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# 免疫和細胞治療新進展學術會議

# International Symposium on New Advances in Immune Cell Therapy

時　　間：113 年 6 月 23 日(星期日) 09:00~12:00
地　　點：臺北榮民總醫院 致德樓一樓第一會議室

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| ***08:30-09:00*** | ***報到*** | |
| ***09:00-09:10*** | ***貴賓、長官致詞 紀念合影*** | |
| | **座長：鄭子豪 副校長 (Tzu-Hao Cheng)**<br>**黃奇英 教授 (Chi-Ying Huang)**<br>**陳正豐 主任 (Cheng-Fong Chen)** | |
| 09:10-09:40 | 細胞療法新範例<br>Cell Therapy: A New Paradigm | 林欣榮院長<br>Shinn-Zong Lin |
| 09:40-10:10 | 攜帶核酸的標靶細胞外囊泡用於癌症治療<br>Targeted Extracellular Vesicles Carrying Nucleic Acids for Cancer Therapy | 李利教授<br>L. James Lee |
| 10:10-10:40 | 幹細胞在退化性膝關節炎的治療：挑戰與困境<br>Stem Cell Therapy in Knee Osteoarthritis: Challenge and Predicament | 張毓翰主任<br>Yu-Han Chang |
| ***10:40-10:50*** | ***Coffee Break*** | |
| | **座長：顏厥全 主任 (Chueh-Chuan Yen)**<br>**邱士華 主任 (Shih-Hwa Chiou)** | |
| 10:50-11:20 | 半導體技術應用於細胞療法<br>Semiconductor Technology for Cell Therapy | 李鎮宜副校長<br>Chen-Yi Lee |
| 11:20-11:50 | iPS 細胞細胞治療的現況與未來挑戰<br>Current Status and Future Challenges of Cell Therapy Using Induced Pluripotent Stem Cells (iPSCs) | 吉田信介博士<br>Shinsuke Yoshida<br>(日本) |
| ***11:50*** | ***閉幕式*** | |

# Cell therapy: A new paradigm

## 細胞療法新典範

**Shinn-Zong Lin**
**林欣榮**
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*佛教慈濟醫療財團法人 花蓮慈濟醫院 神經醫學科學中心*

Exosomes, the extracellular vesicles secreted by various cells, have diverse biomolecules that modulate cellular functions in recipient cells.

Tumor-derived exosomes play the pivotal role in transferring oncogenic molecules to neighboring cells, leading to the alteration of their phenotype and promoting tumor growth, metastasis, drug resistance, and modulation of tumor microenvironments. Our research on malignant brain tumors has revealed that glioblastoma stem cells (GSCs) transfer their cargoes to tumor non-stem cells or normal cells via extracellular vesicles (EVs), leading to the development of a tumor stem cell subtype with therapeutic resistance and cancerous properties. TZAB-001, a monoclonal antibody produced from GSCs-derived extracellular vesicles, significantly reduce the therapeutic resistance of tumor stem cells by blocking the intercellular propagation of EVs. The TZAB-001 recognized proteins expressed in gliomas almost 60 times higher than other tumors. Immunohistochemical staining and western blot show that TZAB-001 antibody specifically recognizes human GBM stem cells, liver cancer cell line HepG2, pancreatic cancer cell PANC-1, and lung cancer cell line A549, but not normal brain cells. The results reveal that TZAB-001 has the application potential for tumor diagnosis, CarT immunotherapy in cancer stem cells, and ADC drug development to enhance their efficacy.

In regenerative medicine, exosomes derived from stem cells have shown promising results in promoting tissue repair and regeneration. Furthermore, exosomes also modulate the immune response and promote angiogenesis, which are critical processes for tissue regeneration. Our studies in Alzheimer's disease focus on developing a culture medium which can increase the exosomes production. Using mesenchymal stem cells (MSCs) and Trisomy-derived T21 AF-iPS cells co-culture system, we identify an exosome enhancer TZX4 that can significantly increase the production of exosomes. In addition, TZ-008 exosomes selected by small molecule BP, which significantly increase the production of the cytokine IL-34 to aid in treating Alzheimer's disease while reducing inflammatory cytokines such as IL-6 and IL-8. Furthermore, TZ-008 exosomes can directly reduce the production of amyloid beta proteins that lead to Alzheimer's disease.

The application of exosomes in regenerative medicine and cancer holds great promise. Nevertheless, there are still many challenges that need to be overcome. These include optimizing the isolation and characterization of exosomes, understanding their specific functions and mechanisms of action, and developing effective delivery strategies for clinical applications. Further research in these areas is needed to fully realize the potential of exosomes as a new class of therapeutics.

# Targeted extracellular vesicles carrying nucleic acids for cancer therapy

## 攜帶核酸的靶向性細胞外囊泡用於癌症治療

**L. James Lee**

**李 利**

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*美國俄亥俄州州立大學 化學及分子生物工程學系*

Extracellular vesicles (EVs) are cell secreted particulates which contain rich biomolecules. EVs encapsulate genetic and proteomic materials have emerged as promising therapeutic agents because they are more biocompatible and can penetrate physiological barriers compared to synthetic nanoparticles. EVs are also much more affordable with lower immunogenicity than cell- or virus-based therapies. Here we show the development of a new bionanotechnology platform, cell nanoelectroporation (CNP), for highly effective cell transfection and production of EVs aplenty. The use of cell secreted EVs containing targeting ligands and therapeutic mRNAs and small RNAs is demonstrated in pre-clinical treatment of pancreatic cancer and brain caner. The potential of targeted EVs carrying therapeutic nucleic acids in immune therapies such as ADC (antibody-drug conjugate), ICI (immune check point inhibitor) and BiTE (bi-specific antibody T-cell engager) will also be discussed.

