(30)

眼科的先驅進展與未來前沿

Pioneering Advances and Future Frontiers in Ophthalmology

時　　間：114 年 6 月 29 日(星期日) 08:00~12:00
地　　點：臺北榮民總醫院 醫學科技大樓一樓會議室

08:00-08:20	Registration	
08:20-08:30	***Opening Remarks***	陳世真部長 Shih-Jen Chen
	座長：陳世真 部長 (Shih-Jen Chen)	
08:30-08:45	評估大語言模型在醫療任務的應用性 Gauging LLM Readiness in Medical Tasks	張高榮醫師 Kao-Jung Chang
08:45-09:05	First Human Results with the 256 Channel Intelligent Micro Implant Eye (IMIE 256)	Mark S Humayun (USA)
09:05-09:25	Paradigm Shift in Retinitis Pigmentosa	Hossein Ameri (USA)
09:25-09:40	透過基因與多體學技術探索遺傳性視網膜疾病 Exploring inherited retinal diseases through genomics and poly-omics technologies	陳達慶醫師 Ta-Ching Chen
09:40-09:55	眼科用生物醫學微型植入物 Biomedical Microimplants for Ophthalmology	戴聿昌院士 Yu-Chong Tai
10:00-10:30	***Coffee Break***	
	座長：林泰祺 主任 (Tai-Chi Lin)	
10:30-10:50	Studying Retina Using Fluorescence Lifetime Imaging Microscopy	Hossein Ameri (USA)
10:50-11:05	細胞重新程和 iPS 技術在視網膜疾病之開發應用 Cell Reprogramming and iPS Technology in Retinal Diseases	邱士華教授 Shih-Hwa Chiou
11:05-11:25	Long-term Follow-up of a Phase 1/2a Clinical Trial of a Stem Cell-Derived Bioengineered Retinal Pigment Epithelium Implant for Geographic Atrophy	Mark S Humayun (USA)
11:25-11:50	Panel Discussion	陳世真部長 Shih-Jen Chen
11:50-12:00	***Closing Remarks***	陳世真部長 Shih-Jen Chen

Gauging the Large Language Model (LLM) readiness in medical tasks

程評估大語言模型在醫療任務的應用性

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The digitalization of medical information, coupled with the rapid advancements in Multimodal Large Language Models (MLLMs), has led to growing interest in their application to medical tasks. However, as the initial AI hype begins to subside, researchers are critically reassessing whether these models are truly ready for integration into high-stakes healthcare environments. By sharing our first-hand experience in docking MLLMs toward a broad range (general medical QA, surgical decision support) and in depth medical tasks (establish automated radiology report generation), the speaker would walk through the technical objectives, application gaps and future projection of human-computer collaboration between MLLM models and next generation physicians.

First human results with the 256 channel Intelligent Micro Implant Eye (IMIE 256)

Mark S Humayun

USC Ginsburg Institute for Biomedical Therapeutics, USA

USC Roski Eye Institute, USA

Background: To report on the safety and efficacy of the 256-channel Intelligent Micro Implant Eye epiretinal prosthesis system (IMIE 256).

Methods: The IMIE 256 implants were implanted in the right eyes of five subjects with end-stage retinitis pigmentosa. Following implantation, the subjects underwent visual rehabilitation training for 90 days, and their visual performance was evaluated using the grating visual acuity test, Tumbling E visual acuity test, direction of motion, square localization, and orientation and mobility test. To evaluate the safety of the IMIE 256, all adverse events were recorded.

Results: Subjects performed significantly better on all evaluations with the IMIE 256 system on as compared with the performance at baseline or with the system off. There was a steady improvement in performance at each observation interval, indicating that the training and/or practice helped the subjects use the IMIE 256. There were two serious adverse events—electrode array movement and low intraocular pressure in one subject, which resolved with surgery. There were no other adverse events observed except those expected in the course of postoperative healing.

Conclusion: These results show an improved safety and efficacy profile compared with that of the Argus II implant. Further clinical trials are needed to confirm these results in a larger number of subjects and over longer durations

Paradigm shift in retinitis pigmentosa

Hossein Ameri
Keck School of Medicine of USC, USA
USC Retinal Degeneration Center, USA

Retinitis Pigmentosa (RP) is the most common inherited retinal disease, initially presenting with night vision difficulties, followed by progressive peripheral vision loss and eventual central vision impairment. Cystoid macular edema and cataracts further contribute to vision decline. While characteristic fundus findings include bone spicule pigmentation, vascular attenuation, and optic disc pallor, early-stage RP may exhibit a normal retinal appearance.

