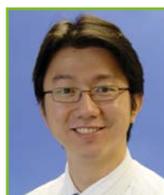


## Examples of successful Letters of Intent

### Clinical Training Award:\*

\*This award has been replaced for the 2013 cycle by the Fellowship Project Award.



**Dr Ning Cheung,**  
Singapore Eye Research Institute

Examples  
of successful  
Letters of  
Intent

**I intend to undertake a 2-year fellowship in both medical and surgical retina in two different countries (Department of Ophthalmology and Visual Sciences, Chinese University of Hong Kong, Hong Kong Eye Hospital, and Singapore Eye Research Institute, Singapore National Eye Centre).**

I will undertake various clinical duties to broaden my experience in diagnosing, evaluating and managing patients with vitreoretinal disorders.

I have already started the first year of my fellowship in Hong Kong (February 2012), for which my clinical duties each week include the following:

- **Three medical retina clinic sessions (including interpretation of FFA/ICG)**
- **Two surgical retina clinic sessions**
- **Three surgical retina operating sessions (hands-on experience with vitrectomy, scleral buckling and others)**
- **One retinal laser/intravitreal injection session (experience in photodynamic therapy, retinal laser and intravitreal injections)**
- **One research/teaching session**
- **Six days/month vitreoretinal oncalls (experience in managing emergency retinal disorders, such as trauma and retinal detachment).**

**I expect these clinical duties to provide me with the experience needed to become a comprehensive retinal specialist**

I expect these clinical duties to provide me with the experience needed to become a comprehensive retinal specialist who is capable of managing patients with a variety of medical and surgical retinal disorders, including macular diseases, retinal vascular diseases, retinal detachment, and others (e.g. retinal oncological disorders, degenerative hereditary disease, infectious retinal disease and trauma).

In addition to the duties described above, I will continue to pursue my academic interest in retinal research in these institutes. Further, the experience with teaching local ophthalmology residents will help me to become a more mature clinical tutor to provide teaching in retinal disorders to ophthalmology trainees.

Professor Tien Yin Wong is my chief mentor, but the fellowship program is also co-mentored by a team of other experienced

clinical retinal specialists (e.g. Dr Chi Wai Tsang, Head of the Vitreoretinal Unit at the Hong Kong Eye Hospital; Associate Professor David TL Liu, Head of the Vitreoretinal Unit at the Prince of Wales Hospital, Hong Kong; Dr Doric Wong, Head of the Vitreoretinal Unit at the Singapore National Eye Centre).

As this is a 2-year plan (most vitreoretinal training needs at least 2 years), I am hoping to apply for the GOAP to obtain support for part of this fellowship program (e.g. for the duration of Sept 2012 to Sept 2013). The GOAP funding will be extremely helpful for me to successfully complete the proposed training to become a comprehensive clinical retinal specialist.

# Research Award: Age-related macular degeneration: analysis of gene expression in the human retina



**Dr Diego Ponzin,**  
Fondazione Banca degli Occhi del Veneto, Italy

Examples  
of successful  
Letters of  
Intent

## Rationale

Age-related macular degeneration (AMD) is a disease caused by degeneration of the retina and choroid, which is chronic, progressive and has a pathogenesis that is still unclear. AMD represents the primary cause of low vision in persons over 50 years in highly-developed countries; in these countries it affects up to 30% of subjects over 70 years of age. Alterations typically affect the macular region, which contains the highest concentration of cone photoreceptors and is principally responsible for central vision. For both forms of the disease (“neovascular or exudative”, and “atrophic or dry”), the most common symptoms are blurred vision, metamorphopsia (distorted vision), and decreased reading ability, especially in dim light. No resolving treatments are so far available.

Lower risk of AMD progression has been associated with intake of antioxidant elements and omega-3 fatty acid-based diets; retinal exudation in advanced neovascular form can be limited with repeated intraocular injections of anti-vascular endothelial growth factor (VEGF). A genetic origin of the disease has been inferred (genes of the immune system, H-factor of the complement, etc.), but related studies have so far been carried out in the genome of peripheral blood cells and never in ocular tissues. The reasons behind this are the huge practical difficulties encountered in obtaining human retina/choroid samples for research purposes, and in rapidly processing the genetic material extracted from these samples.

## Objectives/scope

The aim of this research project is to study potential alterations in gene expression directly in the retinal/choroid tissues of subjects affected by AMD.

