Receptor could halt blinding diseases, stop tumor growth, preserve neurons after trauma

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An international team of researchers has discovered what promises to be the on-off switch behind several major diseases. In the advance online edition of today's *Nature Medicine*, scientists from Sainte-Justine Hospital Research Center, the Université de Montréal and the Institut national de la santé et de la recherche médicale (INSERM) in France report how the GPR91 receptor contributes to activate unchecked vascular growth that causes vision loss in common blinding diseases. These findings could also have wide-ranging and positive implications for brain tissue regeneration.

While investigating the molecular mechanisms that lead to vision loss, the research team uncovered that the GPR91 receptor can mediate irregular vascular growth that is responsible for some of the main causes of blindness in the industrial world: retinopathy of prematurity in infants, diabetic retinopathy in adults (vision loss or blindness that affects up to 90 percent of diabetics) or age-related macular degeneration in seniors (central vision loss).

"We found that GPR91 is a master regulator of blood vessel growth, which upon enhanced activation leads to the unchecked and anarchic proliferation of vascular networks, which is the hallmark of retinopathies. This uncontrolled overgrowth can ultimately cause the retina to detach and a person to lose their sight," says Dr. Mike Przemyslaw Sapieha, the study's lead author and a scientist at the Sainte-Justine Hospital Reserch Center and the Université de Montréal.

"With the identification of GPR91 as a key player in this disease process, we can move forward in designing treatments that block the receptor and consequently stop vision loss," adds Dr. Sapieha. "Inhibition of GPR91 has a great therapeutic potential to halt these blinding diseases."

GPR91 to preserve neurons

The team's study also provides promise that the GPR91 receptor could preserve neurons. "Neurons are key sensors in retina oxygenation and serve as key players in the repair process of the retina," explains Dr. Sylvain Chemtob, director of the study and a neonatal researcher at the Sainte-Justine Hospital Research Center and professor at the Université de Montréal's Department of Pediatrics, Ophthalmology, Pharmacology and the School of Optometry.

"Given the similarities between the retina and the brain, we can envisage applying our findings in retina to the brain," says Dr. Chemtob. "Activation of the GPR91 receptor could be beneficial in helping salvage neurons in damaged brain tissue in stroke or head injury victims."

GPR91 to stop cancer growth

This study is the first to examine the wide-ranging implications of GPR91 and to investigate how the receptor, which is present in neurons, responds to stresses and adjust when in its oxygenation state is compromised. "This is a new concept in vascular biology," says Dr. Sapieha, noting it is conceivable that interfering with the GPR91 receptor could be used to stop cancer growth. "If you stop GPR91 from allowing blood vessels to expand and supply a tumour with nutrients and oxygen, one can significantly hamper growth of the cancer."

While these promising investigations on GPR91 were conducted in animals, the receptor is also found in humans, and Dr. Chemtob surmises

that extension of the research to human clinical investigations could be in three to fours years. "We expect these findings to have an enormous impact," he says.

On the Web:

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