

Sight recovery in mice

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Swiss researchers from the Friedrich Miescher Institute, in collaboration with Inserm researchers from CNRS and UPMC in the Institut de la Vision, have restored sight to mice afflicted with retinitis pigmentosa. The results have been confirmed ex-vivo, on human tissue cultures. Thanks to a complementary clinical approach, the team led by Jose-Alain Sahel (Institut de la Vision/Centre d'Investigation Clinique) has determined the types of patient who could benefit from this therapy.

Retinitis pigmentosa affects over one million people worldwide and is manifested by a progressive loss of sight, eventually leading to blindness. <u>Retinitis pigmentosa</u> is a form of inherited <u>retinal degeneration</u> that affects the light-sensitive cells: photoreceptors.

Photoreceptors are a special type of neuron which convert light into nervous impulses. These impulses are then processed by the retina and transmitted along the nerve fibres to the brain. There are two types of photoreceptors: rods and cones.

As the disease progresses, it leads initially to degeneration of the rods which are responsible for night vision. Then the cones, which are responsible for diurnal vision, become affected. Whereas the rods are destroyed, the cones survive in the organism for extended periods, even after the occurrence of blindness as they cease to function. This inspired the researchers from the Friedrich Miescher Institute (FMI) and the Institut de la Vision to develop a genetic therapy to restore the visual function of the cones which were defective (dormant) but remained present.



Recreating a biological photoelectric system

At the stage of the disease where the researchers have intervened, although the defective cones no longer possess the ability to respond to a luminous stimulation (photo reception function) they do still retain some electrical properties and their connections with the neurons of the inner retina which normally transmit <u>visual information</u> to the brain. Hence, they are able to be activated artificially. Earlier work, carried out by the same team under the direction of Botond Roska (FMI), had shown that light-sensitive ionic channels, identified by the team of Ernst Bamberg (Max Planck Institute, Frankfurt), had the ability to modulate electrical activity from various neurons into which they had been introduced, in response to the level of light.

By combining these two observations, the researchers have succeeded in reactivating cones and thus allowing re-stimulation of the mice's ON/OFF transmission channels. To achieve this, they have introduced a protein, via a genetic therapy vector, which is capable of coupling luminous stimulation to ionic transport, hence reintroducing the phototransduction cascade required for vision. The researchers have therefore recreated a genuine biological photoelectric system.

These results are very promising, particularly as they have been confirmed by Serge Picaud and researchers at the Institut de la Vision using human retina in cultures and therapeutic vectors for which human compatibility has already been demonstrated. The photosensitive protein can be expressed in human cone photoreceptors to which it confers a new sensitivity to light.

"We integrated the clinical approach as soon as we obtained the first fundamental results of this work. So, at the national reference center for rare diseases of the retina, thanks to non-invasive high-resolution retinal imaging techniques, we can now target patients to whom this therapy



could be applied" explains José Alain Sahel, who points out that the transition from mice to man always carries many uncertainties. "The results are also very complementary to the research which has been carried out at the Institute and the CIC by the team of Serge Picaud, which aims to test and improve an artificial retina as well as our research on RdCVF protein which protects the activity of cones".

More information: Genetic reactivation of cone photoreceptors restores complex visual responses in Retinitis pigmentosa, Volker Busskamp et al., Science 24 June 2010

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