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Research update: 3D printed-dispensing aids, and some surprising results... for cancer care

Joanna Hodgkinson, Head of Research

Professor James Morgan of Cardiff University is currently leading two research projects funded by Glaucoma UK. Joanna Hodgkinson, Head of Research, spoke to him to hear more about his findings.

UKEGS 2022 grant: prevention of retinal ganglion cell damage

In 2022, Professor Morgan was awarded £49,293 to investigate a possible mechanism of protecting retinal ganglion cells. He found some surprising results!

What was the aim of the project?

Glaucoma causes the selective loss of retinal ganglion cells (RGCs), the neurons that connect the eye to the brain. The environment around these cells in the retina influences how well they can cope with increased eye pressure. It’s a busy environment, with

lots of different types of cell carrying out different functions, to maintain optimal conditions and make sure all the cells are behaving as they should. Cells called microglia look to be particularly important here. Microglia are like the watchguards of the central nervous system, keeping an eye out for nerve cells which appear to be infected or aren't working properly.

Previous research has shown that microglial cells have both protective and damaging effects on RGC health. For example, one of the first changes in glaucoma seems to be loss of connections between RGCs and the outer retina (where the light-sensitive cells are), and it seems microglial cells might initiate this process. Other neurodegenerative conditions such as Alzheimer's or Parkinson's disease also seem to show similar interactions between microglial cells and cells like RGCs.

We wanted to see whether inhibiting (reducing the activity) of microglial cells would limit RGC damage in glaucoma. To do this, we used a substance called CSF1R (Colony Stimulating Factor 1 Receptor) inhibitor, which stops microglia from operating in the retina and central nervous system (CNS). We hoped to see that inhibiting the microglia would protect the RGCs. If successful, we thought this could be used to find a new therapy or treatment for glaucoma.

What have you found out so far?

The results were surprising, and completely the opposite of what we expected!

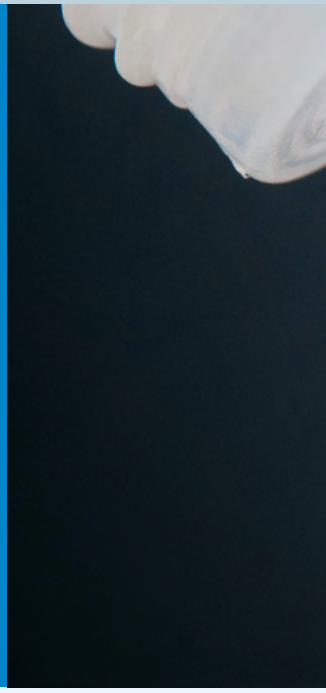
We thought that the CSF1R inhibitor would protect the retinal ganglion cells. In fact, the CSF1R inhibitors in the retina cause significant retinal ganglion cell damage in their own right. The damage is dose-related (more CSF1R results in more RGC damage). When the administration of the CSF1R is stopped the microglial cells recover from the CSF1R inhibitor, but the RGCs remain severely damaged.

Anticipated results:

↓ CSF1R → ↓ microglia activity → ↓ RGC loss → ↑ RGC function

Actual results:

↓ CSF1R → [unknown mechanism] → ↓ RGC function



> We presented the findings at the UKEGS conference in November, and a conference about optic nerves in Austria in December 2023.

The importance of this work is that targeted CSF1R inhibition is unlikely to be useful in the treatment of glaucoma.

We presented the findings at the UKEGS conference in November, and a conference about optic nerves in Austria in December 2023. We're hoping to publish the results soon, and expect there to be some interest, given the results were such a surprise.

Why is this project important or useful to people with glaucoma?

When we set out, we, and others in laboratories around the world, thought we might find a new way to protect retinal ganglion cells, using CSF1R inhibitors. We hoped a possible outcome could have been a new therapy for glaucoma. CSF1R inhibitors are used in some cancer treatments already. However, the findings have blown that out of the water! We know now that CSF1R inhibitors have the opposite effect, and have no role in protecting against glaucoma.