## Methods

Human retina and choroid will be harvested from the donor eyes, the corneas of which will be used for transplantation. Half of each sample will be analysed for histological research of signs of AMD (presence of “drusen” in dry AMD, and of vessels from the choroid in exudative AMD), with the other half being used for RNA extraction. Preliminary results have already validated protocols for extraction of good quality RNA (RIN >8) from retina/choroid samples of

human eye bulbs (Mora P *et al.* *Retina* 2010; 30: 1555). Gene expression in affected subjects will be evaluated by means of microarray (Microarray Scanner System G2565AA), and compared with that of healthy donors. The identification of one or more genes that are “up” or “down”-regulated

might allow us to identify alterations in the molecular patterns of diseased tissues.

## Expected results

So far, no gene expression studies have directly involved the tissues affected with AMD, i.e. the human retina and choroid. Microarray-based analyses will allow identification of the genes most dysregulated in AMD, and might therefore provide a new key to the pathogenesis of the disease. It is worth remembering that the finding of significantly increased levels of VEGF in the vitreous humor of patients with neovascular AMD has been the basis for the therapeutic application of anti-VEGF. Our findings might therefore suggest new potential pharmaceutical targets for patients with AMD, or identify further genes linked to the risk of having/developing AMD.

**Microarray-based analyses will allow identification of the genes most dysregulated in AMD**

# Research Award: Neurological, visual and neurocognitive performance in pediatric HIV-infected patients as compared to healthy controls



**Dr Frank Verbraak,**  
University of Amsterdam, The Netherlands

Examples  
of successful  
Letters of  
Intent

## Rationale

This study will determine the relationship between structural retinal neural damage (optical coherence tomography; OCT), functional retinal loss (contrast sensitivity, and color vision tests), cognitive deficits (neuropsychological examination), and subtle brain alterations (advanced neuro-imaging and evaluation of the cerebrospinal fluid) in HIV-infected children with sustained viral suppression on combination antiretroviral therapy (cART) in comparison to HIV-uninfected controls. The cooperation

with the research groups of the Departments of Infectious Diseases, and Neuro-Imaging of the Academic Medical Center will provide a unique set of data, relating retinal neurodegeneration to a complete review of general health and neurological examination of the patients.

Despite the use of cART, HIV-infected children can present with a broad range of neurocognitive impairments.

In addition to neurocognitive deficits, structural and functional abnormalities of the retina have been described in HIV-infected children on cART without infectious retinitis. Damage to the neuroretina has been demonstrated (loss of retinal nerve fiber layer thickness) and shown to be correlated to electroretinographic abnormalities. The mechanisms underlying these retinal abnormalities are – like neurocognitive deficits – mostly unknown. It is possible that identical mechanisms cause brain alterations and cognitive deficits, as well as retinal neurodegeneration.

## Objectives

To evaluate neurologic and cognitive disorders, neuro-imaging and ophthalmological alterations in perinatally HIV-infected children compared with matched (with respect to age, sex, race, home

environment and socio-economic status) healthy controls. To measure cART concentration levels, and markers of disease activity and nervous tissue damage in cerebrospinal fluid (CSF) and blood, and to correlate the results with the outcome of the neuropsychological assessment, neuro-imaging and ophthalmological tests.

## Methods

In this study, 40 perinatally HIV-infected children will be compared with 40 matched (with respect to age, sex, race, home environment and socio-economic status)

healthy controls and will undergo an extensive ophthalmological examination, including OCT, to measure individual retinal layer thickness. The Pelli Robson test (standard test), Cquant test (a new method) will be performed to assess possible differences in contrast sensitivity. The Lanthony, desaturated panel D-15 test will be used to assess color vision. In addition, an extensive neuropsychological examination will be performed to investigate the existence of cognitive deficits. Advanced imaging techniques, like magnetic resonance

imaging (MRI), diffusion tensor imaging, functional MRI (fMRI) and magnetic resonance spectroscopy, will be used to assess possible correlations between cognitive deficits and (subtle) brain alterations. Finally, all HIV-infected children will be requested to undergo lumbar puncture (spinal tap) for collection of CSF, to evaluate drug levels and markers of disease activity and nervous tissue damage.

## Expected results

If retinal neurodegeneration is related to cognitive loss and subtle brain alterations, this could mean that a relatively simple ophthalmological examination could be used as test to document and predict disease progression elsewhere in the body. Patients at higher risk could be identified more accurately, leading to a stricter follow-up and a higher quality of life.

**This study will determine the relationship between structural retinal neural damage... and subtle brain alterations...in HIV-infected children...**