



朝向健康生命的再生醫學

暨2025年台灣再生醫學學會學術研討會

Toward Health Life by Regenerative Medicine
2025 Annual Meeting of FARM

摘要集

2025
3.29
SAT

主辦：台灣再生醫學學會

協辦： 國立臺北科技大學
高值生醫材料研究與商品化中心

 上海商業儲蓄銀行 文教基金會
THE SHANGHAI COMMERCIAL & SAVINGS BANK, LTD.

 北科大宏裕科技研究大樓
國際會議廳

目 錄

Content

一、 學術研討會會議議程時間表.....	2
二、 學術研討會論文摘要	
Invited Lectures.....	9
Poster Paper.....	27
三、 台灣再生醫學學會入會申請書.....	66

朝向健康生命的再生醫學暨 2025 年台灣再生醫學學會學術研討會
Toward Health Life by Regenerative Medicine / 2025 Annual Meeting of FARM

Scientific Program

Time	Topic	Speaker	Institute	Moderator
08:00	Registration 報 到			
Session 1				
08:30~08:40	Opening Remark			
I-01 08:40~09:10	Transforming Disease Treatment: Mesenchymal Stem Cell Spheroids from Preclinical Models to Scaled-Up, Fully Automated Production	Prof. Seong Keun Kwon	Korean Society for Biomaterials Korean Tissue Engineering & Regenerative Medicine Society	張至宏教授
I-02 09:10~09:40	Rebuilding Immune Resilience in Aging and Cancer: Advancements in Drug Development for Regenerative Health.	Dr. Helen Chen	Stanford University - Alixia	方旭偉教授
I-03 09:40~10:10	Enhancement of BMP-2-Mediated Bone Regeneration and Clinical Study on Osteonecrosis Repair	Prof. Eui Kyun Park	Department of Oral Pathology and Regenerative Medicine, School of Dentistry, Kyungpook National University, Daegu, South Korea	胡育誠教授
10:10~10:30 Group photo / Coffee Break				
Session 2				
I-04 10:30~11:00	Tissue-engineered Tissue Models for Understanding Biological Responses to Nano/Microplastics	Prof. Masaya Yamamoto, PhD.	Graduate School of Engineering Department of Materials Processing Physical Metallurgy and Physicochemistry of Biomolecular and Biomaterial Systems Tohoku University, Japan	楊凱強教授
I-05 11:00~11:20	Angiogenic, Injectable, Granular, Porous Scaffold for Fat Transplantation	劉彥良 教授	中國醫藥大學醫學工程學院	黃玲惠教授 沈家寧教授
I-06 11:20~11:40	Biofabrication of Functionalized Hydrogels: New Frontiers in Regenerative Medicine	林芷歆 副教授	臺北醫學大學奈米醫學工程研究所	
I-07 11:40~12:00	Smart Wound Dressing for Infected Wound Healing and Monitoring Applications	林宗宏 教授	台灣大學醫學工程學系	
12:00 會員大會 / 12:00~13:40 Lunch Break				

Time	Topic	Speaker	Institute	Moderator
Session 3				
I-08 13:40~14:00	Innovative Optical Imaging Technologies: Breakthroughs and Future Perspectives in Blood Microcirculation and Wound Diagnosis	廖倫德 教授	國家衛生研究院生醫工程研究所	何美冷教授 陳志華教授
I-09 14:00~14:20	Comparison of Extracellular Vesicles from Different Stem Cells and Their Potential Use in Bone and Cartilage	陳崇桓 教授	高雄醫學大學骨科學研究中心	
I-10 14:20~14:40	Tracking Mesenchymal Stem Cells with Iron Oxide Nanoparticles: In Vivo Imaging and Applications	蕭仲凱 教授	台北慈濟醫院影像醫學部	
I-11 14:40~15:00	Extracellular Vesicles as a Therapeutic Approach for Cartilage Disorders	廖秀蓉 博士	亞東紀念醫院醫學研究部 國立陽明交通大學生物藥學所	
15:00~15:30 Group photo / Coffee Break				
Session 4				
I-12 15:30~15:50	The Role of CD44-miR146a Axis in Tendinopathy	吳柏廷 教授	成功大學醫學院骨科學科	姚俊旭教授 黃彥華教授
I-13 15:50~16:10	Bioengineered Microrobots for Intelligent Translational Medicine	莊爾元 教授	臺北醫學大學生醫材料暨組織工程研究所	
I-14 16:10~16:30	人工周邊神經再生醫學-中醫學應用典範轉移	陳悅生 教授	中國醫藥大學生物醫學工程學系	
I-15 16:30~16:50	台灣細胞資源整合發展與創新實踐	張育甄 博士	財團法人食品工業發展研究所 生物資源保存及研究中心	
Closing Remarks & Poster Competition Award				

壁報 Poster

評分委員：林泰元教授、施博仁教授、胡尚秀教授、陳敏慧教授、劉澤英教授（依姓氏筆畫排列）

壁報論文作者解說時段：13:00~14:00

No.	Classification	Topic	Authors	Institute
參與競賽				
P-01	Biomaterials	Characterizing Physicochemical Properties of Various Cellulose-containing Thermosensitive Hydrogels	林倩榕 ¹ 林子涵 ¹ 劉怡心 ^{1,2} 蘇真瑩 ^{1,2} 方旭偉 ^{1,2}	國立臺北科技大學化學工程與生物科技研究所 ¹ 高值生醫材料研究與商品化中心 ²
P-02	Biomaterials	Chitosan Nanoparticles as A Targeted Delivery System for Anti-Fibrotic microRNAs in The Treatment of Oral Submucosal Fibrosis	尹品曦 ¹ 鄭詠馨 ² 陳幸佑 ² 楊凱強 ¹	臺北醫學大學牙體技術學系 ¹ 國立臺灣科技大學材料科學與工程系 ²
P-03	Biomaterials	Controlled Fabrication of Gelatin-Based Biodegradable Microspheres: A Comparison of Microfluidic and Emulsification Methods	呂柏融 ¹ 張宥承 ^{1,2} 方旭偉 ^{1,2}	國立臺北科技大學化學工程與生物科技研究所 ¹ 高值生醫材料研究與商品化中心 ²
P-04	Biomaterials	Development of a Supramolecular Hydrogel Incorporating Hybrid Apoptotic Bodies to Enhance the Cancer-Immunity Cycle for Melanoma Immunotherapy	黃偉源 王子威	國立清華大學材料科學與工程學系
P-05	Biomaterials	Establishment of Process Parameters for Polylactic Acid Microparticles Fabrication Using Microfluidic System	吳承翰 ¹ 張宥承 ² 方旭偉 ^{1,2}	國立臺北科技大學化學工程與生物科技研究所 ¹ 高值生醫材料研究與商品化中心 ²
P-06	Biomaterials	Exosome and Oxygen Co-Delivery via a Thermosensitive Hydrogel to Enhance Burn Wound Regeneration	葉政昊 ¹ 陳思恒 ^{1,2*} 林峯輝 ^{1,3*}	台灣大學醫學院和工程學院生物醫學工程研究所 ¹ 長庚大學醫學院長庚紀念醫院整形外科 ² 國家衛生研究院生物醫學工程與奈米醫學研究所 ³
P-07	Biomaterials	Sonoporation-enhanced Pleurodesis	林欣儀 ¹ 廖偉志 ^{2,3} 王浩宇 ¹ 葉秩光 ⁴ 劉彥良 ⁵	中國醫藥大學生物醫學研究所 ¹ 中國醫藥大學附設醫院內科部胸腔科 ² 中國醫藥大學醫學系 ³ 清華大學生醫工程與環境科學系 ⁴ 中國醫藥大學生物醫學工程碩士學位學程 ⁵
P-08	Biomaterials	Studying Cancer Cell Homing Using a Transwell-integrated Alginate Hydrogel Platform	康文 ¹ 呂隆昇 ¹ 楊凱強 ^{1,2,*}	臺北醫學大學生物醫材暨組織工程研究所 ¹ 臺北醫學大學牙體技術學系 ²
P-09	Biomaterials	The Effects of Triple Helix Structure on Modified Gelatin	王韻堯 ² , Yi-Chun Chou ¹ , Yi-Xin Liu ^{2,3} and 方旭偉 ^{2,3*}	國立台北科技大學生物技術研究所 ¹ 國立臺北科技大學化學工程與生物科技研究所 ² 高值生醫材料研究與商品化中心 ³

P-10	Bone marrow stem cells	The role of TNF- α -primed Bone Marrow Mesenchymal Stem Cells in Enhancing Osteogenic and Immunomodulatory Functions for Treating Peri-implantitis	王心妤 ¹ 林妘霏 ¹ 莊漢英 ¹ 蔡孟勳 ² 陳漪紋 ² 王麗姿 ¹	臺北醫學大學醫學檢驗暨 生物技術學系 ¹ 台灣大學臨床牙醫學研究所 ²
P-11	Others	Adipose-derived MSCs Exhibit Enhanced Immunomodulatory Properties Towards CD4 T Cells Via Mitochondrial Transfer	利苑期 莊漢英 陳品瑄 王麗姿	臺北醫學大學醫學檢驗暨 生物技術學系
P-12	Others	An Application Platform of Chinese Medicine Compound to Skin Burns and Scald	劉佳芳 姚俊旭	中國醫藥大學中醫學系
P-13	Others	Concentration Gradient Microfluidics for Neural Stem Cell Applications	張鈺茹 郭奐均 李亦宸*	逢甲大學化學工程學系
P-14	Others	Enhancing Immunomodulation in Umbilical Cord Mesenchymal Stem Cells with Lipopolysaccharide: Therapeutic Prospects for Microbe-associated Inflammatory Diseases	陳品瑄 ¹ 莊漢英 ¹ 蔡孟勳 ² 陳漪紋 ² 王麗姿 ¹	臺北醫學大學醫學檢驗暨 生物技術學系 ¹ 台灣大學臨床牙醫學研究所 ²
P-15	Others	Hypoxia-primed Umbilical Cord Mesenchymal Stem Cells Effectively Modulate CD4 T Cells Through Enhanced Mitochondrial Metabolism	黃孟萱 莊漢英 廖羿婷 王麗姿	臺北醫學大學醫學檢驗暨 生物技術學系
P-16	Others	Immunomodulatory Effects of Umbilical Cord Mesenchymal Stem Cells on Polymorphonuclear Neutrophil Responses in Inflammatory Conditions	Duong Thi Thuy Doan 莊漢英 王麗姿	臺北醫學大學醫學檢驗暨 生物技術學系所
P-17	Others	Therapeutic Potential of Adipose-derived Mesenchymal Stem Cells in Modulating T Cell Responses in Type 2 Diabetes Mellitus	李若宇 ¹ 陳品瑄 ¹ 莊漢英 ¹ 王睦惠 ² 鄭乃禎 ² 王麗姿 ¹	臺北醫學大學醫學檢驗暨 生物技術學系 ¹ 台灣大學醫學院外科 ²
P-18	Others	Umbilical Cord Mesenchymal Stem Cells Modulate Lung Macrophage Responses and Offer Therapeutic Potential for Viral Pneumonia	廖羿婷 ¹ 莊漢英 ¹ 黃瑋琛 ² 王麗姿 ¹	臺北醫學大學醫學檢驗暨 生物技術學系 ¹ 國防醫學院醫學系 ²
P-19	Others	ER Stress Protein TXNDC5 Promotes Skin Fibrosis	劉瀚陽 鄭乃禎	台灣大學醫學院附設醫院
P-20	Regenerative medicine	A Novel 3D Spheroid Imaging Analysis Platform for Assessing the Clinical Potential of Adipose-Derived Stem Cell Spheroids in Regenerative Medicine	羅麗紋 ¹ 沈宜珊 ² 陳星宇 ¹ 沈家寧 ¹ 廖秀蓉 ^{2,3}	中央研究院生醫轉譯研究中心 ¹ 醫療財團法人徐元智先生 醫藥基金會亞東紀念醫院 醫學研究部 ² 國立陽明交通大學生物藥學所 ³
P-21	Regenerative medicine	Adipose Tissue-derived Mesenchymal Stem Cells Show Promise in Diabetic Ulcer Treatment with Targeted Polymorphonuclear Neutrophil Modulation	陳芷榆 ¹ 林妘霏 ¹ 莊漢英 ¹ 王睦惠 ² 鄭乃禎 ² 王麗姿 ¹	臺北醫學大學醫學檢驗暨 生物技術學系 ¹ 台灣大學醫學院外科 ²
P-22	Regenerative medicine	Development of Nicotinamide Mononucleotide Loaded Nanoparticle Applied in Retinal Ganglion Cell Regeneration	朱培欣 ¹ 楊添鈞 ² 曾靖嬋 ^{3*}	臺北醫學大學奈米醫學工程研究所 ¹ 臺北醫學大學解剖學暨細胞生物學科 ² 臺北醫學大學醫材暨組織工程研究所 ³

