Breakthrough in the fight against blindness

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Michel Cayouette and Pierre Mattar. Credit: IRCM

A team of researchers at the IRCM led by Michel Cayouette, PhD, identified one of the genes responsible for producing a type of cell required for vision. The breakthrough, published in the scientific journal *Neuron*, could eventually help overcome obstacles associated with treatments to prevent blindness.

The retina of the eye is made up, in part, of two types of photoreceptors (light-sensing neurons): rods that enable night vision, and cones that are used for high visual acuity and colour daylight vision. The loss of cones is a major cause of blindness associated to various retinal degenerative diseases, and the scientific community is working towards restoring sight through cell replacement therapies.

"Retinal stem cells produce all types of retinal cells, including rod and

cone photoreceptors," explains Pierre Mattar, PhD, first author of the study and postdoctoral fellow in Dr. Cayouette's laboratory. "The scientific community has been successful in generating rods from stem cells and has even used them to restore sight in mouse models of blindness, which shows that this approach is promising. However, the production of a large number of cones continues to be very difficult, for reasons that remain unknown."

During normal development of the retina, stem cells produce the different types of photoreceptors according to a precise time sequence. They produce cones first and, later, will produce rods. The IRCM researchers identified, for the first time, one of the genes involved in this temporal change, the Casz1 gene.

"We discovered a cascade of genes that allows the sequential production of photoreceptors and other retinal cell types over time," says Dr. Cayouette, Associate IRCM Research Professor and Director of the Cellular Neurobiology research unit. "This cascade appears to be conserved from flies to mice, which suggests that it might represent a fundamental mechanism to control stem cell development that could also be conserved in humans."

"The current methods to produce photoreceptors from retinal stem cells do not take into account the temporal identity of stem cells or, in other words, when they are most likely to generate cones or rods," adds Dr. Cayouette. "Our findings now provide a novel way to control this process. Manipulating the Casz1 cascade could allow us, for example, to extend the cone-producing window, thereby increasing the generation of cone cells that could be used in treatments to reverse blindness."

The article published in *Neuron* was prepared in collaboration with Johan Ericson from the Karolinska Institutet in Sweden and Seth Blackshaw from John Hopkins University School of Medicine in the United States.

In the same issue of the journal, a preview manuscript by Claude Desplan and colleagues (Konstantinides et al., 2015, *Neuron*, 85: 447-449) includes comments on the importance of the work conducted by Drs. Cayouette and Mattar.

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