Project: RNA base editing strategies as potential therapeutic of inherited retinal dystrophies

Supervised by: A/Prof Guei-Sheung Liu

Research Group: Genetic Engineering Research

Project Summary: Inherited retinal degenerations (IRDs) are significant contributors to global vision impairment and blindness, with no cure to date. Gene therapy by supplementation is restricted to certain forms of IRDs and therefore alternative therapeutic approaches are required. Specific mutations underlying these conditions have been identified, although efficient strategies to target these mutations have not been developed. Recently, CRISPR base editing has allowed targeted modification of single bases using adenosine and cytosine deaminases without causing sequence breaks. Compact CRISPR systems that target RNA have also been demonstrated to perform efficient and specific base editing. Their compact size allows delivery using a single viral vector which is the delivery method of choice.

The current project aims to compare two established compact CRISPR RNA base editors, to investigate their potential in correcting point mutations present in the retina efficiently and specifically. Successful demonstration of ocular RNA base editing using these systems would provide a novel therapeutic approach against IRDs.

This project would be suitable for medical or biomedical science students who are interested in genetic engineering and biotechnology to engage in translational eye research. Applicants with proficiency in genetics or molecular biology subjects are encouraged to apply.

Project: Optimising adeno-associated virus (AAV) transduction efficacy in cell and tissue models

Supervised by: Dr Thomas Edwards & Dr Doron Hickey

Research Group: Gene Therapy group

Project Summary: A range of cell biology techniques will be used to interrogate the effect of supplementary agents on the in vitro transduction efficacy of AAV. The successful applicant will need laboratory experience and be able to demonstrate independent working.
Project: Genetics detective: are mitochondrial DNA mutations responsible for unexplained vision loss?

Supervised by: Dr Isabel Lopez Sanchez and Sona Samuel

Research Group: Mitochondrial Biology and Disease

Project Summary: In this project, the student will apply molecular biology techniques (PCR, restriction enzyme digestion, gel electrophoresis) to investigate the presence of mitochondrial DNA mutations known to cause blindness, using clinical samples from ~250 patients with unexplained vision loss. This important work may provide a genetic diagnosis to patients affected by vision loss, and will lead the pathway for discovery of novel disease-causing genes.

Project: Automated identification of corneal conditions using Artificial Intelligence

Supervised by: Dr Srujana Sahebjada & A/Prof Mark Daniell

Research Group: Surgical Research Unit

Project Summary: Keratoconus is a common condition that affects the cornea and despite its increasing prevalence, the cause of keratoconus is largely unknown. There are many clinical gaps regarding keratoconus in terms of subclinical detection, clarifying its disease stage and identifying which features should be used to predict its progression. These gaps impact on a clinician's decision-making process for keratoconus disease management. The project aims at developing machine learning algorithms to identify features that define early subclinical keratoconus that are currently refractory as well as identify a series of features that are involved in a) disease staging, as well as b) risk of progression of Keratoconus. It provides an exciting opportunity to be a part of this project which includes collecting data, conducting big data analysis, generating AI model and manuscript writing.

Project: Deep phenotyping of inherited retinal disease using advanced imaging techniques.

Supervised by: Dr Thomas Edwards and A/Prof Lauren Ayton

Research Group: Gene Therapy Unit

Project Summary: Successful candidate will develop and apply multi-modal imaging techniques to characterise inherited retinal disease.