P-23	Regenerative medicine	Enhanced Expansion and Activation of Immune Cell Spheroids Using a One-Step Closed Bioreactor for Immunocellular Therapy	林智妮 ¹ 楊易軒 ² 管哲雍 ² 林峯輝 ^{1,2}	國立臺灣大學醫學工程研究所 ¹ 國家衛生研究院生醫工程與奈米醫學研究所 ²
P-24	Regenerative medicine	Small Extracellular Vesicles Engineered Using Click Chemistry to Express Chimeric Antigen Receptors Show Enhanced Efficacy in Acute Liver Failure	陳姿妤 ¹ 呂彥葶 ¹ 陳雅紋 ² 林郁修 ¹ Duy-Cuong Le ^{3,4,8} 黃彥華 ^{3,5,6,7} 王惠鈞 ² 李政忠 ^{2,8} 林泰元 ¹	國立臺灣大學醫學院藥理學研究所 ¹ 臺北醫學大學醫學科技學院轉譯醫學博士學位學程 ² 臺北醫學大學醫學院國際博士學位學程(細胞治療與再生醫學) ³ Vimtec 高科技中心, Vimtec 醫療系統, 河內, 越南 ⁴ 臺北醫學大學醫學院醫學系生物化學與分子細胞生物學科 ⁵ 臺北醫學大學醫學院醫學科學研究所 ⁶ 臺北醫學大學細胞治療與再生醫學研究中心 ⁷ 臺北醫學大學醫學科技學院國際轉譯科學博士學位學程 ⁸
P-25	Regenerative medicine	Umbilical Cord Mesenchymal Stem Cell Therapy in Porphyromonas Gingivalis-mediated Severe Aspiration Pneumonia Via Modulation of Lung Macrophages	林妘霏 ¹ 莊漢英 ¹ 蔡孟勳 ² 陳漪紋 ² 王麗姿 ¹	臺北醫學大學醫學檢驗暨生物技術學系 ¹ 台灣大學臨床牙醫學研究所 ²
P-26	Tissue Engineering	3D Stem Cell Spheroid-derived Decellularized Matrix as Platform for Loading Delivering Brain-derived Neurotrophic Factor Delivery to Treat Traumatic Brain Injury	林鈺萍 ¹ 高英淇 ¹ 黃玠誠 ¹	國立清華大學生物醫學工程研究所
P-27	Tissue Engineering	Bone Morphogenetic Protein-2 Hybrid Electrospinning Membranes for Applications in Bone Differentiation	謝孟昀 ² 陳映彤 ² 李亦宸 ^{2,*} 姚俊旭 ^{1,*}	中國醫藥大學醫學院生物醫學影像暨放射科學系 ¹ 逢甲大學化學工程學系 ²
P-28	Tissue Engineering	Fabrication of Multi-zonal Cartilage Graft with Chondrocyte Precursors of Different Maturity	蔡宜蓁 ¹ 劉彥良 ² 林峯輝 ³ 劉華昌 ⁴	中國醫藥大學生物醫學工程學系 ¹ 中國醫藥大學生物醫學工程碩士學位學程 ² 國立臺灣大學醫學工程學系 ³ 國立臺灣大學醫學院骨科部 ⁴
P-29	Tissue Engineering	Integrated SOX9 mRNA Lipid Nanoparticles and Porous Cell Carriers: A Novel Approach to <i>In situ</i> Chondrogenesis for Mesenchymal Stem Cell Therapy in Cartilage Defect Repair	陳詩妮 ¹ 劉華昌 ² 劉彥良 ³	中國醫藥大學醫學檢驗生物技術學系 ¹ 國立臺灣大學醫學院骨科部 ² 中國醫藥大學醫學工程學院生物醫學工程碩士學位學程 ³
P-30	Tissue Engineering	The Synthesis of Gelatin-diamine Couple to Sialic acid to formed the Composed Polymer Based that the Physicochemical Characterization by NMR Spectroscopy, for Cell Functional Evaluated by Cell Viability and Cell Migration Test	蕭淑敏 方旭偉*	國立臺北科技大學化學工程與生物科技研究所

不參與競賽				
P-31	Biomaterials	Evaluation of 3-D Printed Scaffolds Grafted with EGCG on Osteoblast Activity	陳秀敏 ¹ 姚俊旭 ² 程正鑫 ³	中國醫藥大學醫學工程學院生物醫學工程碩士學位學程 ¹ 中國醫藥大學生物醫學影像暨放射科學學系 ² 臺南市立安南醫院委託中國醫藥大學興建經營 ³
P-32	Biomaterials	Liquid Foam as Carrier of Immune Cells and Anti-cancer Agents for Intraperitoneal Immunotherapy	沈雅涵 ¹ 洪明奇 ² 林峯輝 ¹ 劉彥良 ³	國立台灣大學醫學工程學系 ¹ 中國醫藥大學生物醫學研究所 ² 中國醫藥大學生物醫學工程碩士學位學程 ³
P-33	Biomaterials	Regenerative Efficacy of Supercritical Carbon Dioxide-Collagen Matrix on Gingival keratinization in Comparison with CTG Technique	Chou Yu Shang ¹ , Srinivasan Periasamy ² , Ko-Chung Yen ² , Dar-Jen Hsieh ^{2,*}	School of Dentistry, College of Dental Medicine, Kaohsiung Medical University, Taiwan ¹ R&D Center, ACRO Biomedical Co. Ltd, 33Kaohsiung City 82151, Taiwan ²
P-34	Biomaterials	Stem Cell Spheroid-derived 3D Decellularized Matrix with Polydopamine Nanoparticle Dressing Promotes Brain Tissue Repair by Antioxidative and Immunomodulatory Potential	楊蓓青 黃玠誠*	國立清華大學生物醫學工程研究所
P-35	Biomaterials	Supercritical Carbon Dioxide-Derived Acellular Dermal Matrix-Based Neuromorphic Device with Ultralow Voltage, Ion Channel Emulation, and Synaptic Forgetting Visualization Computation	Lei Li ¹ , Yihua Xu ¹ , Qunkai Peng ¹ , Pei Huang ¹ , Xinqing Duan ¹ , Mingqiang Wang ¹ , Yu Jiang ¹ , Jie Wang ¹ , Srinivasan Periasamy ² , Kuan-Chang Chang ¹ , Dar-Jen Hsieh ^{2,*}	Guangdong Provincial Key Laboratory of In-Memory Computing Chips, School of Electronic and Computer Engineering, Peking University, Shenzhen 518055, P. R. China ¹ R&D Center, ACRO Biomedical Co. Ltd, Kaohsiung City 82151, Taiwan ²
P-36	Regenerative medicine	An Immune Microenvironment-modulating Plants-derived EVs with re-epithelialization for Diabetic Wound Therapy	廖秀蓉 ^{1,2} 蔡維妮 ² 吳廣俠 ² 張至宏 ^{3,4*} 黃奇英 ^{2*}	亞東紀念醫院醫學研究部 ¹ 國立陽明交通大學生物藥學所 ² 亞東紀念醫院骨科部 ³ 元智大學生物工程與技術研究所 ⁴
P-37	Tissue Engineering	Bioinspired Scaffold Biomimicking Native Cartilage Extracellular Matrix Enhances Chondrogenesis of Human Synovium-Derived Stem Cells	陳怡儒 楊雅婷 王禎麒	台北慈濟醫院骨科部
P-38	Tissue Engineering	Wharton's Jelly Mesenchymal Stem Cells Secrete Extracellular Vesicles Enhance Cell Proliferation and Reduce Oxidative Stress in Chondrocytes	伍哲緯 ^{1,2,3} 傅尹志 ^{1,3,4} 邵佩琳 ⁵ 張玲華 ^{1,3} 鄒亞璇 ^{1,3} 曹雲雅 ^{1,3} 吳順成 ^{1,3*}	高雄醫學大學再生醫學與細胞治療研究中心 ¹ 元培醫事科技大學食品科學系 ² 高雄醫學大學骨科學研究中心 ³ 高雄醫學大學骨科 ⁴ 亞洲大學護理學系 ⁵

Invited Lectures

08:40~09:10

I-01

Transforming Disease Treatment: Mesenchymal Stem Cell Spheroids from Preclinical Models to Scaled-Up, Fully Automated Production

Seong Keun Kwon

Korean Society for Biomaterials

Korean Tissue Engineering & Regenerative Medicine Society

Abstract :

Clinical translation of stem cell therapy has been disappointing thus far due to limited in vivo efficacy. Many researches have been undertaken to improve stem cell activity using gene transfection; nevertheless, gene modification is coupled with a safety risk, which precludes clinical application of stem cell treatment. As a result, spheroidal formation has gained popularity as a method of boosting function without risking safety. As a result of the central hypoxic situation, spheroids express a high quantity of vascular endothelial growth factor (VEGF), a cytokine that promotes angiogenesis. A mesenchymal stem cell-based spheroid secretes cytokines that increase cell survival, proliferation, differentiation, and extracellular remodeling.

In this talk, I would like to demonstrate the method for precise control of spheroid size, which is critical for hypoxia induction. If size control fails and the diameter is too small, hypoxia will not occur, and if the diameter is too large, spheroid survival will decrease. Compared to 2D cultured MSCs, spheroids released significantly increased VEGF, and it increased angiogenesis in both in vitro and various animal disease models.

In addition, I would like to cover a comprehensive automation system for standardized fabrication of spheroid and a surface modified microwell technology for mass production of spheroid. Polymer dot based fast sensing method will be discussed for spheroid quality assurance. These tools will facilitate clinical translation of stem cell therapy.

Keywords: *Stem Cell, Spheroid, Angiogenesis, Mass Production, Automation*



09:10~09:40

I-02

Rebuilding Immune Resilience in Aging and Cancer: Advancements in Drug Development for Regenerative Health

Helen Chen, Ph.D.

Stanford University – Alixia

Abstract :

Inflammatory monocytes are highly plastic adult stem-like cells with critical roles in immune surveillance and tissue repair. However, their dysregulation is a hallmark of immune aging and disease progression. Increased monocyte dysfunction predicts survival outcomes in cancer patients and is implicated in the pathogenesis of age-related disorders, including frailty and Alzheimer's disease. Using single-cell RNA sequencing, we identified a 27-gene signature associated with dysfunctional monocytes exhibiting mitochondrial leakage, a key trigger of inflammasome activation and systemic inflammation. Here, we describe a novel inflammasome inhibitor capable of reprogramming monocytes, restoring immune balance, and reducing their inflammatory state. In vivo, this therapeutic approach effectively suppressed cancer metastases, while in a frailty mouse model, treatment improved immune resilience to lipopolysaccharide challenge, enhanced physical activity, and increased lung capacity. These findings highlight the potential of targeting inflammatory monocytes to restore immune balance and promote tissue regeneration, offering a promising therapeutic strategy for regenerative medicine applications.



09:40~10:10

I-03

Enhancement of BMP2-mediated Bone Regeneration and Clinical Research on Osteonecrosis Repair

Eui Kyun Park

Department of Pathology and Regenerative Medicine, School of Dentistry, Kyungpook National University *epark@knu.ac.kr*

Abstract :

Bone regeneration can be effectively achieved by either enhancing osteoblast function or inhibiting osteoclast activity. Bone morphogenetic protein 2 (BMP2) is widely used in clinical applications to promote osteoblast differentiation. However, its clinical use requires supraphysiological doses of recombinant human BMP2, which can lead to adverse effects such as inflammation, pain, adipose tissue formation, bone resorption, wound complications, and even tumorigenesis. Therefore, precise regulation of BMP2 signaling is essential to optimize bone regeneration while minimizing side effects. Since BMP2 activates multiple signaling pathways, and its biological response is highly dependent on microenvironmental conditions.

To enhance BMP2 efficiency, various approaches have been explored. Most strategies involve combining BMP2 with biomaterials to improve its stability and ensure its sustained release in the body. Another approach focuses on regulating BMP2 signaling pathways. We took the latter strategy, and one of our research demonstrated that glycine, a major component of collagen, and its derivatives exhibit synergistic effects with BMP2 in bone regeneration. Notably, glycinamide, which carries a positive charge, promotes BMP2-mediated bone regeneration more effectively than glycine. This is likely due to its ability to form nanoparticles with BMP2, facilitating cellular uptake and amplifying BMP2 signaling. Additionally, we aimed to potentiate BMP2 signaling by regulating the role of DOCK5 (dedicator of cytokinesis 5), a guanine nucleotide exchange factor for Rac1. The specific role of Rac1 in osteogenesis and bone regeneration remains unclear. However, our research demonstrated that C21, a DOCK5 chemical inhibitor, significantly enhanced osteoblast differentiation and mineral deposition in mouse MC3T3-E1 cells and in both human and mouse bone marrow mesenchymal stem cells (BMSCs). Dock5 knockout (KO) mice exhibited increased bone mass and a higher mineral apposition rate, with their BMSCs demonstrating enhanced osteoblast differentiation. In vivo models revealed significantly improved bone regeneration by BMP2 in Dock5 KO mice compared to wild-type (WT) mice. Mechanistically, DOCK5 inhibition promotes bone formation by suppressing Rac1 under TAK1 and activating MKK3/6 and p38, which are key components of the BMP2 signaling pathway. These findings suggest that DOCK5 negatively regulates osteoblast differentiation and bone regeneration, providing novel insights into potential therapeutic strategies.

