Project Details	
Project Code	MRCNMH26Ca Mead
Title	SONIC-Glaucoma: Stimulation Of Neuroprotective & Immunomodulatory Cargos via Ultrasound in Glaucoma
Research Theme	NMH
Project Type	Wet lab
Summary	Glaucoma causes progressive retinal ganglion cell (RGC) loss and remains without effective neuroprotective therapy. While platelet-derived growth factor (PDGF) and brain-derived neurotrophic factor (BDNF) show strong protective effects in preclinical models, their short half-lives make frequent injections impractical. These factors are enriched in platelets and released in extracellular vesicles (EVs), which naturally cross the blood-retinal barrier. We hypothesize that platelet-derived EVs can serve as endogenous delivery vehicles for PDGF and BDNF. Moreover, we propose that focused ultrasound can non-invasively trigger EV release at the eye, enabling targeted neuroprotection of RGCs in glaucoma.
Description	**Background and Unmet Need** Glaucoma is a progressive eye condition that damages the optic nerve and causes irreversible blindness, affecting over 80 million people worldwide. Central to the disease is the gradual loss of retinal ganglion cells (RGCs), the nerve cells that transmit visual signals from the eye to the brain. While treatments exist to lower intraocular pressure (IOP), the main risk factor, there are no approved therapies that directly protect RGCs from degeneration. This is a major limitation for patients who continue to lose vision despite well-managed IOP. Neurotrophic factors such as platelet-derived growth factor (PDGF) and brain-derived neurotrophic factor (BDNF) have shown strong protective effects in experimental models. However, their clinical use is limited due to short half-lives and the need for frequent eye injections, which is unsuitable for chronic conditions. PDGF and BDNF are enriched in blood platelets and can be released inside extracellular vesicles (EVs), which naturally cross the blood-retinal barrier and deliver therapeutic proteins to retinal tissue. Excitingly, studies show that focused ultrasound, a safe, non-invasive technology, can stimulate platelets to release EVs into circulation. _____ **Key Research Question** Can non-invasive ultrasound be used to stimulate the release of EVs from platelets, enabling the delivery of PDGF and BDNF to the retina and preventing RGC degeneration in glaucoma? _____ **Project Aims and Objectives** This project proposes a novel, multi-disciplinary approach to develop a non-invasive, repeatable neuroprotective treatment for glaucoma. The work is structured into two research objectives, each with distinct stages that the student will lead or co-develop. _____ **Research Objective 1 – Year 1** Develop an ultrasound protocol to trigger therapeutic EV release from platelets

- WP1A (Cardiff):

The student will isolate EVs from commercially sourced human platelets and characterise them using ultracentrifugation, nanoparticle tracking analysis (NTA), ELISA, and Western blotting. These EVs will be tested for PDGF and BDNF content and evaluated for neuroprotective effects in human and rodent RGC in vitro models.

- WP1B (Bristol):

In collaboration with biomedical engineers, the student will test ultrasound parameters (frequency, intensity, duration) to optimise EV release from platelets in vitro. These ultrasound-triggered EVs will undergo the same characterisation and neuroprotection testing.
Student ownership: The student will lead protocol development and in vitro validation, gaining hands-on experience across cell biology, molecular assays, and ultrasound design. They'll have flexibility to explore variables such as dosing and stimulation schedules.

_____

Research Objective 2 – Years 2 and 3

Apply the optimised ultrasound protocol in animal models of glaucoma

- WP2A (Bristol):

The student will apply ultrasound to healthy rats and collect blood to confirm EV release. Targeted ultrasound will then be directed at the eye's blood supply. Retinal tissue will be analysed for EV uptake and PDGF/BDNF content.

- WP2B (Cardiff):

The student will test whether this approach prevents vision loss in a rodent glaucoma model using magnetic bead–induced IOP elevation. Ultrasound treatment will be compared to controls, with outcomes measured using Brn3a staining, DiOlistic dendritic imaging, and ERG-based visual function.
Student ownership: The student will refine ultrasound application in vivo, determine treatment frequency, and lead therapeutic outcome analysis, including statistical design and interpretation.

_____

Training Environment and Skill Development

The student will work across Cardiff and Bristol universities, gaining unique cross-disciplinary experience in neuroscience, regenerative medicine, exosome biology, and ultrasound engineering. Core skills include:

- Stem cell and retinal cell culture
- EV isolation and analysis (NTA, EM, ELISA)
- Immunohistochemistry and advanced microscopy
- In vivo glaucoma surgery and retinal physiology
- Ultrasound instrumentation and optimisation
- Data analysis, presentation, and scientific writing

Students will attend at least one international conference (e.g., ARVO) and contribute to peer-reviewed publications.

_____

Why This Project?

This is a truly interdisciplinary project combining biomedical engineering with retinal neuroscience to develop a first-in-kind, non-invasive

	treatment for glaucoma. It addresses a clear clinical gap and aligns with patient feedback for home-based, injection-free therapy. The project is well-suited for students interested in translational research, vision science, or neurotechnology, and offers flexibility for independent exploration within a supportive, collaborative supervisory team.
Supervisory Team	
Lead Supervisor	
Name	Dr BEN MEAD
Affiliation	Cardiff
College/Faculty	Biological Life Sciences
Department/School	Optometry and Vision Sciences
Email Address	MeadB@cardiff.ac.uk
Co-Supervisor 1	
Name	Dr Daniel Whitcomb
Affiliation	Bristol
College/Faculty	Health and Life Sciences
Department/School	Bristol Medical School
Co-Supervisor 2	
Name	
Affiliation	
College/Faculty	
Department/School	
Co-Supervisor 3	
Name	
Affiliation	
College/Faculty	
Department/School	