# Stem cell therapy in knee osteoarthritis challenge and predicament

# 幹細胞在退化性膝關節炎的治療：挑戰與困境

**Yu-Han Chang**

**張毓翰**

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*林口長庚紀念醫院 骨科部 關節重建骨科*

Stem cell therapy presents a promising avenue for treating knee osteoarthritis (OA), a widespread degenerative joint condition impacting millions globally. However, despite encouraging findings in preclinical studies and early clinical trials, numerous hurdles and uncertainties persist regarding its application in knee OA treatment.

Firstly, the absence of a standardized protocol for stem cell therapy in knee OA complicates result comparison across studies and clinics, casting doubt on treatment consistency and quality. Secondly, the efficacy and durability of stem cell therapy for knee OA remain under scrutiny, with varying outcomes reported. While some studies demonstrate significant pain relief and functional improvement, others yield only modest benefits or none at all. Furthermore, the duration of therapeutic effects remains uncertain, raising questions about the necessity for additional treatments over time.

Thirdly, the lack of FDA regulation in the United States leaves stem cell therapy for knee OA without standardized guidelines, resulting in divergent treatment approaches and potential safety risks. Lastly, the substantial cost associated with stem cell therapy poses a significant barrier to access, especially for patients without sufficient financial means or insurance coverage.

In essence, while stem cell therapy holds promise for knee OA treatment, numerous challenges persist. Further research is imperative to ascertain its safety and efficacy, alongside the development of standardized protocols and regulatory oversight. Additionally, efforts to improve access to stem cell therapy are crucial to ensure equitable treatment availability. In this presentation, I will also share my personal journey and experiences with utilizing allogeneic or autologous adipose-derived stem cell therapy for knee osteoarthritis (OA).

# Semiconductor technology for cell therapy

## 半導體技術應用於細胞療法

**Chen-Yi Lee**

**李鎮宜**

*Institute of Electronics, College of Electrical and Computer Engineering, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC*

*國立陽明交通大學 電機學院 電子研究所*

This talk will introduce the recent advances in semiconductor biochips realized by standard CMOS process. In the first part of this talk, several basic function modules such as location sensing, microfluidic operations, thermal control, tw-DEP sorting, and magnetic extraction will be introduced. Then bio-protocols for target medical tests can be derived from these basic functions to achieve better test accuracy and reliability. Two selected examples, LAMP COVID-19 test and stem cell quality detection, will be used to demonstrate the capability of the proposed semiconductor biochips. With more integrated functions in the proposed semiconductor chips and joint research in multidisciplinary collaboration, it is expected to see more successful stories in emerging medical applications in the very near future.

# Current status and future challenges of cell therapy using induced pluripotent stem cells (iPSCs)

## iPS 細胞細胞治療的現況與未來挑戰

**Shinsuke Yoshida**

**吉田信介**

*Research and Development Center, CiRA Foundation, Kyoto, Japan*

*研究開發中心 公益財團法人京都大學 iPS 細胞研究財團*

One of promising applications of human induced pluripotent stem cells (iPSCs) is cell therapy for many diseases. Many researchers have tried to generate cells or tissue-like structures, including organoids, which help to ameliorate target diseases. In Japan, the world's first autologous transplantation of iPS cell-derived cells (RPE cells) was carried out in 2014, and more than dozen clinical studies of allogeneic transplantation of iPS cell-derived cells have already been conducted, starting with also RPE cells since 2017. Until now (May, 2024) any severe adverse events related to transplanted cells have been reported.

To promote such allogeneic cell therapies, we, Center for iPS Research and Application (CiRA), Kyoto University, and CiRA Foundation spun out from there, have been contributed by establishing a clinical-grade haplobank of 27 iPSC lines from seven donors who were homozygous for one of the four most frequent human leukocyte antigen (HLA) haplotypes in Japan (Yoshida et al., 2023). This haplobank, which is in accordance with regulations and has been released since 2015, can provide HLA (HLA-A/HLA-B/HLA-DRB1) -matched iPSC lines to nearly 40% of the Japanese population. To overcome the HLA matching coverage limitations of this haplobank, we have also released other cell lines, including genome-edited hypoimmunogenic iPSCs covering a wider population.

We have another ongoing challenge, my iPS Project for low-cost autologous cell therapies through automation. Together with the findings on automation, we expect that many of the results of this project would be transferable to allogenic therapies as well. On the other hand, unlike the general-purpose haplobank for allogeneic transplantation, this project can focus more than ever on particular differentiated cells as well as iPSC, that would lead a better understanding of the quality of iPSC lines which is truly necessary for clinical applications. We expect that semiconductor technology can play an important role in achieving these two progress.