Furthermore, we explored the potential of autologous BMSCs seeded onto calcium phosphate ceramic scaffolds for treating osteonecrosis of femoral head (ONFH). Beginning in the early 2000s, a total of 7 patients (9 hips) with ONFH were implanted with a median number of 10.1×10^7 BMSCs. A

20-year follow-up clinical research demonstrated that the combination of autologous BMSCs and calcium phosphate ceramics showed promising outcomes for the treatment of pre-collapsed and early-collapsed stage ONFH with medium-to-large size, mainly located in weight-bearing areas.



10:30~11:00

I-04

Tissue-engineered Tissue Models for Understanding Biological Responses to Nano/Microplastics

山本 雅哉 (Masaya YAMAMOTO)

東北大學大學院工學研究科 (Graduate School of Engineering, Tohoku University)

Introduction : The blood-brain barrier (BBB) plays a crucial role in maintaining the homeostasis of the brain environment by regulating the entry of substances. Recent studies have discovered that nanoplastics (NPs) can traverse biological barriers, including the BBB (*Cell Reports*, **42** (2023) 112346). Therefore, this research aims to fabricate an *in vitro* BBB model to investigate the biological effects of NPs.

Materials and Methods : Low-density polyethylene (LDPE) film was immersed in a potassium peroxodisulfate solution and stirred at 65°C. Potassium peroxodisulfate was added every 12 or 24 h, for a total of 20 times for the NPs and 10 times for microplastics (MPs). After the treatment, the salts in the immersion solution were removed using a dialysis tube, followed by 7-d ultrasonication. After ultrasonication, each sample was allowed to settle and then freeze-dried to obtain dry powdered samples.

Lyophilized powdered decellularized aorta (dAorta) and brain (dBrain) were dissolved in pepsin-HCl solution for 48 h. The solubilized solution was centrifuged to remove undissolved material, then applied to a Transwell insert and incubated at 37°C for 24 h to coat the membrane surface. For BBB model construction, pericytes (1.5×10^4 cells/cm²) were seeded on the bottom of the insert membrane, followed by endothelial cells (1.5×10^5 cells/cm²) on the upper side. After a 3-d culture, the experimental group was exposed to LDPE-NPs or Interleukin-1 beta (IL-1 β) for 24 h. The integrity of the tight junctions was then evaluated by transepithelial/transendothelial electrical resistance (TEER), immunofluorescent staining, hematoxylin and eosin staining, scanning electron microscopy (SEM), transmission electron microscopy (TEM) and western blot analysis.

Results and Discussion : Advanced Oxidation Processes treatment generated NPs with an average size of 497 nm and MPs with an average size of 23 μ m. Zeta potential analysis indicated that NPs exhibited a higher value, likely due to the increased surface oxidation groups compared to MPs. Differential scanning calorimetry data revealed significantly lower crystallinity in NPs (13.56%) compared to MPs (36.22%), which is likely due to the smaller size of NPs, resulting in higher surface energy and a larger amorphous fraction.

In the non-treated group, cell adhesion was low, while adhesion was significantly enhanced on the decellularized extracellular matrix (dECM)-coated membrane. This indicates that dAorta or dBrain could promote earlier maturation of BBB model. Following exposure to LDPE-NPs, all groups showed a marked reduction in TEER values, suggesting substantial disruption of tight junctions by the NPs.

Conclusions : These results suggest that the BBB model utilizing tissue engineering could be a methodology to investigate the biological effects of NPs.



11:00~11:20

I-05

Angiogenic, Injectable, Granular, Porous Scaffold for Fat Transplantation

Yen-Liang Liu^{1,2,3}

¹Master Program for Biomedical Engineering, China Medical University, Taichung, Taiwan

²Cancer Biology and Precision Therapeutics Center, China Medical University, Taichung, Taiwan

³Graduate Institute of Biomedical Sciences, China Medical University, Taichung, Taiwan

Abstract :

Regenerative aesthetics is an emerging field focused on rejuvenating aging tissues using regenerative medicine, with a particular emphasis on facial aesthetics. Autologous fat grafting has been applied to plump up sunken areas with a more natural appearance than dermal fillers. However, this technique is limited by ischemia-induced cell death and gradual absorption, resulting in long-term volume loss of the grafted fat. To address this issue, we have developed a microbubble-based biological scaffold with properties of porosity, injectability, expandability, and angiogenesis support. This scaffold encapsulates fat tissue and promotes neovascularization by carrying vascular endothelial growth factor (VEGF), thus enhancing nutrient delivery to the grafted area and increasing fat graft survival.

Using a microfluidic device, we created microbubble scaffolds with controlled, uniform pore sizes. This method is simple, rapid, and does not require templates or complex setups. Our microbubble scaffold accommodates micronized fat tissue and contains VEGF-loaded nanoshells to enhance the scaffold's pro-angiogenic capability. Our results demonstrate that this scaffold exhibits favorable properties for fat grafting, including biocompatibility, biodegradability, high porosity, injectability, stretchability, and angiogenic potential. PrestoBlue™ and LDH assays confirm the biocompatibility and non-toxicity of the scaffold. The results of the HUVEC tube formation assay and the CAM assay indicate that VEGF-loaded nanoshells promote vascular network formation and angiogenesis. Subcutaneous implantation in mice shows that grafted fat combined with VEGF-enriched scaffolds maintains greater volume and generates more vasculature over time than traditional fat grafting. Overall, these findings highlight the potential of the microbubble scaffold as a promising adjunct in fat grafting applications for sustained implant volume and enhanced long-term outcomes.

Keywords: microbubble scaffold, dermal filler, fat grafting, VEGF, nanoshell, angiogenesis



11:20~11:40

I-06

Biofabrication of Functionalized Hydrogels: New Frontiers in Regenerative Medicine

Joshua Lim, Sasinan Bupphathong, Hsuan-Ya Tao, Chen-En Yeh, and **Chih-Hsin Lin***

Graduate Institute of Nanomedicine and Medical Engineering, College of Biomedical Engineering,
Taipei Medical University, Taipei 110, Taiwan

Abstract :

Gelatin methacrylate (GelMA) is a widely utilized photocrosslinkable hydrogel in 3D bioprinting, recognized for its biocompatibility, tunable mechanical properties, and ability to support cell adhesion and proliferation. However, a major challenge in tissue engineering is the lack of vascularization, which limits the survival and function of large-scale engineered tissues. To address this, we developed functional GelMA-based bioinks by modulating their mechanical properties and conjugating angiogenic growth factors, including vascular endothelial growth factor (VEGF₁₆₅) and basic fibroblast growth factor (bFGF), via EDC/NHS coupling. These modifications enhanced cell viability, proliferation, and vascular network formation while maintaining structural integrity. Additionally, to improve vascular integration and mitigate tissue necrosis in large-volume fat grafting, we engineered a 3D-bioprinted GelMA scaffold. To optimize vascularization within the scaffold and better support embedded cells, we compared the effects of different culturing systems using human adipose-derived stem/stromal cells (ASCs), human umbilical vein endothelial cells (HUVECs), and cocultures of ASCs and HUVECs in 3D-bioprinted GelMA hydrogel constructs. The coculture system significantly enhanced blood vessel formation in both *in vitro* and *in vivo* models, with the highest vessel density observed in murine implants containing HUVEC and ASC cocultures. Furthermore, GelMA was functionalized with silanized hydroxyapatite (Si-HAp) and silanized bioglass to promote osteogenesis and improve 3D bioprinting resolution. Collectively, these advancements highlight the potential of GelMA-based functional bioinks as a scalable and adaptable platform for regenerative medicine, integrating molecular design with vascularized tissue engineering strategies.



11:40~12:00

I-07

Smart Wound Dressing for Infected Wound Healing and Monitoring Applications

Zong-Hong Lin*

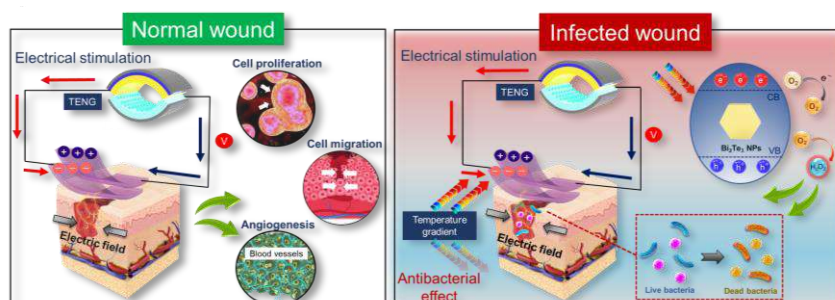
Department of Biomedical Engineering, National Taiwan University, Taipei, Taiwan

*E-mail zhlin@ntu.edu.tw

Abstract :

Electrical stimulation (ES)-based therapy is recognized for its ability to expedite the healing process of chronic wounds. However, its widespread use is hindered by the necessity for bulky, power-consuming sources, often requiring patient hospitalization. To address these limitations, we have developed a self-powered, multi-functional wound dressing capable of activation through wearable nanogenerators, providing electrical stimulation to accelerate wound closure. Additionally, a wireless measurement module is incorporated into the system, enabling remote, non-invasive monitoring of wound recovery. The proposed self-powered wound dressing represents a versatile and responsive strategy for personalized wound treatment, leveraging temperature gradients and mechanical stimuli. The design adopts a layer-by-layer approach, featuring a thermocatalytic layer comprising Bi_2Te_3 nanoplates (NPs) and a mechanical energy harvesting layer consisting of chitosan-coated carbon fiber fabrics (CFFs). For normal skin wounds, ES-mediated therapy was applied by connecting the electrodes to the arch-shaped triboelectric nanogenerator (a-TENG). In the case of infected wounds, a hybrid treatment strategy involving both the TENG and temperature gradient was implemented, simultaneously triggering the Bi_2Te_3 NPs and chitosan/CFF to combat bacteria and promote healing. The pulsed ES from the a-TENG significantly accelerated wound closure by about threefold for both normal and infected wounds compared to control groups. We present a next-generation wearable self-powered wound dressing designed to be activated by diverse stimuli from the patient's body, offering on-demand treatment for both normal and infected wounds. Triggered by the surrounding temperature difference, it controllably generates hydrogen peroxide, effectively inhibiting bacterial growth at the wound site. The integrated electrodes are connected to a wearable triboelectric nanogenerator, providing electrical stimulation to accelerate wound closure by enhancing cellular proliferation, migration, and angiogenesis.

Keywords : Smart dressing, self-powered system, wound healing, infection prevention



[1] S. R. Barman, S.-W. Chan, F.-C. Kao, H.-Y. Ho, I. Khan, A. Pal, C.-C. Huang, Z.-H. Lin* (2023)
“A Self-powered Multifunctional Dressing for Active Infection Prevention and Accelerated Wound Healing” *Sci. Adv.*, 9, eadc8758.

[2] Y.-J. Lin[†], I. Khan[†], S. Saha, C.-C. Wu, S. R. Barman, F.-C. Kao, Z.-H. Lin* (2021)
“Thermocatalytic Hydrogen Peroxide Generation and Environmental Disinfection by Bi₂Te₃ Nanoplates” *Nat. Commun.*, 12, 180 (Editor’s Highlight).



13:40~14:00

I-08

Innovative Optical Imaging Technologies: Breakthroughs and Future Perspectives in Blood Microcirculation and Wound Diagnosis

Lun-De Liao

國家衛生研究院生醫工程研究所 (IBEN, NHRI, Taiwan.)

Abstract :

Regenerative medicine, recognized as a key field of the 21st century, aims to restore damaged tissues and organs. Effective wound healing assessment is critical for clinical decision-making, yet traditional methods rely on subjective evaluation, lacking microvascular insight and delaying intervention—challenges exacerbated in mass casualty incidents like the Formosa Fun Coast explosion. This study introduces Laser Speckle Contrast Imaging (LSCI) for non-contact, real-time monitoring of superficial blood circulation, revolutionizing wound assessment. LSCI quantifies blood flow by analyzing speckle pattern changes, offering objective, large-area evaluation. A major clinical challenge—patient movement affecting assessment accuracy—was addressed using the Channel and Spatial Reliability Tracking (CSRT) algorithm, ensuring robust ROI tracking. Clinical validation showed high tracking consistency (ICC: 0.798-0.917 for acute wounds, 0.628-0.849 for chronic wounds). LSCI significantly reduces assessment time, predicting healing potential within 3-5 days instead of 14, with a necrotic threshold of 21,045.77 AU (AUC=0.918, accuracy=79.48%). Compared to traditional Laser Doppler Flowmetry (LDF), LSCI achieves non-contact skin perfusion pressure (SPP) measurement, providing a comprehensive microcirculation assessment ($r=0.74$ correlation with LDF). Beyond wound care, LSCI integrates with regenerative medicine, evaluating stem cell therapy-induced angiogenesis, biomaterial tissue perfusion, and real-time blood flow in tissue engineering. Future AI integration will enable precise prediction models, advancing personalized treatment and accessible wound care solutions worldwide.

