Biomere

COMMUNITY BLOG

OPSIN EXPRESSION IN RETINAL GANGLION CELLS: A SURROGATE FOR RESTORING VISION

Vedere Bio was founded in June 2019 with $21 million series A funding and was acquired by Novartis in a lucrative deal valued at up to $280 million ($150 million upfront)[1] 18 months later. This is exceptional even in the fast-paced M&A world and one contributing factor may be that Vedere's technology has the potential to be a game changer in gene therapy. Vedere's novel opto-genetics platform could be used to develop novel gene therapies for retinal disorders like age-related macular degeneration (AMD) and retinitis pigmentosa that can lead to blindness. It's well known that cataracts and retinal eye diseases are the most common causes of permanent blindness, and while cataracts are treated surgically, retinal eye diseases typically do not have a standard treatment regimen. In developed countries, retinal diseases are the most common cause of irreversible blindness and AMD is the most common retinal eye disease in older people. AMD does have a few therapeutic options such as laser photocoagulation and anti-angiogenic therapies (for wet AMD) but there is an unmet clinical need for long-term therapies and the more prevalent dry form of AMD has very limited therapeutic options. Gene therapies are being actively investigated but one of the complications is the fact that there are several therapeutic targets for retinal disease - more than 250 different genetic mutations have been reported for retinitis pigmentosa alone. Gene therapy that targets a specific disease driver gene would be beneficial only to the patients with that mutation, thus limiting the addressable patient population.

Vedere Bio's technology is unique in that it does not depend on the presence of specific genetic mutations and can address a broader patient population. Some retinal diseases like AMD and retinitis pigmentosa can cause widespread death of photoreceptor cells (rods and cones) resulting in vision loss. Vedere's strategy is to target retinal cells that are not destroyed during the disease process. The technology was originally developed at UC Berkeley in the labs of Ehud Isacoff and John Flannery and focuses on the development of adeno-associated virus (AAV) vectors that express light sensing opsin proteins and can be directly injected into the vitreous space. The goal of this approach is to reverse blindness by using an AAV expressing green cone opsin targeted to retinal ganglion cells in the inner retina. Normally, these cells are not sensitive to light but the presence of the green cone opsin protein makes them light sensitive, so they are able to function as surrogates for photoreceptor cells and generate electrical signals for the brain to interpret as vision.

Another unique feature is the AAV vector that was engineered to specifically infect cells in the inner retina. The AAV serotype 2 viruses with tissue specific opsin expression infect the retinal ganglion cells in the inner retina– the tissue specific expression simplifies the delivery method as the virus can be directly injected into the vitreous space instead of the subretinal area, which is a more complicated process. The use of the green cone opsin is a technological innovation as optogenetic methods have used microbial opsins that have high response rates but need a strong light stimulus which could damage the retina. Conversely, rhodopsin and melanopsin from retinal ganglion cells are sensitive but have a slow response to light. The medium wavelength green cone opsin solves both challenges as it is sensitive to dim light and has a fast response rate. An added benefit is that the green cone opsin protein allows visual adaptation in normal light for 3D object visualization.

This opens up the possibility that people with advanced retinal disease may be able to see again and regain a better quality of life so Vedere's innovative technology could be a true game changer in ocular gene therapy.

Interested in reading more about the development and testing of the AAV in the rd1 mouse model of blindness? Check out the original **paper** from March 2019.

1 https://www.prnewswire.com/news-releases/novartis-acquires-vedere-bio-a-novel-optogenetics-aav-gene-therapy-company-301162269.html