Traditionally, RP diagnosis relied on clinical examination, electroretinography (ERG), and family history to determine inheritance patterns—autosomal recessive, autosomal dominant, or X-linked. However, variations in genetic mutations can lead to diverse disease courses, even within the same inheritance category. Treatment options were historically limited, with studies suggesting potential benefits of Vitamin A, though recent reanalysis has invalidated these findings, leading to its discontinuation as a recommended therapy.

Advancements in imaging, including ultra-wide-field fundus photography and fundus autofluorescence, now enable early and more precise RP detection. A key finding in RP is the symmetrical loss of peripheral retinal vessels, which serves as a reliable diagnostic marker. Genetic testing has transformed RP diagnosis by identifying causative mutations in approximately 50% of cases and aiding in prognosis.

Recent breakthroughs in RP management include gene therapy for RPE65-mediated RP and retinal prostheses, though the latter is no longer commercially available. Ongoing gene therapy trials aim to target both specific mutations and broader, gene-agnostic approaches. Additionally, stem cell transplantation and oral medications, such as the NAC Attack trial investigating N-acetylcysteine (NAC), offer new treatment avenues. Future prospects include Natural History studies to refine disease understanding, potential approval of RPGR-targeted gene therapy in 2025 or 2026, and emerging therapies like optogenetics, modifier gene therapy, and next-generation retinal prostheses. These advancements mark a paradigm shift in RP diagnosis and treatment.

Exploring inherited retinal diseases through genomics and poly-omics technologies

透過基因與多體學技術探索遺傳性視網膜疾病

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Inherited retinal diseases (IRD) encompasses a group of monogenic disorders that lead to the progressive dysfunction of rod and cone photoreceptors, ultimately resulting in blindness. Affecting over 2 million individuals worldwide, more than 300 genes have now been implicated in IRD, making molecular diagnosis essential for clinical management and for determining eligibility for participation in gene therapy trials.

With advancements in next-generation sequencing (NGS) technologies, a variety of genetic testing methods are now accessible for IRD diagnosis. Although the genetic basis is fixed, the progression of IRD remains dynamic. In an era where precise genetic diagnosis has become more achievable, a critical question arises: How can we effectively monitor disease progression in IRD patients to enhance their chances of benefiting from emerging therapies?

In this short talk, I would like to share the experience we found about current evidence surrounding the prediction of therapeutic windows for individual patients, taking genetic, phenotypic, and surgical factors into account. Additionally, we have integrated metabolomics—a comprehensive analysis of biochemical products—demonstrating that common IRD conditions can be distinguished based on unique metabolite heatmaps. Lastly, we would like to share some clinical experience from gene-specific therapies and trials. Hopefully, patients of this field could get more chance in restoring vision in the near future.

Biomedical microimplants for ophthalmology

眼科用生物醫學微型植入物

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The field of microdevices, specifically Micro/Nano-Electro-Mechanical Systems (MEMS/NEMS), has advanced tremendously for the last 30 years. Most noticeably, however, the field has mostly advanced in microsensors such as pressure sensors, accelerometers, gyros, microphones for cell phone and smart instrumentation applications. Looking forward though, one promising direction for microdevices is for biomedical applications. Specifically, the new and exciting possibility are "microimplants for ophthalmology or eye diseases," which are small devices to be put on or inside eyes to interface with and/or replace defective intraocular tissues that are important for eye functions. However, the optics of a human eye involves many parts and hundreds of million cells so many diseases can blind an eye. Specifically, according to WHO, four major eye diseases cause ~80% of world blindness, and they are cataract, glaucoma, retinitis pigmentosa (RP)/age-related macular disease (AMD), and diabetic retinopathy. This work reviews the author's research on microimplant research on these four diseases. Covered in this talk will be microdevices including accommodative intraocular liquid lens (aIOLL for Cataract), implantable pressure sensor for continuous monitoring of intraocular pressure (IOP for Glaucoma), retinal prosthetic implant for partial vision recovery (for RP/AMD), and oxygen-transporting implant (for Diabetic Retinopathy). Details of materials, technology, principles, and preliminary results on these devices will be discussed.

Studying Retina Using Fluorescence Lifetime Imaging Microscopy

Hossein Ameri
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USC Retinal Degeneration Center, USA

Fluorescence lifetime imaging microscopy (FLIM) has emerged as a powerful technique for studying tissue metabolism and structure at a cellular level. By measuring the fluorescence lifetimes of nicotinamide adenine dinucleotide (NAD(P)H) and flavin adenine dinucleotide (FAD), FLIM enables the assessment of metabolic states, providing insight into oxidative phosphorylation and glycolysis. In addition to metabolic activity, FLIM is also useful for studying retinal structure. This talk will explore recent advancements in FLIM for retinal imaging, highlighting key findings from studies on both healthy and diseased retinas.