Keywords : Laser Speckle Contrast Imaging, Skin Perfusion Pressure, Microcirculation, Wound Healing, Diabetic Foot, Non-invasive Measurement, Regenerative Medicine



14:00~14:20

I-09

Comparison of Extracellular Vesicles from Different Stem Cells and Their Potential Use in Bone and Cartilage

陳崇桓

高雄醫學大學骨科學研究中心

Abstract :

We compare the miRNA profiles of exosomes derived from human iPSCs, BMSCs, and ADSCs (hiPSC-Exos, hBMSC-Exos, and hADSC-Exos) and their functional effects on human articular chondrocytes (hACs). hiPSC-Exos, hBMSC-Exos, and hADSC-Exos were collected from the appropriate cells cultured in 10% bovine exosome-depleted FBS (de-Exo-FBS) for 48 hours. NGS and bioinformatics were used to analyze the small RNA profiles of these exosomes. The biological functions of hACs were examined after a 12-day treatment with exosomes. hBMSC-Exos and hADSC-Exos had similar miRNA profiles but were largely different from hiPS-Exos. There were 17 highly expressed miRNAs in hiPSC-Exos, 13 miRNAs in hADSC-Exos, and 11 miRNAs in hBMSC-Exos. Among them, 7 miRNAs overlapped between the hBMSC-Exos and hADSC-Exos, and only 3 of them (hsa-miR-16-5p, hsa-miR-25-3p, and hsa-miR-93-5p) overlapped among all 3 exosomes. The putative target genes of the 3 overlapping exosomal miRNAs, and high-scoring target genes, including MAN2A1, ZNFX1, PHF19, GPR137C, ENPP5, B3GALT2, FNIP1, PKD2, and FBXW7, were identified. GO and KEGG enrichment analyses revealed that these genes are involved in cell growth, bone ossification, and cartilage development/differentiation, possibly via the MAPK signaling pathway. Accordingly, we confirmed the biological effect on cartilage differentiation and found that hiPSC-Exos, hBMSC-Exos and hADSC-Exos maintained hAC viability, prevented senescence, promoted the formation of a normal cartilage matrix (glycosaminoglycan and type II collagen), and downregulated fibrocartilage matrix (type I collagen) in normal hACs. Comparatively, hBMSC-Exos had the greatest effect on hAC function. Bioinformatics revealed differences and possible mechanisms of action of exosomes derived from pluripotent hiPSCs, multipotent hADSCs and multipotent hBMSCs and these exosomes effectively suppressed cell senescence and promoted normal functional extracellular matrix formation in hACs. We also found EV from hypoxia cultured ADSCs and umbilical cord MSC can improve osteoarthritic phenotype chondrocyte and osteoarthritis. We also found EV from iPSC and ADSCs can enhance osteogenic differentiation of MSC in vitro and bone defect healing in vivo.



14:20~14:40

I-10

**Tracking Mesenchymal Stem Cells with Iron Oxide Nanoparticles:
In Vivo Imaging and Applications**

Jong-kai Hsiao

Dept. Medical Imaging, Taipei Tzuchi Hospital, New Taipei City, Taiwan.

Abstract :

Iron oxide nanoparticles (IONs) offer a transformative approach to tracking and enhancing mesenchymal stem cell (MSC) therapies for brain disorders, as demonstrated in our comprehensive research. This presentation showcases our advancements in labeling human and rat MSCs (hMSCs and rMSCs) with Ferucarbotran and Ferucarbotran-protamine (Fer-Pro) complexes to monitor their brain trafficking and therapeutic impact via magnetic resonance imaging (MRI). Our studies reveal that ION labeling preserves MSC viability, proliferation, and differentiation while enabling high-resolution, non-invasive tracking in vivo. In a murine glioma model, Fer-Pro-labeled hMSCs exhibit targeted migration to tumors via SDF-1/CXCR4 signaling, detectable by clinical 1.5-T MRI, and display intrinsic tumor inhibition. For neural repair, ION-labeled hMSCs differentiate into neural-like cells (NCs) with intact electrophysiological function and neural marker expression (e.g., GFAP, TH, TuJ1). Most strikingly, in an ischemic stroke rat model, Ferucarbotran-labeled rMSCs (Fer-RFP⁺ rMSCs) not only migrate to ischemic sites—tracked by 3T MRI—but also, when isolated ex vivo, exhibit spontaneous neuronal firing activity and NeuN expression, suggesting functional neuronal differentiation. These cells correlate with reduced infarct volumes and improved neurological scores, highlighting a potential cell replacement mechanism alongside bystander effects. Collectively, our work demonstrates that ION labeling, particularly with Ferucarbotran, enhances MSC-based therapies for brain tumors and stroke by enabling precise trafficking and revealing novel functional integration, bridging preclinical promise to clinical potential.



14:40~15:00

I-11

Extracellular Vesicles as a Therapeutic Approach for Cartilage Disorders

廖秀蓉

亞東紀念醫院醫學研究部 / 國立陽明交通大學生物藥學所

Background and Objectives : Osteoarthritis (OA) and rheumatoid arthritis (RA) are chronic inflammatory joint diseases leading to cartilage degradation and joint dysfunction. OA is characterized by cartilage damage and joint pain, while RA involves autoimmune-driven synovial inflammation and cartilage destruction. There are no effective disease-modifying osteoarthritis drugs (DMOADs) currently available. This study investigates the potential of extracellular vesicles (EVs) derived from mesenchymal stem cells (MSCs) primed with a novel peptide (Patent 1-P) for cartilage repair and inflammation regulation in OA and RA models.

Materials and Methods : Patent 1-P-primed MSC-EVs were isolated using tangential flow filtration (TFF) and characterized according to the International Society for Extracellular Vesicles' guidelines. Therapeutic effects were evaluated in OA and RA models, including an ACLT-induced OA model and a CIA-induced RA model. High-throughput RNA sequencing (RNA-seq) and miRNA sequencing were performed to analyze the molecular mechanisms in RA.

Results : In OA models, Patent 1-P enhanced chondrogenesis by activating receptor X signaling pathways, upregulating key cartilage markers like collagen type II, COMP, and SOX9. Intra-articular injections of Patent 1-P reduced OA severity, and the therapeutic benefit was improved with Patent 1-P-MSC-EV administration, resulting in thicker cartilage and reduced MMP13 activity, suggesting Patent 1-P-MSC-EVs as a potential DMOAD.

In RA models, ADSC-EVs inhibited osteoclast differentiation by modulating key factors such as C-CBL, cathepsin K, and miRNAs (miR-X, miR-Y, miR-Z), which suppressed RANK signaling. RNA-seq analysis showed downregulation of RANK signaling and Ca^{2+} oscillations. In CIA rats, combined ADSC-EVs and etanercept treatment led to disease remission and cartilage repair. In RA patients unresponsive to etanercept, engineered ADSC-EVs reduced osteoclast activation.

Conclusions : Patent 1-P-MSC-EVs promote chondrogenesis and cartilage repair in OA, while engineered ADSC-EVs modulate osteoclast differentiation and inflammation in RA. These results suggest MSC-derived EVs, particularly Patent 1-P-primed and engineered miRNA-loaded ADSC-EVs, as a promising treatment strategy for OA and RA by enhancing cartilage regeneration and reducing inflammatory bone destruction.



15:30~15:50

I-12

The Role of CD44-miR146a Axis in Tendinopathy

Po-Ting Wu

Department of Orthopaedics, College of Medicine, National Cheng Kung University, Tainan, Taiwan

Department of Orthopaedics, National Cheng Kung University Hospital, College of Medicine,
National Cheng Kung University, Tainan, Taiwan

Department of Biomedical Engineering, National Cheng Kung University, Tainan, Taiwan

Department of Biochemistry and Molecular Biology, College of Medicine, National Cheng Kung
University, Tainan, Taiwan.

Medical Device Innovation Center, National Cheng Kung University, Tainan, Taiwan

Abstract :

Tendinopathy is a degenerative condition characterized by apoptosis, chronic inflammation, and cellular senescence, leading to extracellular matrix (ECM) disruption and tendon dysfunction. CD44, a principle hyaluronan receptor, has been implicated in regulating apoptosis and inflammation, while microRNA-146a (miR-146a) plays a crucial role in mitigating IL-1 β -driven senescence. Our previous studies reveal the roles of CD44 and miR-146a in tendinopathy and their interactions in modulating apoptosis, inflammation, senescence, and ECM homeostasis. CD44 expression was positively correlated with tendinopathy severity in human long head biceps (LHB) tendons, with apoptotic cells co-localized in CD44-expressing regions. Blocking CD44 signaling induced apoptosis, elevated cleaved caspase-3, and increased pro-inflammatory mediators, including IL-1 β , IL-6, TNF- α , and MMP family members, while reducing tenogenic markers and phosphorylated AKT. Furthermore, CD44 overexpression in tendinopathic tenocytes and a rat Achilles tendinopathy model suppressed senescence-associated secretory phenotypes (SASPs), downregulating p53, p21, p16, COX-2, and phospho-NF- κ B while enhancing tenomodulin and collagen type I. Similarly, miR-146a expression negatively correlated with tendinopathy severity, and its overexpression suppressed IRAK-4/TRAF6/NF- κ B signaling, protecting tenocytes from senescence and SASPs. Mechanistically, CD44 and miR-146a cooperatively reduced apoptosis through the CD44-AKT-miR-146a axis by suppressing Smad4 expression. These findings highlight CD44 and miR-146a as crucial regulators of tendon homeostasis, offering potential therapeutic targets for mitigating apoptosis, senescence, and inflammation in tendinopathy.



15:50~16:10

I-13

Bioengineered Microrobots for Intelligent Translational Medicine

Andrew E.-Y. Chuang

Graduate Institute of Biomedical Materials and Tissue Engineering, College of Biomedical Engineering, Taipei Medical University, New Taipei City, Taiwan
eychuang@tmu.edu.tw

Abstract :

The advent of bioengineered microrobots has revolutionized the landscape of translational medicine, offering unparalleled precision, adaptability, and multifunctionality in addressing complex biomedical challenges. These microrobots, designed with advanced bioengineering principles, integrate intelligent systems for targeted diagnostics, therapeutic interventions, and minimally invasive procedures. By combining innovative materials, bio-compatible designs, and responsive functionalities, microrobots can navigate complex biological environments, deliver therapeutics with high spatial accuracy, and monitor physiological responses in real time. This paradigm shift toward intelligent microrobotics aligns with the goals of translational medicine by bridging the gap between experimental research and clinical applications. Key advancements in microrobot fabrication, including biocompatible nanomaterials, programmable actuation mechanisms, and adaptive sensing technologies, have enhanced their potential for personalized medicine. Furthermore, these systems are now being explored for diverse applications such as precision drug delivery, regenerative medicine, and immune modulation, with promising results in preclinical models. This work highlights the state-of-the-art developments in bioengineered microrobots, focusing on their integration into intelligent translational medicine. We discuss current innovations, address challenges such as scalability, biocompatibility, and regulatory considerations, and explore future directions to accelerate the clinical adoption of these transformative technologies.

