# ORIA funding addresses unmet needs in ophthalmology research

In 2019 ORIA invested $641,739 on 12 research projects. This snapshot of 4 of the funded projects illustrates how ORIA is addressing unmet needs in ophthalmology research.

## Blocking the genes that cause blindness

Retinitis pigmentosa (RP) is an inherited eye condition that causes the light-sensitive cells at the back of the eye to slowly degenerate. RP affects 1 in 3,000 people worldwide and there are 8,000 patients in Australia. Although more than 100 genes may cause RP, a gene called PRPF31 is one of the most commonly implicated.

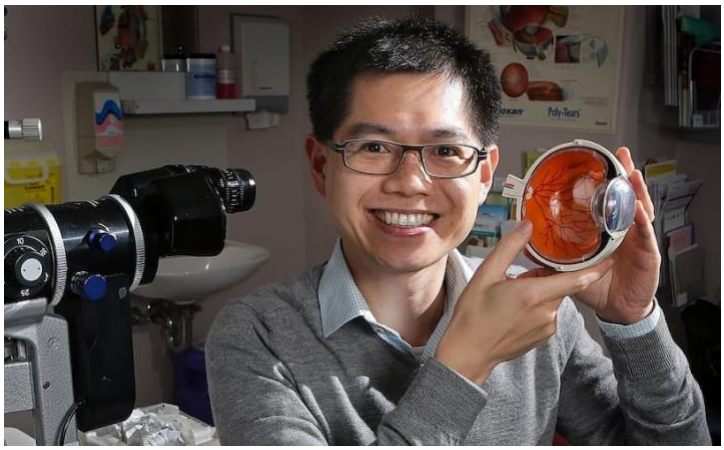
Lead researcher, Dr Fred Chen has studied DNA from families with this gene and found that not all family members (up to 30%) who carry the gene develop RP. This intriguing observation led to the discovery that another gene called CNOT3 is a negative regulator of the PRPF31 gene and is an excellent candidate for new therapeutic strategies. By interfering with CNOT3 function using specially developed RNA fragments, the PRPF31 gene can still function adequately.

“The aim of this study is to induce partial knock-down of CNOT3...and thereby increase PRPF31 expression from the normal allele in retinal cells from patients,” said Dr Chen.

In the laboratory, specially cultured retinal cells from RP patients will then be studied to determine whether gene and cell function improve.

“No treatments are currently available for these diseases,” explains Dr Chen.

“Successful completion of this project will generate essential pilot data to support *in vitro* and *in vivo* pre-clinical animal testing of an Australian made lead drug candidate.”



**Dr Fred Chen,** Centre for Ophthalmology and Visual Science (Lions Eye Institute), The University of Western Australia

## Understanding vision loss caused by the dengue virus

Worldwide, deaths due to dengue virus infection have increased by around 50% between 2005 and 2015, to 18,400. In Australia, the number of dengue virus infections is at a 20-year high. At present no approved vaccines or anti-viral drugs are available to treat dengue virus.

Dengue virus infection may cause an array of different dengue eye diseases.

“Retinopathy, and particularly pathology involving the macula, is well described and most likely to adversely impact the vision,” explains Prof Smith.

“Ultimately any retinal inflammation resolves, but the prognosis of dengue retinopathy is highly variable, ranging from full resolution to permanent vision loss, irrespective of medical interventions to reduce inflammation.”

Prof Justine Smith and colleagues at Flinders University have planned a program of laboratory research to investigate exactly how dengue virus interacts with retinal cells at the molecular level. They are particularly interested in the immune response to the virus.

“Defining the interactions between DENV and retinal pigment epithelial cells represents a first step towards developing effective treatment for dengue retinopathy,” said Prof Smith.

**Prof Justine Smith,** Flinders University, South Australia

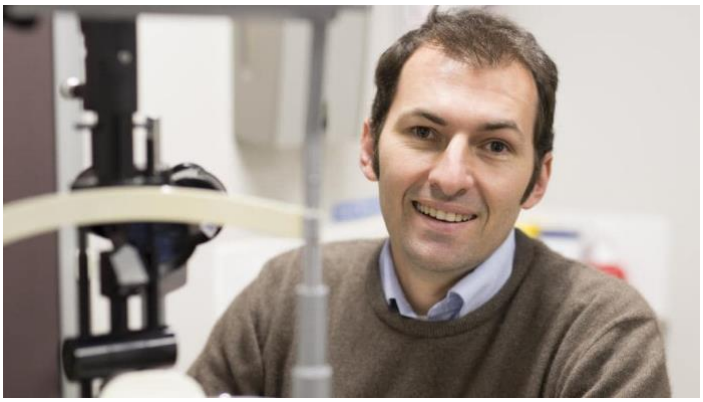
## Decoding the genetic risk for giant cell arteritis

Giant cell arteritis (GCA) is an inflammatory disease causing headaches, joint and facial pain, fever and may cause permanent vision loss. It is the most common form of vasculitis in elderly people, with most patients over the age of 50 and making a timely diagnosis and intervention crucial to prevent vision loss.

“If untreated, GCA can cause catastrophic complications including blindness, strokes, as well as aortic dissection and rupture. GCA represents one of the few true ophthalmic emergencies,” explained Prof Hewitt.

“Even after successful treatment with corticosteroids, GCA relapses in 20-30% of patients. There is a significant need for more effective and safer treatments for GCA.”

In ground-breaking pilot work, Prof Hewitt and his research team have identified a novel locus on chromosome 15 that is associated with GCA. Two implicated genes in this region (milk fat globule-EGF factor 8 MFGE8 and hyaluronan and proteoglycan link protein 3; HAPLN3) will be studied in this project to further elucidate the molecular mechanisms that may be involved.



**Prof Alex Hewitt,** Centre for Eye Research Australia, Melbourne, Victoria

## Targeting inflammation to prevent age-related macular degeneration

Age-Related Macular Degeneration (AMD) is the leading cause of vision loss in the Western world.

“There are two forms of the disease, 'wet' AMD, characterised by choroidal neovascularisation, and 'dry' AMD, in which an atrophic retinal lesion develops,” explained Dr Nilisha Fernando, The John Curtin School of Medical Research, The Australian National University, Canberra.

“There are no treatments for dry AMD, it has been suggested that targeting retinal inflammation, a key feature of disease progression, could lead to the development of novel therapeutics,” she said.

In this study the research team will investigate microRNAs (miRNAs) which are ‘master regulators’ of gene expression. On microRNA in particular, called miR-223, is known to regulate inflammasome - a critical inflammatory pathway that has been strongly linked to the progression of retinal degeneration. Using tissue from people with AMD in combination with an animal model, the therapeutic potential of miR-223 will be investigated.

“These findings could be of major importance in shaping the therapeutic landscape for the treatment of retinal degenerations such as AMD, as well as other neuro-inflammatory diseases where inflammasome activation plays a key role in disease progression,” said Dr Fernando.