Studies using multiphoton FLIM in wild-type (C57BL6/J) and rd10 mice have demonstrated significant metabolic differences during retinal development. In both strains, oxidative phosphorylation initially decreases and later increases, plateauing over time. However, this transition occurs earlier in rd10 mice, suggesting an accelerated metabolic shift associated with retinal degeneration. Additionally, FLIM analysis has revealed a distinct metabolic distribution between the inner and outer retina, with oxidative phosphorylation being more pronounced in the inner layers.

Beyond animal models, FLIM was also applied to postmortem human retinal tissue. A study on a patient with Stargardt disease demonstrated that the macular area had more oxidative phosphorylation relative to the mid-peripheral retina. These findings underscore the potential of FLIM in assessing disease progression and evaluating therapeutic outcomes.

Through these studies, FLIM has proven invaluable for investigating retinal structure, metabolism, and disease mechanisms. This presentation will discuss the role of FLIM in advancing our understanding of retinal disorders and its implications for the development of targeted treatments.

Cell reprogramming and iPS technology in retinal diseases

細胞重新程和 iPS 技術在視網膜疾病之開發應用

Shih-Hwa Chiou

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In recent years, due to advances in regenerative medicine and stem cell technology, as well as the use of health big data, cell therapy has broken through the barriers and bottlenecks in the treatment of many diseases and physiological research in the past, creating various possibilities for personalized precision medicine, and has become the focus of global medical competition. It is also a key policy direction for the government to promote innovative medical care in Taiwan.

The Ministry of Health and Welfare of the Executive Yuan promulgated the " Measures for the Administration of the Implementation or Use of Specific Medical Technical Inspection Instruments " (referred to as the Special management method) in 107, and formulated a draft of the " Regulations on the Administration of Regenerative Medicine Preparations " to promote Taiwan's regenerative medicine industry and emerging organisms. The basis for technological development. In recent years, Taiwan and Japan have been promoting economic structural reforms and industrial innovation measures. It is hoped that this exchange of Taiwanese clinical trials will help Japan's successful experience in implementing the regenerative medicine industry and provide more complete domestic regenerative medicine products. Benefit the domestic public.

In the future, multi-center and cross-field clinical treatment can be carried out in Taiwan, which is expected to improve the treatment level for Taiwan's stem cell industry.

Long-term follow-up of a phase 1/2a clinical trial of a stem cell-derived bioengineered retinal pigment epithelium implant for geographic atrophy

Mark S Humayun

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USC Roski Eye Institute, USA

Purpose: To report long-term results from a phase 1/2a clinical trial assessment of a scaffold-based human embryonic stem cell-derived retinal pigmented epithelium (RPE) implant in patients with advanced geographic atrophy (GA).

Design: A single-arm, open-label phase 1/2a clinical trial approved by the United States Food and Drug Administration.

Participants: Patients were 69-85 years of age at the time of enrollment and were legally blind in the treated eye (best-corrected visual acuity [BCVA], ≤ 20/200) as a result of GA involving the fovea.

Methods: The clinical trial enrolled 16 patients, 15 of whom underwent implantation successfully. The implant was administered to the worse-seeing eye with the use of a custom subretinal insertion device. The companion nonimplanted eye served as the control. The primary endpoint was at 1 year; thereafter, patients were followed up at least yearly.

Main outcome measures: Safety was the primary endpoint of the study. The occurrence and frequency of adverse events (AEs) were determined by scheduled eye examinations, including measurement of BCVA and intraocular pressure and multimodal imaging. Serum antibody titers were collected to monitor systemic humoral immune responses to the implanted cells.

Results: At a median follow-up of 3 years, fundus photography revealed no migration of the implant. No unanticipated, severe, implant-related AEs occurred, and the most common anticipated severe AE (severe retinal hemorrhage) was eliminated in the second cohort (9 patients) through improved intraoperative hemostasis. Nonsevere, transient retinal hemorrhages were noted either during or after surgery in all patients as anticipated for a subretinal surgical procedure. Throughout the median 3-year follow-up, results show that implanted eyes were more likely to improve by > 5 letters of BCVA and were less likely to worsen by > 5 letters compared with nonimplanted eyes.

Conclusions: This report details the long-term follow-up of patients with GA to receive a scaffold-based stem cell-derived bioengineered RPE implant. Results show that the implant, at a median 3-year follow-up, is safe and well tolerated in patients with advanced dry age-related macular degeneration. The safety profile, along with the early indication of efficacy, warrants further clinical evaluation of this novel approach for the treatment of GA.