Keywords: Bioengineered Microrobots, Intelligent Systems, Translational Medicine, Precision Drug Delivery, Biomedical Applications



16:10~16:30

I-14

人工周邊神經再生醫學-中醫學應用典範轉移

陳悅生

中國醫藥大學生物醫學工程學系

摘要：

周邊神經損傷 (Peripheral Nerve Injury, PNI) 是由於事故、創傷和其他原因導致周邊神經結構與功能喪失，導致感覺、運動和自主神經功能部分或完全失去功用以及神經性疼痛的臨床問題。目前仍缺乏確保神經功能完全恢復的可靠治療方法，目前外科手術治療的黃金標準是使用自體神經移植，但鑒於自體移植來源的的侷限性，因此神經導管已被認為是自體神經移植的替代治療方法之一。先前使用中醫藥與生醫材料的結合來促進神經再生，而近年來生物列印技術已被廣泛應用於神經導管的製作。借助這項技術，我們可以將常見的膠原蛋白、褐藻糖、明膠等高生物相容性材料，與各種細胞結合，形成三維結構以支持神經再生。此外，還可以在材料中摻入不同的導電材料，並配合體外刺激，為神經再生提供全新的促進策略，過程中進一步了解不同培養及刺激模式影響神經細胞所釋放外泌體的差異，進一步瞭解神經損傷時，是否能影響周邊免疫反應的調控，讓巨噬細胞分化為促進組織再生的 M2 型，進而提高神經再生的效果。總而言之，結合多種技術及治療策略，希望能將細胞治療結合導電材料與組織工程等相關技術，開發出具有生物相容性的神經導管，得到最佳的治療效果，進而為神經損傷修復提供有效的資源和替代方法。



16:30~16:50

I-15

台灣細胞資源整合發展與創新實踐

張育甄

財團法人食品工業發展研究所
生物資源保存及研究中心

摘要：

生物材料為生物醫學研究的重要基礎，生物資源保存及研究中心(BCRC)自 1982 年成立以來，一直從事遺傳資源的保存、鑑定和提供等工作，包括微生物、細胞和基因資源。其中細胞資源，由 1996 年國家衛生研究院委辦細胞庫核心設施平台起，完成主要庫藏架構，使各界便利地使用各類細胞資源。更於符合布達佩斯條約的條件下，成為台灣唯一專利委辦之寄存機構，致力於提升台灣在全球生物資源保存和研究方面的地位。隨著國內生技醫藥領域之發展，除自行開發羊水幹細胞與神經幹細胞之建立技術外，更拓展收存範圍建置多樣化的細胞資源，滿足國人日益增長的研發需求，因此遵循法規並克服技術挑戰，完備包括特殊收藏(special collection)、胚胎幹細胞庫、醫用細胞資源等多項資源。2016 年起與中央研究院於國科會經費下共同建置人類疾病誘導型多潛能幹細胞服務聯盟，目前 iPSC 庫藏量已達全球第五。在品質要求方面，BCRC 藉由通過 ISO 9001、ISO17025 和 ISO 17034 多項認證和能力驗證等，建立多項完整的品質系統。跟隨近年再生醫療領域的開展，力求由傳統的資源中心轉型，跨足轉譯醫學領域服務，建立符合藥典規範之分析，並著重於細胞治療產品的檢測與評估服務，同時藉由建置 GTP 細胞處理中心，積極與產業界結合，協助特管辦法或臨床試驗之執行。未來將持續創新技術與服務，以資源平台為細胞產品增值，永續台灣細胞資源之發展。



Poster Paper

不同纖維素比例溫敏感水凝膠之物化特性分析
**Characterizing Physicochemical Properties of Various Cellulose-containing
Thermosensitive Hydrogels**

林倩蓉¹ 林子涵¹ 劉怡心^{1,2} 蘇真瑩^{1,2} 方旭偉^{1,2}
國立臺北科技大學化學工程與生物科技研究所¹ 高值生醫材料研究與商品化中心²

Introduction : Hydrogels are three-dimensional, cross-linked hydrophilic polymers that absorb large amounts of water without disintegration, offering excellent biocompatibility. Smart hydrogels respond to external stimuli like temperature and pH, altering their structure. Among them, thermosensitive hydrogels are widely used, as they gel within a specific temperature range and regulate hydrophilic-hydrophobic interactions to control drug release, making them ideal for biomedical applications.

Materials and Methods : The thermosensitive hydrogel based on 20% Pluronic F127 by incorporating 5% Pluronic F68, 1% hyaluronic acid, 3% carboxymethyl cellulose, and adjusting the ratios of hydroxypropyl methylcellulose (HPMC) and methylcellulose (MC). The experiment will include physicochemical property testing. Physicochemical tests will assess gel viscosity, gelation temperature, and gelation time.

Results : The research results show that the gelation point of the hydrogel ranges from 25 to 27°C, with a gelation stability temperature between 35 and 38°C. At room temperature, the hydrogel exhibits low viscosity, which increases as the temperature rises. Among the five tested formulations, the gelation time met the experimental target, with 2 mL of hydrogel forming a gel within 60 seconds and 5 mL within 150 seconds.

Discussion : According to the rheometer results, the gelation point decreases with the addition of MC when HPMC is not present. When HPMC is added, the sample containing 0.7% MC exhibits the lowest gelation point. Regarding gelation stability temperature, the addition of MC causes a decrease in stability temperature as HPMC concentration increases. In the absence of MC, the sample with 0.7% HPMC shows the lowest gelation stability temperature. In terms of viscosity, both HPMC and MC contribute to an increase in viscosity, while maintaining relatively low viscosity at room temperature, which increases as the temperature rises. The gelation results indicate that the addition of HPMC and MC accelerates the gelation process.

Conclusions : In summary, the addition of MC lowers the gelation point temperature, while HPMC reduces the gelation stability temperature. Both HPMC and MC increase hydrogel viscosity and accelerate the gelation process. Next, in vitro tests will be conducted on the five selected formulations, focusing on degradation and drug release. The study will compare the release profiles of natural antimicrobial agents and antibiotics, aiming for a positive correlation between release rate and degradation rate, ensuring sustained drug release. These findings will help enhance the therapeutic efficacy of the hydrogel and expand its applications in various medical fields.

幾丁聚醣奈米粒作為微小核糖核酸靶向傳遞系統於口腔黏膜下纖維化治療的運用
Chitosan Nanoparticles as A Targeted Delivery System for Anti-Fibrotic microRNAs in The Treatment of Oral Submucosal Fibrosis

尹品曦¹ 鄭詠馨² 陳幸佑² 楊凱強¹
臺北醫學大學牙體技術學系¹ 國立臺灣科技大學材料科學與工程系²

Introduction : Oral submucous fibrosis (OSF), a precancerous disease, is characterized by excessive extracellular matrixes (ECM) deposition. Dysregulation of microRNAs (miRs) is involved in the progression of OSF, and miR manipulation could be a promising therapeutic approach. However, the negative charge miR may hamper cellular uptake, and exogenous miRs can be degraded shortly *in vivo*. Therefore, we proposed delivering miRs by chitosan nanoparticles (NPs) as a treatment for OSF.

Materials and Methods : The miR-negative control (miR-NC)/chitosan NPs were fabricated by the ionic gelation method and characterized by dynamic light scattering. Human oral submucosal fibroblasts were first subjected to arecoline stimulation to induce myofibroblast differentiation and then transfected with miR-145 inhibitor or miR-424 inhibitor using chitosan NPs.

Results : For chitosan NPs loaded with miR-NC, the particle size ranged from 121.9 ± 0.1 nm with a polydispersity index of 0.162 ± 0.004 and a zeta potential of $+22.4 \pm 0.5$ mV. Transfection of these two miRs downregulated the mRNA levels of transforming growth factor-beta1 (*TGFBI*), alpha-smooth muscle actin (*ACTA2*), collagen type I alpha 1 (*COL1A1*), *COL3A1*, *COL4A1*, matrix metalloproteinase-2, tissue inhibitor of metalloproteinase-2, and zinc finger E-box binding homeobox 1 in myofibroblasts. Western blot analysis revealed that the miRs/chitosan NP transfection decreased α -SMA and type 1 collagen protein products. Furthermore, stimulated cells' wound closure ability was inhibited upon transfection.

Discussion : The most significant innovation of this study is the use of anti-fibrotic chitosan as a raw material to produce the nanoparticles. Results of qPCR showed that transfection of chitosan NP (with miR-NC) downregulated fibrotic genes. Chitosan NP transfection also inhibited cell migration stimulated by arecoline. Finally, chitosan NP is a good delivery vehicle for miR transfection.

Conclusions : Transfection of miR-145 inhibitor and miR-424 inhibitor, which inhibited the TGF- β /Smads signaling pathway and decreased ECM component productions, can be a promising treatment for OSF.

可控制的明膠微粒製備：微流體與乳化法比較研究
**Controlled Fabrication of Gelatin-Based Biodegradable Microspheres: A Comparison of
Microfluidic and Emulsification Methods**

呂柏融¹ 張宥承^{1,2} 方旭偉^{1,2}

國立臺北科技大學化學工程與生物科技研究所¹ 高值生醫材料研究與商品化中心²

Introduction : Gelatin-based microspheres are widely used in biomedical applications, including embolization, hemostatic agents, and drug delivery. Their performance depends on particle characteristics, influenced by fabrication methods. Emulsification often results in broad size distributions, affecting degradation and drug release, while microfluidics provides better control and uniformity. This study compares these methods in terms of size distribution, dispersibility, and morphology.

Materials and Methods : Type A gelatin was used to form water-in-oil droplets. Microfluidics utilized an X-section microchannel for shear-controlled droplet formation, while emulsification relied on mechanical stirring. Glutaraldehyde stabilized the microspheres. Scanning Electron Microscope(SEM) analyzed morphology, ImageJ measured size distribution, and optical microscopy assessed dispersibility via suspension stability.

Results : Both methods successfully produced monodisperse gelatin microspheres. However, microfluidics demonstrated superior control over particle size distribution, with a coefficient of variation (CV) $< 5\%$, significantly lower than the emulsification method (CV $\approx 55\%$). The microfluidic-fabricated microspheres exhibited a more uniform and narrow size distribution. Furthermore, the dried particles maintained stable suspension for approximately 3 minutes, indicating improved dispersibility.

Discussion : The results indicate that flow rate in the microfluidic system and stirring speed in the emulsification process directly influence droplet formation and particle size. Higher flow rates or stirring speeds promote finer droplet breakup, increasing particle yield while reducing size variation. Despite the advantages of microfluidic techniques in precision and uniformity, scalability remains a challenge, as high-throughput production requires parallelization of microfluidic channels. Conversely, emulsification methods, although less precise, offer easier scale-up for industrial applications.

Conclusions : This study elucidates the influence of fabrication parameters on the production of gelatin-based microspheres using microfluidic and emulsification techniques. The ability to precisely control particle size distribution could impact degradation rates and application-specific performance in biomedical fields. By optimizing flow conditions and shear forces, microfluidic techniques offer a promising approach for tailoring gelatin microspheres for various biomedical applications, opening new avenues for controlled drug release and tissue engineering scaffolds.

開發雜合凋亡小體之超分子水凝膠以增強癌症免疫循環並提升黑色素瘤免疫治療效果
**Development of a Supramolecular Hydrogel Incorporating Hybrid Apoptotic Bodies to
Enhance the Cancer-Immunity Cycle for Melanoma Immunotherapy**

黃偉源 王子威

國立清華大學材料科學與工程學系

Introduction : Melanoma's aggressive nature and immune evasion limit treatment efficacy. To address these challenges, we developed an injectable PEG-Upy-based hydrogel incorporating Hy-ApoBDs to enhance immunotherapy by modulating the cancer-immunity cycle. This system integrates doxorubicin (DOX)-induced immunogenic cell death (ICD), Hy-ApoBDs functionalized with calreticulin and CX3CL1, and PD-L1 blockade, collectively enhancing antigen presentation, recruiting immune cells, and sustaining T-cell activation to suppress melanoma progression.

Materials and Methods : Apoptotic bodies were isolated from B16-F10 melanoma cells and decorated with calreticulin and CX3CL1 via click chemistry and electrostatic adsorption. After functionalization of 4-arm-PEG with ureidopyrimidinone (Upy), the PEG-Upy hydrogel was formulated by incorporating DOX, hybrid apoptotic bodies (Hy-ApoBDs), and an aPD-L1/laponite complex for enhanced melanoma immunotherapy.

Results : The supramolecular hydrogel, leveraging hydrogen bonding interactions, enables injectable and localized drug delivery. Through surface modification, Hy-ApoBDs exhibited enhanced immunostimulatory properties, increasing the secretion of immunomodulatory cytokines and upregulating dendritic cell activation compared to ApoBDs. In vivo, this hydrogel system significantly reduced tumor burden, enhanced immune activation, and increased immune cell infiltration into tumor sites.

Discussion : Our study highlights a multi-faceted melanoma immunotherapy strategy that overcomes limitations of single-agent treatments. DOX-induced ICD promoted tumor antigen release, while Hy-ApoBDs enhanced antigen presentation and immune recruitment. PD-L1 blockade sustained T-cell activation, counteracting immunosuppression within the tumor microenvironment. This combination therapy effectively promoted local tumor eradication and systemic immunity, with potential applications in other cancers. These findings underscore the potential of integrating chemotherapy and immunotherapy for enhanced anti-cancer efficacy.

Conclusions : We developed a supramolecular hydrogel-based immunotherapy platform integrating chemotherapy and immunotherapy to enhance anti-cancer immunity. This system induces ICD, enhances antigen presentation, and recruits immune cells, leading to robust tumor suppression. In vivo studies demonstrated significant tumor regression and systemic immune activation. These findings support further exploration of this hydrogel system for melanoma and other cancers.

使用微流道系統製作聚乳酸微粒的參數設立
**Establishment of Process Parameters for Polylactic Acid Microparticles
Fabrication Using Microfluidic System**

吳承翰¹ 張宥承² 方旭偉^{1,2}

國立臺北科技大學化學工程與生物科技研究所¹ 高值生醫材料研究與商品化中心²

Introduction : Microparticles have various medical applications, including drug delivery, dermal fillers, and embolization, making them essential in biomaterials. Currently, the emulsification method is the primary method for microparticle fabrication. However, microparticle prepared by the emulsification method have wide size distribution. In contrast, microfluidic system provide a fixed flow rate, resulting in the microparticles with a more uniform particle size distribution.

