Retina Australia Research Report 2025

Project Title: Advancing Usher syndrome type 1B gene therapy with split intein

Lay description

This project focused on developing a better gene therapy approach for Usher syndrome type 1B, an inherited condition caused by faults in the MYO7A gene. A major challenge in treating this disease is that the MYO7A gene is too large to fit inside the small viral delivery tools commonly used in gene therapy, called AAV vectors. Another challenge is getting the treatment into the right cells in the retina, especially the light-sensing cells known as photoreceptors. In this project, we tackled both problems at the same time. We worked on a way to split the large MYO7A gene into two parts so it could be delivered more effectively, and we also developed an improved AAV vector designed to reach photoreceptors more efficiently through a simple injection into the eye. This work is aimed at creating a safer, less invasive and more practical path toward future gene therapy for Usher syndrome and other inherited retinal diseases caused by large genes.

What we achieved this year?

1. We identified the most effective way to split the MYO7A gene.

Because MYO7A is too large for one standard AAV vector, we explored a “split gene” strategy, where the gene is divided into two parts and reassembled inside cells after delivery. During this funding period, we successfully identified the most efficient split site in the MYO7A protein. This was an important milestone because it enabled the highest level of MYO7A protein production in cells that we have achieved so far. In practical terms, this means we are now much closer to building a gene therapy that can deliver the full MYO7A protein in a workable and reliable way. This is a key step forward, because without strong reassembly of the gene and protein inside cells, the therapy would be unlikely to succeed.

2. We developed a better AAV delivery vector for photoreceptors.

Even the best gene construct is only useful if it can reach the right cells. Photoreceptors are the critical cells for vision, but they are also some of the hardest cells to reach safely using a simple injection into the vitreous, the gel-like substance inside the eye. In this project, we developed an improved AAV vector that can transduce, or enter, photoreceptors more efficiently through intravitreal injection. This is important because intravitreal injection is less invasive than surgery under the retina and is more practical for future clinical use. Better photoreceptor delivery brings us closer to a treatment that could be easier to administer while still reaching the cells that matter most for preserving vision.

3. We addressed two of the biggest barriers in retinal gene therapy at once.

Many inherited retinal diseases remain difficult to treat because of two common problems: some disease genes are too large for standard AAV delivery, and many vectors do not reach enough photoreceptors after injection into the eye. Our work

directly addressed both of these barriers. By improving both the gene design and the delivery vector, this project has laid the groundwork for a new type of treatment approach that could be useful not only for Usher syndrome type 1B, but also for other inherited retinal diseases caused by large genes. This makes the project important not just for one condition, but as part of a broader platform for retinal gene therapy.

Why this matters for patients and families?

For people living with inherited retinal diseases, one of the greatest frustrations is that many promising genes are still considered too difficult to treat. Large genes such as MYO7A have remained especially challenging because they do not fit neatly into current gene therapy systems. This project helps move that barrier. By showing that MYO7A can be split more effectively and delivered using a better retinal vector, we have taken meaningful steps toward a future treatment that may be safer, less invasive and more effective. While more work is still needed before this can reach patients, these results provide a strong foundation for the next stage of testing in animal models and for longer-term translation toward human treatment.

Next steps

The next phase of the work will build on these results by testing the lead MYO7A gene therapy design in disease models and continuing to evaluate safety, durability and real-world treatment potential. The ultimate goal is to develop a therapy that restores full-length MYO7A in retinal cells and protects vision in a way that could realistically be used in the clinic. Support from Retina Australia has been instrumental in enabling this progress and in helping move this work toward the next stage of development.

JiangHui (Sloan) Wang

30/03/2026