

## Eye cells believed to be retinal stem cells are misidentified

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Cells isolated from the eye that many scientists believed were retinal stem cells are, in fact, normal adult cells, investigators at St. Jude Children's Research Hospital have found. If retinal stem cells could be obtained, they might provide the basis for treatments to restore sight to millions of people with blindness caused by retinal degeneration. Stem cells are immature cells capable of producing large numbers of adult cells, such as retinal cells. Researchers believe that stem cells offer the promise of regenerating tissue in organs such as the eye, brain and heart, damaged by trauma or disease.

The new findings suggest that research on cell therapies to restore blindness should not concentrate on these eye cells previously believed to be retinal <u>stem cells</u>. More promising, the scientists said, is research aimed at re-engineering stem cells to develop into the light-sensitive photoreceptor cells that are lost as a result of retinal degeneration. Such studies could lead to implantation of such engineered photoreceptor cells into the eye to restore sight.

Led by Michael Dyer, Ph.D., the researchers published their findings March 30, 2009, in the online early edition of the <u>Proceedings of the</u> <u>National Academy of Sciences</u>. Dyer is a member of the St. Jude Department of Developmental Neurobiology.

In studies reported in 2000, scientists proposed that the layer of ciliary epithelial cells lining the inside of the eye, contains retinal stem cells because when grown in culture dishes these cells formed tiny spheres of



about a thousand cells, said Dyer, the paper's senior author. These spheres, in turn, could be cultured to give rise to more spheres, reminiscent of the self-renewing capability of stem cells. Also, the cultured sphere cells showed activation of genes characteristic of adult eye cells.

"The first clue that these cells were not stem cells was that they were pigmented," Dyer said. "<u>Neural stem cells</u>, in general, and retinal progenitor cells, in particular, are not pigmented. Nevertheless, the previous finding was met with a tremendous amount of enthusiasm because of the promise of introducing these cells into the eye to regenerate photoreceptors lost to blindness."

In their studies, Dyer and his colleagues analyzed the sphere-forming cells in detail to determine whether they were really retinal stem cells. Painstaking microscopy studies of each cell in the spheres revealed all were pigmented and had features of ciliary epithelial cells. The researchers also compared the structure of the sphere-forming cells with those of confirmed stem cells and other immature cells in the developing retina called progenitor cells. That comparison revealed fundamental differences between the sphere-forming cells and established stem or progenitor cells.

The researchers also found that simply culturing the sphere-forming cells in the same growth medium as is used for stem cells caused them to activate genes characteristic of stem cells, yet remain adult ciliary epithelial cells.

Dyer said that a particularly promising alternative is the possibility of taking samples of adult cells—such as fibroblasts that form connective tissue—from a patient with retinal degeneration and exposing them to genetic cues that induce them to revert to stem cells. Those induced pluripotent stem cells could then be manipulated to develop into light-



sensing photoreceptor cells that could then be transplanted into the patient's eyes to restore vision.

"This approach would solve many problems of developing cell-based therapy for blindness," Dyer said. "First, these cells are immortal, so they can be grown indefinitely to produce large amounts of cells for treatment. And secondly, they would be immunologically matched to the patient, so there would be no danger of rejection. And thanks to some excellent research during the past 15 years, we know a lot about how to reprogram such stem cells to make them into photoreceptors."

Source: St. Jude Children's Research Hospital

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