Materials and Methods : This study used both a microfluidic system and an emulsification method to fabricate Polylactic Acid(PLA) microparticles. Meanwhile, the PLA concentration and PVA flow rate would be adjust in the microfluidic system. Finally, to create porous microparticles, ammonium bicarbonate(NH_4HCO_3) would be added.

Results : In this study, PLA microparticles with average sizes of $40.7 \pm 35.5 \mu\text{m}$ and $27.6 \pm 1.8 \mu\text{m}$ were fabricated by emulsification and the microfluidic system, respectively. Meanwhile, as continuous phase flow rate increased and dispersed phase concentration decreased, particle size would decrease. Additionally, based on the SEM image, the microparticles which incorporate NH_4HCO_3 led to the formation of pores, with the pore size increasing as the NH_4HCO_3 concentration increased.

Discussion : Firstly, PLA microparticles prepared by the microfluidic system were confirmed to have a more uniform particle size distribution than those fabricated by the emulsification method. Furthermore, in the microfluidic system, a higher continuous phase flow rate increases shear force, reducing particle size, while a lower dispersed phase concentration enhances emulsification, further decreasing size. Additionally, the decomposition of NH_4HCO_3 generated NH_3 and CO_2 gases, which indicates that higher NH_4HCO_3 concentrations lead to the formation of more pores in PLA microparticles.

Conclusions : In this study, PLA microparticles with a uniform particle size distribution were fabricated using a microfluidic system. By adjusting different parameters, microparticles of various sizes were produced. Additionally, NH_4HCO_3 was incorporated into the dispersed phase to create porous microparticles, and the pores could be controlled by varying the NH_4HCO_3 concentration. From an application perspective, the microfluidic system enables the rapid development of uniform microparticles. Furthermore, the adjustable porous structure allows these microparticles to be used as new soft tissue fillers or drug carriers in future applications.

透過溫敏性水膠共同輸送外泌體和氧氣以增強燒傷傷口再生
**Exosome and Oxygen Co-Delivery via a Thermosensitive Hydrogel to
Enhance Burn Wound Regeneration**

葉政昊¹, Shih-Heng Chen^{1,2*} and Feng-Huei Lin^{1,3*}

台灣大學醫學院和工程學院生物醫學工程研究所¹ 長庚大學醫學院長庚紀念醫院整形外科²
國家衛生研究院生物醫學工程與奈米醫學研究所³

Introduction : Burn injuries are a significant global health issue. Effective wound management is crucial due to challenges like oxidative stress and inflammation. Adipose-derived stem cell exosomes are promising therapeutic agents, reducing oxidative stress and enhancing intercellular communication. They promote wound healing by modulating inflammation, angiogenesis, and enhancing cell proliferation. However, exosomes require adequate oxygen levels to be effective. Hyperoxia devices, such as hyperbaric oxygen therapy, are beneficial but have limitations. Continuous oxygen delivery methods, like using perfluorodecalin with exosomes, offer a promising solution for sustained wound healing.

Materials and Methods : Emulsify perfluorodecalin to create an emulsified perfluorodecalin, oxygenated perfluorodecalin emulsion, and then mix it with exosomes and Pluronic F127 to form the PDOE hydrogel.

Results : In material experiments, this material can maintain a wound site for 60 hours, continuously releasing exosomes and oxygen, and keeping the wound in a hyperoxic state. In cellular experiments, it can enhance exosome uptake under hypoxic conditions, reduce ROS expression, and promote the proliferation and migration of HUVECs, HDFs, and HaCaTs, as well as angiogenesis. Animal experiments demonstrate that it accelerates wound healing, reduces inflammatory responses, promotes angiogenesis, and facilitates the conversion of type III collagen to type I collagen.

Discussion : Thermal injuries from burns create localized hypoxic regions, hindering wound healing. The PDOE hydrogel mitigates hypoxia by reducing HIF-1 α and activating the Nrf2/ARE pathway, enhancing antioxidant capacity. Hyperoxia reduces ROS and inflammation by suppressing TNF- α and IL-1 β . Exosomes in PDOE hydrogel contain antioxidant enzymes and miRNAs that neutralize ROS and regulate gene expression, promoting angiogenesis and cell proliferation. Oxygen supplementation enhances exosome uptake, and their synergistic effect improves wound healing by promoting collagen synthesis and remodeling.

Conclusions : This study explores combining exosome therapy with hyperbaric oxygen therapy for wound recovery. The PDOE hydrogel, loaded with oxygen and exosomes, reduces ROS, promotes angiogenesis, and facilitates granulation tissue contraction. It effectively addresses hypoxic cell issues and converts type III to type I collagen. In vivo and in vitro results support its clinical potential, but further research is needed to understand the underlying mechanisms.

超聲波聲穿孔增強肺肋膜沾黏術 Sonoporation-enhanced Pleurodesis

林欣儀¹ 廖偉志^{2,3} 王浩宇¹ 葉秩光⁴ 劉彥良⁵

中國醫藥大學生物醫學研究所¹ 中國醫藥大學附設醫院內科部胸腔科² 中國醫藥大學醫學系³
清華大學生醫工程與環境科學系⁴ 中國醫藥大學生物醫學工程碩士學位學程⁵

Introduction : Malignant pleural effusion (MPE), caused by cancer metastasis, leads to respiratory distress. Treatments like surgery, chemotherapy, and pleural catheter drainage can cause complications. Pleurodesis, using sclerosing agents, is the primary treatment, but its efficacy and side effects are limited. This study developed an ultrasound-responsive foam to enhance drug delivery, improving pleurodesis outcomes. Animal tests confirmed its ability to promote inflammation and tissue adhesion, showing potential for better MPE treatment.

Materials and Methods : A retrospective cohort analysis was conducted using the TriNetX database to compare cancer patients with and without MPE. Additionally, *in vitro* and *in vivo* experiments were performed to develop and assess an ultrasound-triggered foam carrier for targeted drug delivery and pleurodesis. The effectiveness of the formulation was evaluated through flow cytometry, histological analysis, and enzyme-linked immunosorbent assays (ELISA), which demonstrated its capacity to enhance localized inflammatory responses and fibrosis, thereby improving treatment efficacy.

Results : The proposed ultrasound-triggered microbubble-based method significantly improved drug delivery and pleural adhesion. Optimization of microbubble size facilitated enhanced sonoporation, leading to superior drug penetration and fibrotic tissue formation. *In vivo* studies demonstrated that ultrasound stimulation increased drug dispersion, fibrosis, and overall pleurodesis effectiveness. The ultrasound-assisted pleurodesis resulted in a more homogeneous pleurodesis effect, higher fibrosis levels, and fewer adverse effects compared to conventional approaches. Furthermore, dynamic immune responses were observed, with neutrophils and macrophages exhibiting distinct temporal activation patterns that contributed to tissue repair and fibrosis development.

Discussion : This study demonstrates that ultrasound-responsive foam, incorporating tigecycline-loaded microbubbles, significantly enhances drug delivery for pleurodesis. The cavitation effect of the microbubbles, activated by 1 MHz ultrasound, facilitated deeper tissue penetration and triggered robust inflammatory responses, thereby promoting pleural adhesion and collagen fiber deposition. This novel approach effectively addresses the limitations associated with conventional sclerosing agent administration, particularly the challenge of uneven drug distribution in pleurodesis procedures.

Conclusions : Ultrasound-responsive foam provides a promising method for improving pleurodesis, addressing issues with drug distribution and adhesion. Tigecycline-loaded foam, combined with ultrasound, offers enhanced therapeutic outcomes through deeper tissue penetration and efficient collagen fiber formation, potentially improving MPE treatment.

使用 Transwell 整合海藻酸鹽水凝膠平台研究癌細胞歸巢
Studying Cancer Cell Homing Using a Transwell-integrated Alginate Hydrogel Platform

康文¹, Long-Sheng Lu¹, Kai-Chiang Yang^{1,2,*}

Graduate Institute of Biomedical Materials & Tissue Engineering, Taipei Medical University¹
School of Dental Technology, College of Oral Medicine, Taipei Medical University²

Introduction : Metastasis is a major cause of high cancer mortality due to the ability of malignant cells to "home" to distant organs. The homing process is critical for cancer progression, and understanding its mechanisms is crucial for developing effective therapeutics. Therefore, this study utilized a transwell-based alginate hydrogel (TAH) platform to mimic the cancer microenvironment and investigated the homing behavior and metastatic potential of gastric cancer stem cells (CSCs).

Materials and Methods : In this study, the TAH model was used to co-culture gastric cancer cell lines MKN45 or AGS with endothelial cells (HMEC-1) or mesothelial cells (MeT-5A). This platform mimics the tumor microenvironment and promotes cell-cell interactions between different culture chambers. The upper chamber contained endothelial or mesothelial cells, while the lower chamber was used to culture cancer cells. Any cancer cells that migrated into the alginate hydrogel were identified as the CSC population. Finally, the homing index was evaluated based on the migration and adhesion of these CSCs.

Result : After applying the TAH model, MKN45 co-cultured with HMEC-1 or MeT-5A showed higher migration and adhesion abilities to CSC compared with AGS. When co-cultured with HMEC-1 or MeT-5A, the homing index of MKN45 was 0.63 and 0.75, respectively. Under the same conditions, AGS showed negative homing indexes of -0.45 and -0.43, indicating that MKN45 had a stronger homing ability.

Discussion : The results showed that the homing index of MKN45 was higher than that of AGS, which was associated with its metastatic potential. Furthermore, the TAH model provides valuable insights into CSC dynamics and highlights the importance of microenvironmental cues in homing behavior.

Conclusion : The TAH model provides a powerful tool for studying cancer metastasis and evaluating potential therapeutic approaches, representing a critical step toward understanding and combating tumor spread.

分子結構對修飾明膠的影響
The Effects of Triple Helix Structure on Modified Gelatin

王韻堯², Yi-Chun Chou¹, Yi-Xin Liu^{2 3} and Hsu-Wei Fang^{2 3*}

Institute of Biotechnology, National Taipei University of Technology, Taiwan 10608 Taiwan¹
Department of Chemical Engineering and Biotechnology National Taipei University of Technology,
Taipei 10608 Taiwan²

High-value Biomaterials Research and Commercialization Center, National Taipei University of
Technology, Taipei 10608, Taiwan³

Introduction : Gastrointestinal bleeding, particularly gastric hemorrhage, remains a clinical challenge due to difficulties in precise localization and the non-degradability of existing hemostatic powders. This research investigates the structural modulation of gelatin-based hemostatic powders by incorporating polyacrylic acid (PAA) and calcium carbonate (CaCO₃) to improve water absorption, thermal stability, and mechanical strength. By optimizing gelatin's molecular configuration, we aim to enhance its hemostatic performance and assess the impact of structural variations.

Materials and Methods : Gelatin was dissolved in deionized water and stirred at varying temperatures (30°C–90°C), with CaCO₃ added to adjust the pH of PAA. The mixture was frozen and freeze-dried to obtain the final powder. Structural properties were analyzed using circular dichroism (CD) spectroscopy and scanning electron microscopy (SEM).

Results : Powders prepared at 50°C exhibited a water absorption ratio of 2060%, increasing to 2088% at 90°C. CD and SEM analyses confirmed that structural modulation improved stability and absorption capacity. Adjusting temperature and pH influenced the triple-helix structure, affecting hemostatic efficiency.

Discussion : The integration of PAA and CaCO₃ stabilized the gelatin network, enhancing mechanical strength and resistance to gastric peristalsis. Increased water absorption facilitated rapid clot formation. Ca²⁺ served as a coagulation cofactor, further promoting platelet aggregation. These structural modifications offer potential advantages over traditional hemostatic powders in terms of biocompatibility and degradation.

Conclusions : This study demonstrates that modulating the molecular structure of gelatin-based powders can significantly impact water absorption, mechanical integrity, and stability. While the results indicate promising hemostatic potential, further refinement of synthesis conditions and structural assessments via thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) are required to confirm the impact of structural quantity variations.

TNF- α 能增強骨髓來源間質幹細胞的免疫調節功能和骨分化能力有效治療植體周圍炎
The Role of TNF- α -primed Bone Marrow Mesenchymal Stem Cells in Enhancing Osteogenic
and Immunomodulatory Functions for Treating Peri-implantitis

王心妤¹ 林妘霏¹ 莊漢英¹ 蔡孟勳² 陳漪紋² 王麗姿¹
臺北醫學大學醫學檢驗暨生物技術學系¹ 台灣大學臨床牙醫學研究所²

Introduction : Bone marrow mesenchymal stem cells (BMMSCs) have gained attention as a promising therapy for bone diseases and immune-related conditions due to their ability to differentiate into osteoblasts and modulate immune responses. Mitochondrial metabolism plays a critical role in influencing osteogenesis and immunomodulation of BMMSCs. Peri-implantitis, characterized by inflammation of tissues surrounding dental implants and accompanying bone loss, is often exacerbated by the cytokine TNF- α . While BMMSCs have demonstrated enhanced therapeutic functions in response to inflammatory cytokines like TNF- α , the mechanisms through which TNF- α -primed BMMSCs address peri-implantitis remain unclear.