Although it's a dead-end in terms of glaucoma therapies, there are some actions we need to take. People receiving CSF1R inhibitors as a cancer treatment may need to be monitored, for example through OCT and visual field tests, to detect any possible damage to the retinal ganglion cells at the earliest opportunity. So we need to work with our colleagues in cancer care to make them aware of this.

What are the next steps for the research?

The results surprised us, so we don't fully understand what has happened! We're trying to understand how and why the RGCs have been damaged by CSF1R inhibition. We're sending the optic nerves to a specialist lab for independent assessment to understand more about how the structure of the cells has been affected. Our method was just looking

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at the connections to other cells. We anticipate further research will look at how the nerve cells in the visual cortex of the brain are affected by CSF1R inhibition. This aspect of the project is important because we need to know if CSF1R inhibition has a general effect on brain function. While this is not directly relevant to glaucoma it is important for those receiving CSF1R inhibitors for the treatment of cancer.

Royal College of Nursing 2019 grant: developing an electronic monitoring device for eye drop adherence

In 2019, we awarded specialist eye nursing researcher Professor Heather Waterman £49,354 for her investigation into a new electronic way of monitoring whether people are using their eye drops as prescribed. The project was delayed due to COVID, and Professor Waterman has since retired. Professor Morgan is now leading on the project. Here’s where he’s got to.

What was the aim of the project?

Many people with glaucoma find eye drops difficult to manage, and don’t always put them in every day as prescribed by their doctor. We know that this could be putting them at risk of losing more sight. However, it’s very difficult to measure adherence accurately. We don’t have a “gold standard” way of saying how well patients are putting in their drops. This means it can be hard for nurses and other glaucoma professionals to identify who needs additional support, and what this should look like.

We developed a prototype label device to put on the eye drop bottle, containing an electronic membrane and a memory chip. The label records when patients squeeze it. This means we can measure when someone put eye drops in their eye (or at least, when they attempted to!).

The aims of the study were to see whether:

1. The label works reliably;
2. It registers each eye drop instillation accurately;
3. Patients use the label according to the instructions;
4. People with different diagnoses respond similarly to the device;
5. It changes how adherent people are with their eye drops.

We also wanted to check what patients and clinicians felt about the device, whether they found it helpful and practical to use.

We want to ensure that if the label were used more widely on eye drop bottles, it would help patients be more adherent in using their eye drops, and help clinicians in identifying those who need more support.

What have you found out so far?

The project has changed significantly since we started in 2019. We've had lots of staff changes, notably the retirement of our primary investigator, Heather. Unfortunately, we haven't completed the project yet because I've taken it on in addition to my other commitments.

Despite that, we have made significant progress, and the project has evolved, I think to provide a better, more useful device to help patients. When we started the study, it quickly became apparent that lots of people were having real difficulties in putting the eye drops into their eye. So instead of just putting a label on the bottle to monitor when someone was squeezing it, we've changed the device to being a dispensing aid. So the aid can detect when it's squeezed, but it also helps patients hold the bottle securely and squeeze it. We've used 3D printing for this, which makes it really easy to adjust the design based on feedback. It's much quicker than traditional manufacturing methods.

Why is this project important or useful to people with glaucoma?

We know that many people with glaucoma struggle with using their eye drops every day. We want to be able to provide more bespoke support for people to manage their glaucoma and protect their vision, by identifying what they're struggling with. For example, we will be able to identify if someone isn't putting in their eye drops every day – perhaps they need more help to put them in. Other people might be putting in their drops every day, but they aren't lowering the eye pressure. If we find that, we can give them a different type of eye drop, or perhaps another type of treatment. However, we need to make sure that patients are comfortable with this approach.

What are the next steps for the research?

The next steps are to find out whether these devices are acceptable to patients. Does it work as a dispensing aid? Would you feel self-conscious using this in public? Do they want feedback from the device about their adherence? We're also asking clinicians such as doctors and nurses about how well they feel the device works in monitoring whether a patient is using their eye drops regularly.

If the results of this work are positive, we would take the device to suppliers so that it can be mass produced. The idea is that patients would bring the device to the clinic where we could download the drop use history and then plug this into their electronic record. We can then work with patients to find the best way to administer drops and target training and support when needed.