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THE Current

May 20, 2011
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# By UCSB Scientists Make Strides in Vision Research

New research at UC Santa Barbara is contributing to the basic biological understanding of how retinas develop. The study is part of the campus's expanding vision research.

The new studies are published in recent online versions of The Proceedings of the National Academy of Sciences (PNAS), and Investigative Ophthalmology and Visual Science (IOVS).

The scientists document how they used mice as a research model organism to show that the size of different populations of retinal neurons display wide-ranging variability among individuals. In the PNAS article, they demonstrate a nearly two-fold variation in the number of interneurons called horizontal cells. In the IOVS article, they report a conspicuous variation in the number of cone photoreceptors.

"These studies individually demonstrate the genetic determinants of nerve cell number," said Benjamin E. Reese, senior author and professor with the Neuroscience Research Institute and the Department of Psychological and Brain Sciences. "Together, they show that different nerve cell types are modulated independent of one another."

Using recombinant inbred mice, Irene Whitney, graduate student and first author of both articles, and Mary Raven, staff scientist and co-author, have been able to

identify genomic loci where polymorphic genes must contribute to such natural variation. In the IOVS article, they describe this natural variation for the population of cone photoreceptors, and identify two potential causal genes that may modulate cone photoreceptor production on chromosome 10.

In the PNAS article, the scientists –– working will colleagues from four other U.S. institutions –– identify a promising candidate gene at a locus on chromosome 13, a transcription factor gene called Islet-1. This gene was confirmed to be critical for regulating horizontal cell number in genetically modified mice, in which the Islet-1 gene was rendered nonfunctional. The scientists verified that expression of this gene differs between these strains of mice during the developmental period when horizontal cells are produced. They also showed that the source of this variable expression must be due to a genetic variant within a regulatory region of the gene itself. Finally, they identified such a single nucleotide polymorphism creating an E-box, a DNA sequence bound by a family of transcription factors that have recently been shown to play a role in retinal development.

The team explained that such natural variation in the ratio of nerve cells requires a degree of plasticity in the process of forming neural connectivity, to ensure that the entire visual field is served by neural circuits that mediate our visual abilities. A series of other published and submitted studies from the Reese lab document this very plasticity in different strains of mice and in genetically modified mice.

Efforts to use genetic engineering and stem cell biology to repair diseased retinas depend upon a fuller appreciation of the developmental biology of the retina, explained Reese.

"These particular studies are just one contribution in an enormously complex process," said Reese. "Our fundamental interest is in the development the retina

–– how you ‘build' this neural tissue that, when fully mature, will mediate our visual abilities."

Vision research at UCSB has been steadily expanding in recent decades. "Since I arrived here in 1971, UCSB's vision research has grown to include dozens of scientists, in a number of labs, contributing to an explosion of research in the field," said Steven Fisher, professor emeritus in the Department of Molecular, Cellular, and Developmental Biology, and professor in the Neuroscience Research Institute.

The National Eye Institute of the National Institutes of Health funded both of the above studies.

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† Top photo: Whole mouse retina labeled to reveal the terminals of cone photoreceptors (in blue), and one of their post-synaptic partners, the horizontal cells (in red).

The dendritic branches of the horizontal cells make fine contacts with each cone terminal.

Credit: Confocal micrograph by Patrick Keeley

†† Bottom photo: From the left: Irene E. Whitney, Mary A. Raven, and Benjamin E. Reese

Credit: George Foulsham, Office of Public Affairs, UCSB

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