Cell transplantation allows mice to see again in daylight
Transplantation of cone photoreceptors into the mammalian retina represents a new promising strategy for treatment

Degeneration or loss of the light-sensitive cells of the retina, the so-called photoreceptors, inevitably leads to vision impairment and blindness with no curative therapy currently available. On of the main causes for disability in industrialized societies is the loss of cone photoreceptors that are responsible for daylight vision. The team of Professor Marius Ader of the DFG-Research Center for Regenerative Therapies Dresden – Cluster of Excellence at the TU Dresden (CRTD) in collaboration with Dr. Günther Zeck of the Natural and Medical Sciences Institute (NMI) at the University of Tübingen, now report the successful transplantation of cone-like photoreceptors into the retina of recipient mice with disrupted daylight vision. They demonstrated that donor cells correctly integrated in the host tissue that resulted in recovered signal processing under daylight conditions. These results represent an important step towards the development of cell-based strategies for the treatment of retinal degenerative diseases. The study was recently published in the journal „Stem Cells“ (DOI: 10.1002/stem.1824.).

Human daylight vision depends on cone photoreceptors and their degeneration results in severe visual impairment as observed in several eye diseases including age-related macular degeneration, cone-rod dystrophies, or late stage retinitis pigmentosa. The adult mammalian retina, including humans, does not intrinsically regenerate and thus dying photoreceptors result in permanent vision loss with no treatments currently available. Several therapeutic approaches are currently being developed to treat retinal degenerative diseases. However, most require the existence of target cells and despite indications for visual improvements a continuous degeneration of photoreceptors was observed. Thus, cell-based therapies aiming to replace lost photoreceptors represent a promising alternative and treatment strategy.

So far the majority of retinal transplantation studies focused on rod photoreceptors. Rods, however, are adapted to dim light conditions at dawn and night, hence they dominate the retina of the night-active mouse. In contrast, since human daylight vision depends predominantly on cone photoreceptors, Marius Ader and his team used genetically engineered mice that possess solely cones. They transplanted isolated cone-like photoreceptors from these mice into recipient mice whose cones were degenerated or non-functional. By using
electrophysiological measurements the Dresden neurobiologist together with his partners from Tübingen could demonstrate for the first time functional integration of transplanted cones into the host tissue mediating responses to high-light stimuli, that were correctly processed within the retina.

„The results of this study are highly important for the development of cell replacement therapies for blinding disorders as they provide the first evidence that daylight vision can be principally restored by cell transplantation in the mammalian retina. The first step is done, but we still have a long way to go before such approach can be used in patients“, says Marius Ader.

Next, it will be important to increase the number and lifespan of integrated donor cells and to establish a reliable cell source for obtaining a sufficient number of donor photoreceptors for clinical applications. The development of cone photoreceptors from induced pluripotent and embryonic stem cells for future transplantation studies is expected to play a crucial role for this approach.

The presented results provide a proof-of-principle that transplantation of cone photoreceptors into the mammalian retina may represent a promising strategy for the treatment of previously incurable diseases of the retina.

Publication
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Photo
Transplanted cone-like photoreceptors (green) integrate functionally into the retina (blue) of mice with degenerated cones and mediate daylight responses. ©CRTD/Marius Ader

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The **Center for Regenerative Therapies Dresden (CRTD)** at the TU Dresden, founded in 2006, has passed the third phase of the excellence initiative as Cluster of Excellence and DFG Research Center. The director of this institute is Ely Tanaka, professor for Regeneration. Aim of the CRTD is to explore the capacity for regeneration of the human body and to develop novel regenerative therapies for so far incurable diseases. The center’s major fields of research are focused on hematology/immunology, diabetes, neurodegeneration, and bone regeneration.

Currently, six professors and eleven group leaders are working at the CRTD, they are integrated into a network of over 75 member labs at seven different institutions in Dresden. In addition, eight partners from industry are supporting the network. The synergies in the network allow for a fast translation of results from basic research to clinical applications. [www.crt-dresden.de](http://www.crt-dresden.de)