Materials and Methods : Bioinformatics analysis was employed to investigate the role of TNF- α in mediating peri-implantitis and its effects on BMMSCs. T cell activation and proliferation assays were performed to evaluate the immunomodulatory effects of BMMSCs using flow cytometric analysis. Additionally, the mitochondrial functions of BMMSCs were assessed to link their capabilities to immunomodulation and osteogenesis.

Results : Transcriptomic analysis indicated that TNF- α is critical in peri-implantitis and enhances the immunomodulatory properties of BMMSCs. Functional assays revealed that TNF- α primes BMMSCs to more effectively suppress T cell activation and proliferation. Notably, mitochondrial content was significantly increased in TNF- α -primed BMMSCs, suggesting improved immunomodulatory and osteogenic potential.

Discussion : Further research is needed to elucidate the complex mechanisms underlying BMMSC therapy for peri-implantitis, particularly involving mitochondrial transfer and metabolism in immunomodulation and osteogenesis.

Conclusion : This study aims to develop novel therapeutic strategies for treating peri-implantitis and to clarify the mechanisms involving BMMSCs and mitochondrial activity, ultimately enhancing treatment efficacy for inflammatory conditions.

脂肪間質幹細胞透過粒線體轉移展現增強的 CD4 T 細胞免疫調節能力

Adipose-derived MSCs Exhibit Enhanced Immunomodulatory Properties Towards CD4 T Cells Via Mitochondrial Transfer

利苑期 莊漢英 陳品瑄 王麗姿
臺北醫學大學醫學檢驗暨生物技術學系

Introduction : Mesenchymal stem cells (MSCs) hold significant promise for tissue repair and immune regulation, making them valuable for treating immune-related diseases. While bone marrow (BM) MSCs are the traditional source used in clinical trials due to their extensive research background, adipose-derived MSCs (AdMSCs) are becoming increasingly attractive because of their abundance and accessibility. This study aims to compare the immunomodulatory properties of those two adult MSC sources and to explore the role of mitochondria in their immunomodulatory effects.

Materials and Methods : Bioinformatics analysis was conducted to elucidate the mitochondrial metabolism and immunomodulatory properties of AdMSCs and BMMSCs. T cell inhibition assays were performed to evaluate MSC immunomodulation using flow cytometric analysis. Mitochondrial transfer from MSCs to T cells was assessed to validate their immunomodulatory functions.

Results : *In silico* analysis revealed that AdMSCs exhibit greater immunomodulatory potential and enhanced mitochondrial function compared to BMMSCs. Functional assays confirmed that AdMSCs more effectively inhibit T cell activation. Notably, AdMSCs transfer more active mitochondria to CD4 T cells than those present in their original state.

Discussion : Further investigations will focus on uncovering the molecular mechanisms of mitochondrial metabolism that drive the enhanced immunomodulation of AdMSCs, aiming to provide a comprehensive understanding of their therapeutic potential in cellular therapy.

Conclusion : Our research aims to elucidate the mechanisms behind the therapeutic potential of AdMSCs in immunological disorders.

以中醫藥複方建立皮膚燒燙傷應用平臺之研究
An Application Platform of Chinese Medicine Compound to Skin Burns and Scald

劉佳芳 姚俊旭
私立中國醫藥大學中醫學系

Introduction：皮膚是動物面積最大的器官，動物皮膚面積遭受大量破壞，會致使體內水分、電解質自傷口大量滲出，產生感染、循環血量減少及電解質不平衡等情形，引起休克進而造成死亡。

Materials and Methods：以老鼠為動物模型建立皮膚二度燙傷研究平台為研究主題，建立動物的燙傷試驗模型，採用麵粉為試驗藥品，麵粉性味歸經功效甘涼除熱通淋，入心、脾、腎經、養心、益腎、等進行探究。

Results：麵粉之特別適合用來治療燒燙傷，是因為麵粉的性質甘涼除熱通淋，所以可以滅火毒；同時麵粉有「直降下行，走而不守」的特點，可以將身體的火毒迅速帶走，排出體外，火毒就不會瘀滯與局部造成燙傷，或者即使是有了燙傷，麵粉也能迅速將燙傷部位的熱毒以及身體在熱毒的刺激下產生的過多分泌物清除，皮膚會很快癒合而不留疤痕。

Discussion：傳統醫家把燒燙傷視為外來的火毒造成的皮膚傷害，初期的處理方式，與西醫思維有所不同，治療方式也差異甚大。誠如清朝的《外科證治全書》記載「湯火傷」「此證最忌涼水、涼藥浸敷，致令熱毒伏內，輕則皮肉臭爛，重則神昏氣喘多成不救。」(藍士哲，榮大夫，2016)²。

Conclusion：本研究企圖藉由傳統醫藥內外配體探究協助提供增強對於皮膚燒燙傷診療之效益。茲此當代全球生醫界正積極投入精準醫療(Precision medicine)探究之際，本研究亦研以傳統醫藥作為內外配體對於皮膚燒燙傷受體之療效評估及其機制探究，呼應精準醫療(Precision Medicine)內涵意旨。

濃度梯度微流道於神經幹細胞培養之應用
Concentration Gradient Microfluidics for Neural Stem Cell Applications

張鈺茹 郭奐均 李亦宸*
逢甲大學化學工程學系

Introduction：化合物或藥物濃度的刺激反應對於幹細胞培養的研究中一個非常重要的步驟。目前常使用於濃度篩選的方法是先人工手動配製不同濃度的化合物或藥物後，再與細胞進行混合培養並監測它們對細胞的影響。但人工配製可能含有人為誤差以及高人力的需求，為了解決此問題，近期，微流體技術提供了一個可自動化、降低了試劑使用和操作時間的方法來減少上述問題的發生。

Materials and Methods：本研究利用離心力作為驅動力的方式設計了一個無幫浦的藥物篩選平台。該平台內部含有類樹枝結構用於產生具有化合物或藥物濃度梯度的培養基，而產生的培養基在離心平台的幫助下可將其送到細胞培養室之中。爾後，這些經由離心平台產生的濃度梯度培養基對於神經幹細胞的增生及分化行為影響將進一步以死活細胞定量及免疫螢光染色進行分析。

Results and Discussion：本研究中，我們開發的一個離心式平台，可利用調整離心速度產生十種線性的濃度梯度。爾後，實驗結果顯示該平台所產生的濃度梯度，不論是使用高毒性或低毒性的化合物，對於纖維母細胞、癌細胞及神經幹細胞存活性的影響均可以被分辨。更進一步，若使用生長因子與神經分化誘導試劑，本研究的離心式平台產生的濃度梯度也能夠使得神經幹細胞具有不同的增生能力以及神經元的分化程度。這些結果均驗證本平台的可行性。

Conclusions：在這項研究中，我們驗證了使用離心式平台產生濃度梯度並用於細胞培養的概念，該平台能夠在 10 秒內生成十種線性的藥物濃度。而且在產生濃度梯度與分配液體的過程中，顯示離心旋轉不會對細胞造成顯著的損傷。該平台也顯示分配藥物濃度時，可以減少人工手動造成誤差的可能行及節省時間，而且在可成功長時間觀察藥物濃度對於神經幹細胞行為的影響。因此，本平台為幹細胞培養及藥物篩選的應用提供了一個的潛在的策略選擇。

利用細菌脂多醣提升臍帶間質幹細胞之免疫調節能力：
探討微生物相關發炎疾病的治療機制

Enhancing Immunomodulation in Umbilical Cord Mesenchymal Stem Cells with Lipopolysaccharide: Therapeutic Prospects for Microbe-Associated Inflammatory Diseases

陳品瑄¹ 莊漢英¹ 蔡孟勳² 陳漪紋² 王麗姿¹
臺北醫學大學醫學檢驗暨生物技術學系¹ 台灣大學臨床牙醫學研究所²

Introduction : Mesenchymal stem cells (MSCs) are recognized for their immunomodulatory properties and biocompatibility, making them a key focus in clinical trials for immune and inflammatory diseases. The transition toward allogeneic umbilical cord (UC) MSCs offers promising therapeutic opportunities. However, most ongoing UCMSC trials are still in the early stages, indicating limited immunomodulatory effectiveness. Priming strategies, such as exposure to lipopolysaccharide (LPS), have been explored to enhance MSC functions, though results and depend on the source of the MSCs. This study aims to clarify the therapeutic effects of LPS-treated UCMSCs in microbe-associated inflammatory diseases.

Materials and Methods : Bioinformatics analysis was used to elucidate the immunomodulatory properties of UCMSCs and bone marrow (BM) MSCs. T-cell suppression assays evaluated MSC immunomodulation in the presence or absence of *Porphyromonas gingivalis* (*Pg*) LPS using flow cytometric analysis. TLR-4 knockdown was conducted to confirm the role of *Pg* LPS-mediated UCMSC immunomodulation *in vitro* and in a murine model of peri-implantitis.

Results : Bioinformatics analysis indicated that UCMSCs possess enhanced immunomodulatory properties related to bacterial response and LPS being highly enriched in UCMSCs. Both BMMSCs and UCMSCs suppressed T cell proliferation triggered by T cell receptor signaling; however, UCMSCs exhibited a significantly stronger inhibitory effect on T cell activation with *Pg* LPS in co-cultures. TLR-4 knockdown in UCMSCs resulted in a loss of their ability to inhibit T cell immunity both *in vitro* and in a murine model of peri-implantitis with *Pg* LPS.

Discussion : Further investigations will focus on uncovering the molecular mechanisms driving the enhanced immunomodulation of UCMSCs exposed to LPS, aiming to provide a comprehensive understanding of their therapeutic potential in cellular therapy.

Conclusion : These findings indicate that UCMSCs are a promising therapeutic source for treating microbe-associated inflammatory diseases due to their potent immunomodulatory properties, particularly in modulating T cell responses.

利用低氧預處理優化臍帶間質幹細胞粒線體功能達到有效調節 CD4 T 細胞
**Hypoxia-primed Umbilical Cord Mesenchymal Stem Cells Effectively Modulate CD4 T Cells
Through Enhanced Mitochondrial Metabolism**

黃孟萱 莊漢英 廖羿婷 王麗姿
臺北醫學大學醫學檢驗暨生物技術學系

Introduction : Due to their strong regenerative and immunomodulatory properties, mesenchymal stem cells (MSCs) have emerged as a promising therapeutic approach for inflammatory diseases associated with tissue hypoxia. Allogeneic umbilical cord MSCs (UCMSCs) are increasingly recognized as a leading source in recent clinical trials for various immune-related conditions. MSCs have shown the ability to modulate immune responses, particularly in CD4 T cells, through mitochondrial transfer. However, the role of hypoxic conditions in modulating MSC immunomodulation via mitochondrial mechanisms remains unclear.

Materials and Methods : Bioinformatics analysis was conducted to evaluate the effects of hypoxia treatment on UCMSCs. Deferoxamine was used to induce hypoxic signaling in UCMSCs, and the resulting immunomodulatory effects on CD4 T cell activation and proliferation, as well as mitochondrial functions, were assessed.

Results : Transcriptomic analysis indicated that hypoxia reduced several immune-related pathways and the capacity to activate inflammatory T cells. Functional assays showed that UCMSCs enhanced the inhibition of CD4 T cell activation and proliferation under hypoxia-mimicking conditions induced by hypoxic signaling. Furthermore, UCMSCs exposed to hypoxia-inducing signals exhibited increased mitochondrial content and potentially enhanced metabolic activity.

Discussion : Further investigation is necessary to elucidate the complex mechanisms underlying hypoxia-primed UCMSC therapy for immune-related diseases, particularly concerning mitochondrial transfer and metabolism in CD4 T cells.

Conclusion : A deeper understanding of these mechanisms could facilitate the development of novel therapeutic strategies utilizing UCMSCs to effectively treat immune-related diseases and improve patient outcomes.

臍帶間質幹細胞對嗜中性球在炎症狀況下反應的免疫調節效果
**Immunomodulatory Effects of Umbilical Cord Mesenchymal Stem Cells on
Polymorphonuclear Neutrophil Responses in Inflammatory Conditions**

Duong Thi Thuy Doan, 莊漢英 王麗姿
臺北醫學大學醫學檢驗暨生物技術學系所

Introduction: Mesenchymal stem cells (MSCs) display intricate and context-dependent interactions with polymorphonuclear neutrophils (PMNs), the most abundant immune cells in humans, which are increasingly recognized for their vital roles in immune responses beyond traditional antibacterial functions. The respiratory burst process is crucial for PMNs' defense mechanisms against infections, driving pathogen destruction. However, the excessive production of reactive oxygen species (ROS) during this process can lead to local tissue damage. However, the modulation of PMN respiratory bursts by MSCs is influenced by several factors, particularly the source of the MSCs.

