and mature retina and restricts axon growth throughout life [b]. Another leucine-rich cell adhesion molecule identified in our screens is AMIGO2, which we found to be selectively expressed in starburst amacrine and rod bipolar cells. We identified AMIGO2 as a dendritic scaling factor that selectively controls dendrite territories and their overlap between neighboring neurons of the same type (i.e., coverage) through loss-of-function experiments. Furthermore, we showed that dendrite coverage is a key determinant of feature-selective computations in the retina [c]. We found that the related protein, AMIGO1, determines the size of horizontal cell axons and transsynaptically shapes rod bipolar cell dendrites in a novel homeostatic mechanism (i.e., territory matching). [d].

a. Soto F, Watkins KL, Johnson RE, Schottler F, **Kerschensteiner D**. (2013) NGL2 regulates pathway-specific neurite growth and lamination, synapse formation, and signal transmission in the retina. ***Journal of Neuroscience***; 33(29):11949-11959 [PMID 23864682]

b. Soto F, Zhao L, **Kerschensteiner D**. (2018) Synapse maintenance and restoration in the retina by NGL2. ***eLife***; Mar 19;7 [PMID 29553369]

c. Soto F, Tien NW, Goel A, Zhao L, Ruzycki PA, **Kerschensteiner D**. (2019) AMIGO2 scales dendrite arbors in the retina. ***Cell Reports***; 29(6):1568-1578 [PMID 31693896]

d. Soto F, Shen N, **Kerschensteiner D**. (2022) AMIGO1 promotes axon growth and territory matching in the retina. ***Journal of Neuroscience***; Mar 30;42(13):2678-2689 [PMID 35169021]

5. Patterned spontaneous activity

Patterned spontaneous activity propagates through many parts of the developing nervous system and refines emerging circuits. In the visual system, waves of spontaneous activity originating in the retina dictate activity patterns up to primary visual cortex. Across many species, retinal waves mature in three stereotypic stages (I - III). In each stage, distinct mechanisms give rise to unique activity patterns that serve specific functions in the organization of visual circuits. We discovered that within each stage III wave, neighboring RGCs with opposite light responses (ON and OFF) fire asynchronous bursts of action potentials in a fixed order: ON before OFF [a]. We then used dual patch-clamp recordings and two-photon imaging to define intersecting vertical inhibitory and lateral excitatory circuits that generate, propagate, and pattern stage III waves [b]. The specific patterns of stage III waves appear well suited to guide ON/OFF segregation in the early visual system.

a. **Kerschensteiner D**, Wong RO. (2008) A precisely timed asynchronous pattern of ON and OFF retinal ganglion cell activity during the propagation of retinal waves. ***Neuron***; 58(6):851-858 [PMID:18579076]

b. Akrouh A, **Kerschensteiner D**. (2013) Intersecting circuits generate precisely patterned retinal waves. ***Neuron***; 79(2):322-334 [PMID:23830830]

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/daniel.kerschensteiner.1/bibliography/43350598/public/?sort=date&direction=descending

D. Research Support

Active

R01 EY026978 Kerschensteiner (PI)
09/01/16 – 03/31/26
Synaptic organization and function of retinal interneurons and downstream visual pathways
Role: PI

R01 EY027411 Kerschensteiner (MPI)
04/01/17 – 12/31/26
Synapse rescue and neuroprotection in the retina
Role: PI

R01 EY034001 Kerschensteiner (PI)
04/01/22 – 03/31/26
Visual pathway cooperation to align viewing strategies and processing specializations for predation
Role: PI

T32 EY013360 Kerschensteiner (MPI)
09/30/00 – 03/31/27
Interdisciplinary training in vision science
Role: PI

T32 NS121881 Kerschensteiner (MPI)
07/02/21 – 06/30/26
Neuroscience training program at Washington University
Role: PI