Research Highlight #2008

Dr. Kara Cerveny

Reed College

Light-sheet fluorescence microscopy as a tool to study development in the visual system

Dr. Kara Cerveny's lab at Reed College aims to unpack one very large, yet very important, question: how do cells transition from a proliferation state to a differentiation state? Dr. Cerveny approaches this question through the lens of the visual system, more specifically looking into how neuronal stem and progenitor cells behave in a growing zebrafish retina. She is interested in using light-sheet fluorescence microscopy on the developing zebrafish eye to study the plane of cell division within both early retinal neuro-epithelial cells, as well as in leader cells, acting as STEM and progenitor cells, that are maintained throughout the life of the fish. Zebrafish are useful models to understand growth mechanisms involved in tissue development to the proper size and composition because the embryos are transparent, develop outside of the mother, and can easily be genetically and embryologically manipulated. Additionally, zebrafish continuously grow and develop throughout their lifetime, which further enhances their suitability for developmental research.

> "Zebrafish have this amazing ability to continue to grow throughout their life. They can do this because they have specialized stem cell niches in particular areas of the body that fuel that lifelong growth. We're really interested in all kinds of questions about how those cells, once they're established, then build neurons that integrate seamlessly into the existing circuitry."

The Luxendo light-sheet microscope allows for faster and gentler imaging of a specimen compared to confocal microscopy, making it well-suited for Dr. Cerveny's applications in developmental biology. The gentle nature of the imaging supports the integrity of the live zebrafish for imaging experiments lasting several hours. The high time resolution enables imaging at a timescale reflective of the developmental process.

> "The light-sheet is going to be amazing for us to be able to follow the plane of cell division in real time, actually watching dividing cells and seeing how the angle of cell division shifts over time, in response to various local cues. The light-sheet microscope being so gentle and fast is really nice for us, because with the confocal we have some preliminary data, but our time resolution was so limited. Because the light-sheet is super-fast, we can catch those divisions and really know if more proteins are being inherited on one side or the other, for instance, really know precisely how the cell is dividing."

In addition to looking at cell division in real time, Dr. Cerveny also plans to investigate the interplay between various tissues in the forming eye, including local signal influence on proliferation and differentiation decisions. The eye is comprised of a neuro-epithelial cell sheet (a single layer that develops into cells that send light and then signals back to the brain) as well as a thin epithelial layer (the retinal pigmented epithelium) that mainly supports the photoreceptors. There are also other complex tissues that originate from neural crest cells and make muscle, mesodermal-derived cells from bone, and

ABOUT THE RESEARCHER

Kara Cerveny, Ph.D., is an Associate Professor of Biology at Reed College in Portland, Oregon. She earned her B.S. in Biology and B.A. in Chemistry from Duke University and her Ph.D. in Biochemistry, Cellular, and Molecular Biology from Johns Hopkins School of Medicine. Before her current role, Dr. Cerveny held positions of grade school science teacher, editor for the journal *Cell*, and post-doctoral fellow of Cell and Developmental Biology at University College London, UK.

Website: Visit Dr. Cerveny website

Recent Publications

Barrett C, Hellickson I, Ben-Avi L, Lamb DB, Kranhenbuhl M, Cerveny KL. Impact of low-level ionizing radiation on cell death during zebrafish embryonic development *Health Phys.* 2018 Apr;114(4):421-428.

Valdivia, L.E., Lamb, D.B., Horner W., Wierzbicki, C., Tafessu A., Williams, A.M., Gestri, G., Krasnow, A.M., Vleeshouwer-Neumann, T.S., Givens, M.B., Young, R.M., Lawrence, L.M., Stickney, H.L., Hawkins, T.A., Schwarz, Q., Cavodeassi, F., Wilson, S.W., Cerveny, K.L. Antagonism between Gdf6a and retinoic acid pathways controls timing of retinal neurogeneis and growth of the eye in zebrafish. *Development.* 2016 Epub 2016 Feb 18.

connective tissue in the form of blood vessels and lymphatic vessels. The interplay between these complex tissues during development is a particularly interesting area of study for Dr. Cerveny, and she already has collected some exciting data regarding signaling between the vasculature and the retina.

> "We can get time-resolved images that are collected over 24 hours of development, and it's super gentle so the fish survive and seem to be okay. What's nice is that we're seeing similar data that we had from the confocal, but we're also able to see new things. For instance, when we look at blood vessel growth, we're able to see a lot more 'starts and stops' and retractions, and then another vessel that grows and then retracts. We're seeing much more dynamics than we ever saw with a confocal, and that is really exciting."

In addition to using light-sheet imaging, Dr. Cerveny performs experiments using embryological genetic manipulation. For example, she takes cells from one embryo and places them in another embryo to investigate how the cells can survive in a different environment. She also uses mutant embryos to study how signaling molecules can result in cell shape changes and differentiation effects. Studying the development of the visual system has implications in human health, including in the potential for strengthening the understanding of neurodegeneration and disease associated with improper development. Using light-sheet microscopy to investigate cell division and the interplay between systems, such as the vascular, immune, and nervous systems, will contribute to advances in the field of cell and development biology.

Learn more

To learn more about light-sheet fluorescence microscopy and Luxendo's light-sheet microscopes, visit: https://www.bruker.com/light-sheet

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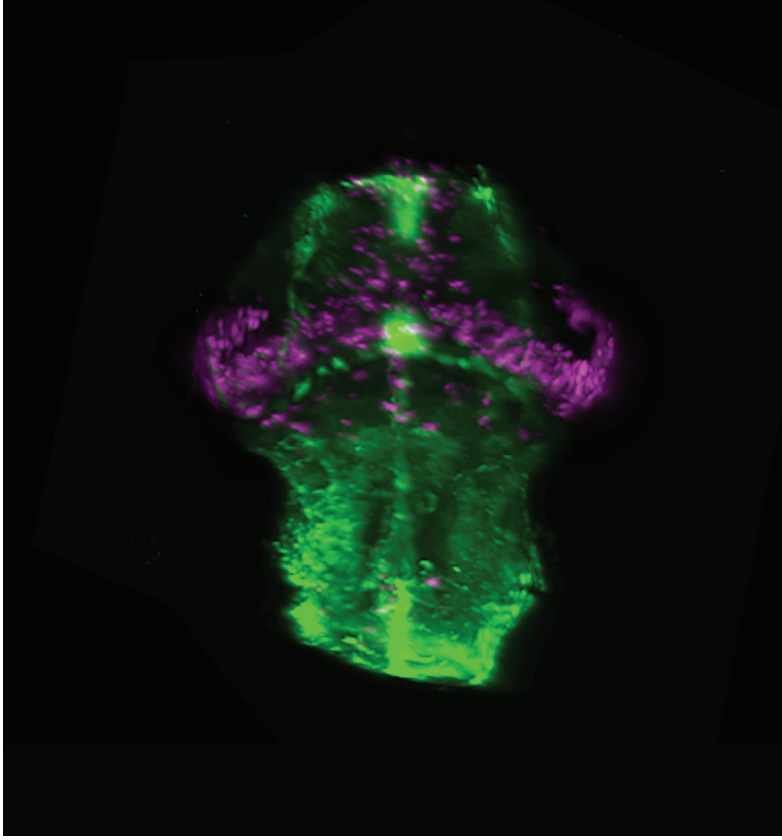

FIGURE 1

Proliferating stem cells in the brain (magenta) in relation to a glia marker (green) in zebrafish.