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Neuronal Migration: How Do You Build a Brain?

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By Sravya Uppalapati

Senior biology major Alex Burkard is working in the Walsh Neurodevelopment Laboratory at VCU to help answer the question, 'How do you build a brain?' Burkard is researching neuronal migration in Zebrafish and how cellular polarity affects hindbrain development.

Burkard developed an interest for the evolutionary process in his sophomore year, specifically how the brain grows but the skull size remains the same. He worked with Dr. Jonathan Moore to study warblers in the spring of 2014, and also met with Dr. Gregory Walsh. Burkard was presented the UROP Fellowship award to continue his research in the Walsh Laboratory in summer 2014.

"The Zebrafish serves as a good model organism in this lab because what is unique about zebrafish is that they are transparent from fertilization to 24 hours," Burkard said.

Burkard adds PTU (a melanosynthesis inhibitor) into the water to elongate the period of transparency for observation. PTU keeps the Zebrafish transparent for a few days longer by blocking the production of melanocytes, cells responsible for skin color and providing camouflage.

Burkard studies motor neurons in the hindbrain that change direction upon contact with another during the process of neuronal migration, formally known as contact inhibition of locomotion (CIL). To visualize this developmental event, Burkard uses green fluorescence protein (GFP) that is fused to these migrating neurons.

"They basically act as a tag," he said. "We can see how the (neuronal) migration patterns are altered when we knock out different known polarity proteins."

To study this process, the laboratory utilizes a "knock-out approach" process with the use of microinjections. The process functions via the injection of DNA into the embryo at the one-cell stage which blocks gene expression and inhibits the function of the protein as the embryo develops.

"By breeding these gene deficient Zebrafish for generations, we were able to create a line of zebrafish that naturally doesn't have the (Nhsl1b) protein," said Burkard. In addition to Nhsl1b, the lab works with Vangl2, Prickle, and other polarity proteins.

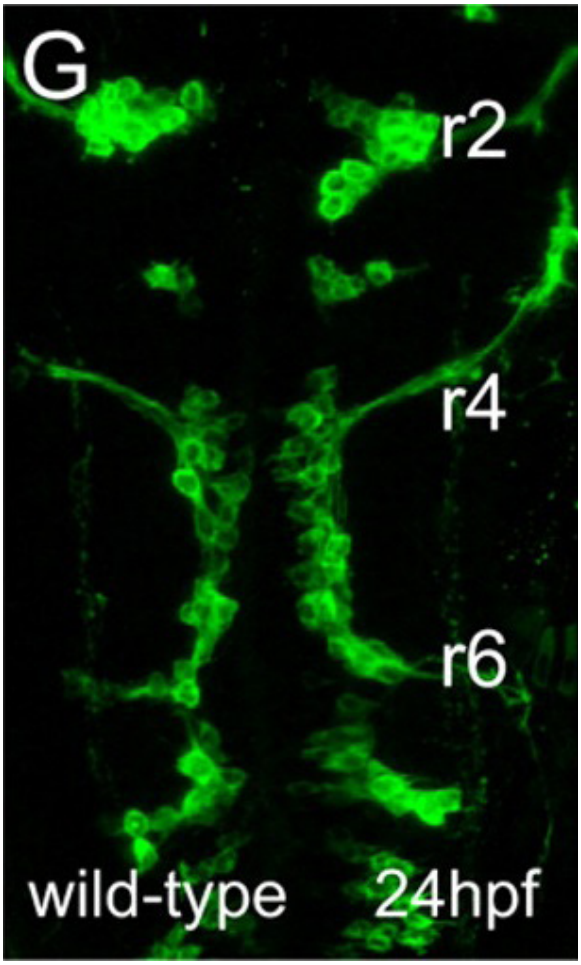
The goals of the project include characterizing the dynamic activity of neurons when various polarity proteins are "knocked out" and determining the

functionality of the brain's neural circuitry. Burkard suggests that the research can be applied to medicinal advances in Nance-Horan syndrome, a congenital disease that causes face dragging and cataracts.

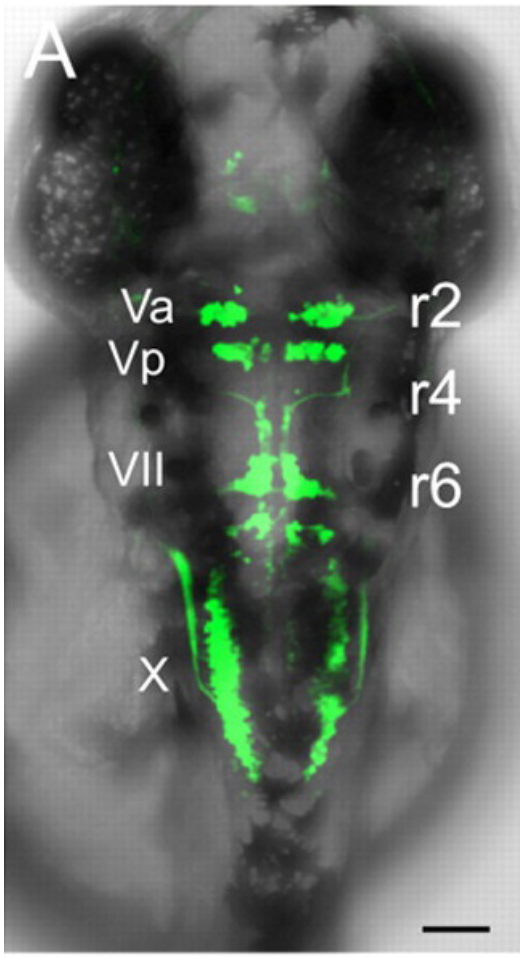
Through trial-and-error, Burkard learned to problem solve and use creative ways to approach a conclusion in his research.

"It's pretty conclusive that nothing works the first time and probably the second time and third time," Burkard said when asked about the research process.

Burkard will present his research in Boston for the American Society for Biochemistry and Molecular Biology conference in March.



The image shows the motor neurons in the hindbrain of a wild-type embryo at 24 hours post-fertilization using confocal microscopy.



Burkard tags green fluorescent protein to motor neurons in the Zebrafish embryo at 24 hours post-fertilization. The image was taken with a combination of light and confocal microscopy.