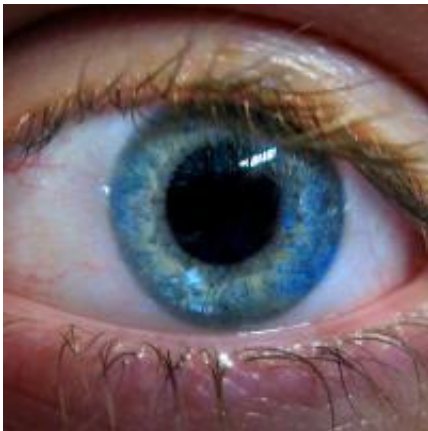


Development of four early retinal cell types integral to normal vision

October 30 2014, by Ellen Goldbaum



University at Buffalo researchers have discovered what regulates generation of the early neurons in the retina during embryonic development. The findings provide clues to how cellular diversity is created in the central nervous system.

Published in September in *Proceedings of the National Academy of Sciences*, the study shows how two related transcription factors, a class of specific proteins regulating gene activity, redundantly regulate cellular diversity in the retina, meaning they have overlapping responsibilities for the same cells.

The results also suggest how cellular formation is driven in other parts of

the nervous system, since the particular transcription factors involved in this study are expressed in other tissues during development, including in the spinal cord.

"Transcription factors are the most important regulators in development of various organs, including the vision system in mammals," explains Xiuqian Mu, PhD, senior author and assistant professor in the Department of Ophthalmology, Ross Eye Institute and the Department of Biochemistry in the UB School of Medicine and Biomedical Sciences. "They turn on and off the genes in the genome that are required for normal development."

Mu and his co-authors were studying the transcription factors called *Onecut1* and *Onecut2* using knockout mice, which lacked either or both of the transcription factors. Previously, they had discovered that *Onecut1* and *Onecut2* were responsible for normal development of horizontal cells, which make it possible for eyes to adjust to see well in both bright and dim light conditions.

In the current research, they found that when mice lacked both transcription factors, there were other significant losses, including abnormal development of cones (one of the retina's two important photoreceptor cell types), [retinal ganglion cells](#) and amacrine cells. "All these cell types are essential for normal vision, and defects in any of them can lead to vision loss, even blindness," explains Mu.

The UB researchers' finding that these two [transcription factors](#) regulate the formation of multiple retinal neurons during [embryonic development](#) suggests that they play an even more significant role than was previously appreciated in the development of the vision system in mammals.

"Development of the vision system, including the retina, is a complex but tightly regulated process," explains Mu. Two waves of cell type

formation are involved as the retina develops, the early wave and the late wave.

"Each wave leads to the development of several cell types," explains Mu, "but it has been a mystery regarding why there are these two waves and what is the genetic basis for them. Our study found that Onecut1 and Onecut2 regulate the first wave, which sheds light on how the generation of different retinal [cell types](#) is coordinated."

Understanding normal development is key to developing therapies for many genetic diseases, including genetic eye diseases, Mu continues. "It is conceivable that in the future we will learn that mutations in these genes cause defects in the human retina," he says.

"One approach under development by many scientists is to generate functional retinal neurons in culture and to use them to replace the diseased ones," says Mu. "Conceivably, what we learned here may in the future be applied to such efforts."

Provided by University at Buffalo

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