Materials and Methods: We employed bioinformatics analysis to explore the modulation of PMNs by bone marrow (BM) and umbilical cord (UC) MSCs. The effects on PMN responses, including ROS production, were assessed through flow cytometric analysis. To identify which MSC sources possess therapeutic potential for preventing immune overreactions during severe bacterial infections, we investigated PMN responses of BMMSCs and UCMSCs in the presence of lipopolysaccharide (LPS).

Results: Transcriptomic analysis revealed that UCMSCs demonstrate strong immunomodulatory capabilities compared to BMMSCs. Notably, UCMSCs reduced PMN activation potential compared to BMMSCs using the transcriptomic data, whereas functional assays indicated that only BMMSCs triggered PMN ROS production. In the context of LPS treatment, UCMSCs significantly decreased PMN ROS production, unlike their BM counterparts.

Discussion: Understanding the delicate balance of MSC-PMN interactions, particularly regarding MSC sources, is crucial for unlocking the full therapeutic potential of MSCs.

Conclusion: UCMSCs not only prevent PMN activation but also mitigate it upon stimulation, making them an exciting candidate for immunomodulating PMN responses and potentially enhancing outcomes in inflammatory conditions.

探討脂肪間質幹細胞透過調節 T 細胞治療第二型糖尿病的潛力
Therapeutic Potential of Adipose-derived Mesenchymal Stem Cells in Modulating T Cell Responses in Type 2 Diabetes Mellitus

李若宇¹ 陳品瑄¹ 莊漢英¹ 王睦惠² 鄭乃禎² 王麗姿¹
臺北醫學大學醫學檢驗暨生物技術學系¹ 臺灣大學醫學院外科²

Introduction : T cells are critical in metabolic inflammation and insulin resistance, with growing evidence linking them to the pathogenesis of type 2 diabetes mellitus (DM). Adipose-derived mesenchymal stem cell (AdMSC) therapy is garnering attention for its immunomodulatory and regenerative properties. In Taiwan, AdMSCs have been approved for clinical use under the Regenerative Medicine Advanced Therapy (RMAT) framework. However, the effectiveness of AdMSCs derived from DM patients in regulating T cells is still unclear.

Materials and Methods : This study employed single-cell RNA sequencing (scRNA-seq) to evaluate the heterogeneity of AdMSCs from DM patients compared to healthy donors (HD). We assessed the ability of these AdMSCs to modulate T cell responses and their mitochondrial functions *in vitro* and established a murine model of diabetic wounds to evaluate the therapeutic potential of AdMSCs from both DM patients and HD.

Results : Our analysis identified at least 11 distinct clusters in the AdMSC populations, many of which were associated with elevated T cell inflammation in DM. Notably, DM-derived AdMSCs significantly increased the frequency of inflammatory T cells, including Th1 and Th17 cells. Consistent with previous findings, high glucose levels were linked to increased mitochondrial metabolism and dysfunctional senescence in MSCs; DM-derived AdMSCs exhibited markedly heightened mitochondrial metabolism compared to HD-derived counterparts. In the murine diabetic ulcer model, AdMSCs from HD demonstrated therapeutic effects by reducing inflammatory T cell responses.

Discussion : Additional studies are necessary to understand the mechanisms driving the therapeutic effects of DM-derived AdMSCs, particularly in their interactions with T cell responses.

Conclusion : Our findings indicate that AdMSCs may offer innovative strategies for treating DM-associated complications through autologous therapy and mitochondrial manipulation.

臍帶間質幹細胞透過調節肺部巨噬細胞群達到治療病毒感染性肺炎的潛力

Umbilical Cord Mesenchymal Stem Cells Modulate Lung Macrophage Responses and Offer Therapeutic Potential for Viral Pneumonia

廖羿婷¹ 莊漢英¹ 黃瑋琛² 王麗姿¹

臺北醫學大學醫學檢驗暨生物技術學系¹ 國防醫學院醫學系²

Introduction : Viral pneumonia and its complications, particularly acute respiratory distress syndrome (ARDS), present significant global health challenges. Proinflammatory pulmonary macrophages (MΦs) worsen the severity of viral pneumonia, yet the responses of specific MΦ subsets are not well understood. Mesenchymal stem cells (MSCs), noted for their immunomodulatory and regenerative properties and migrating to the lungs, show promise as therapies for viral ARDS. However, the heterogeneity of lung MΦ responses and the effects of MSC immunomodulation remain unclear.

Materials and Methods : Bioinformatics analysis was utilized to assess the responses of bone marrow (BM) MSCs and umbilical cord (UC) MSCs to viral infections, as well as the impact of poly I:C treatment on lung MΦ responses. Poly I:C was administered to murine lung-extracted cells to evaluate its influence on pulmonary MΦs using flow cytometric analysis. Additionally, we established a poly I:C virus-like pneumonia murine model to assess UCMSC therapy.

Results : To find the optimal MSC source for treating viral pneumonia, we compared UCMSCs with BMMSCs via transcriptomic analysis, and found that UCMSCs have enhanced virus-defense pathways. Bioinformatics analysis of poly I:C treatment revealed a viral ARDS-like response in monkey and murine lungs, characterized by upregulation of pathways related to viral infections and cytokine production. In lung cells cultured with poly I:C, there was a significant increase in inflammatory M1-type MΦs, while M2-type MΦs remained unchanged. In the intratracheal poly I:C model, UCMSC therapy reduced M1 polarization in lung MΦs and alleviated body weight loss due to poly I:C.

Discussion : The establishment of a poly I:C-induced virus-like pneumonia murine model is crucial for obtaining clinically relevant outcomes when considering UCMSCs for treating emerging viral pneumonia.

Conclusion : These findings confirm that poly I:C effectively mimics viral pneumonia by enhancing M1 polarization. Importantly, UCMSC treatment modulates lung MΦ responses by decreasing M1 polarization in poly I:C-challenged lung cells.

內質網壓力蛋白 TXNDC5 促進皮膚纖維化
ER Stress Protein TXNDC5 Promotes Skin Fibrosis

劉瀚陽 鄭乃禎
臺灣大學醫學院附設醫院

Introduction : Extensive cutaneous fibrosis and scarring, including disfiguring burn scars, hypertrophic scars, and keloids, represent a significant physiological and psychological burden on patients and a considerable public health concern. Thioredoxin domain-containing protein 5 (TXNDC5), initially discovered in mouse human hepatic stellate cells in 2003, has emerged as a crucial regulator of tissue fibrosis in various organ systems. Prof. Yang's research has elucidated a common transforming growth factor-beta-1 (TGF- β 1)-induced fibrosis mechanism in multiple organs. Although systemic evidence supporting the role of TXNDC5 in cutaneous fibrosis is currently lacking, its potential as a key modulator of skin fibrosis warrants further investigation. This study aimed to investigate the role of TXNDC5 in cutaneous fibrosis.

Materials and Methods : The study utilized both in vitro and in vivo approaches. In vitro, we used human dermal fibroblasts (HDFs) to study the effects of TXNDC5 knockdown and overexpression on TGF- β 1-induced fibrogenesis. In vivo, we employed TXNDC5 knockout mice to investigate the role of TXNDC5 in burn-induced skin fibrosis.

Results : The immunofluorescence results and publicly available gene expression data analysis showed that TXNDC5 is upregulated in human burn scars and scleroderma, coinciding with increased expression of α -SMA and ECM components.

In vitro, TXNDC5 was found to be both necessary and sufficient for TGF- β 1-induced fibrogenesis in HDFs. TXNDC5 knockdown attenuated the expression of α -SMA and ECM components, while TXNDC5 overexpression promoted their expression independent of TGF- β 1 stimulation.

In vivo, global TXNDC5 deletion in mice attenuated burn-induced skin fibrosis without impairing wound healing.

Discussion : TXNDC5 was proved to be a crucial regulator of TGF- β 1-induced tissue fibrosis in liver, heart, lung, and kidney. In our in vitro and in vivo experiments, TGF- β 1-induced skin fibrosis is also regulated by this ER protein disulfide isomerase (PDI), via TGF β R1-SMAD pathway. Compared to other organs, skin is a relatively 2D structure, making it difficult to establish a reliable animal model with even fibrogenic insult. But in the other hand, given the accessibility of skin tissue, localized or topical therapies targeting TXNDC5 could offer effective treatment strategies for scar-related conditions.

Conclusions : This study provides compelling evidence for TXNDC5 as a promising therapeutic target for cutaneous fibrosis.

References :

- [1] Lin CC, Ju FS, Mat Sci Eng C 2016, 58:254.
- [2] Cooper LF. J Prosthet Dent. 2000, 84:522.
- [3] Dalby MJ, et al. Nat Mater. 2007, 6:997.
- [4] Chao PG et al, Biofabrication 2014, 6:035008.
- [5] Chang CW et al, Tissue Eng A 2020, 26:102.
- [6] Hoseinpour V and Shariatinia Z, Tissue & Cell 2021, 72:101588.
- [7] Yang J, et al. ACS Nano. 2014.
- [8] Chen P et al. Ecotoxic Environ Safety 2020, 205,:111110.

一種新穎的三維細胞球體影像分析平台-評估脂肪幹細胞球體在再生醫學臨床應用的潛力
**A Novel 3D Spheroid Imaging Analysis Platform for Assessing the Clinical Potential of
Adipose-Derived Stem Cell Spheroids in Regenerative Medicine**

羅麗紋¹ 沈宜珊² 陳星宇¹ 沈家寧¹ 廖秀蓉^{2,3}

中央研究院生醫轉譯研究中心¹

醫療財團法人徐元智先生醫藥基金會亞東紀念醫院醫學研究部²

國立陽明交通大學生物藥學所³

Introduction : Adipose-derived stem cells (ADSCs) are valuable for regenerative medicine, yet preserving their stemness during in vitro expansion remains challenging. Spheroid cultures offer a 3D environment that strengthens cell-cell interactions, replicating native tissue conditions and enhancing stemness, viability, and paracrine activity. We have developed a high resolution imaging platform to optimize this approach, evaluate differentiation potential, and refine spheroid culture protocols. This strategy enhances ADSC functionality by supporting extracellular matrix deposition and improving therapeutic outcomes for cartilage repair and immunomodulation through better cell survival and integration into target tissues.

Materials and Methods : In this study, we utilized human ADSCs to establish 3D cell spheroids through low-adhesion culture techniques. By combining these with tissue clearing technology, we developed a high-resolution 3D fluorescent cell spheroid imaging platform that emulates the in vivo tissue microenvironment. This platform enabled the evaluation of peptide-induced mesenchymal stem cell-derived extracellular vesicles (MSC-EVs) in promoting chondrogenic differentiation, aiming to validate their efficacy in supporting cartilage phenotype generation.

Results : Our results demonstrated that peptide-induced MSC-EVs significantly enhanced the expression of chondrocyte-specific markers, such as SOX9 and Type II collagen, within the 3D spheroids. Additionally, there was a marked increase in thrombospondin-5 (COMP) content. These findings show the potential of peptide-induced EVs to promote chondrocyte differentiation and cartilage tissue formation, underscoring their feasibility as a promising therapeutic candidate for osteoarthritis (OA).

Discussion : Analysis within the 3D spheroid model allowed for a more accurate simulation of the in vivo microenvironment, facilitating an in-depth investigation of the key regulatory factors involved in MSC chondrogenic differentiation. This approach supports the precision development of cartilage repair therapies and provides essential theoretical and technical foundations for advancing precision medicine in OA treatment.

Conclusions : The high-resolution 3D spheroid imaging and analysis platform can accurately evaluate the differentiation potential of adipose-derived stem cell spheroids and optimize culture methods. This approach supports the development of cartilage repair therapies and will aid in more precise pharmacological evaluation in future studies.

脂肪組織來源的間質幹細胞透過調控嗜中性球治療糖尿病性潰瘍

Adipose Tissue-derived Mesenchymal Stem Cells Show Promise in Diabetic Ulcer Treatment with Targeted Polymorphonuclear Neutrophil Modulation

陳芷榆¹ 林妘霏¹ 莊漢英¹ 王睦惠² 鄭乃偵² 王麗姿¹
臺北醫學大學醫學檢驗暨生物技術學系¹ 臺灣大學醫學院外科²

Introduction : Mesenchymal stem cells (MSCs) are known for their potential in tissue repair and immune regulation, with adipose-derived MSCs (AdMSCs) particularly attractive due to their abundance and accessibility. In Taiwan, autologous AdMSCs have received clinical approval under the Regenerative Medicine Advanced Therapy (RMAT) framework. However, the therapeutic efficacy of AdMSCs derived from individuals with metabolic disorders, such as type 2 diabetes mellitus (DM), remains poorly understood.

Materials and Methods : Our study utilized bioinformatics analysis to assess polymorphonuclear neutrophil (PMN) responses that contribute to prolonged inflammation and impaired wound healing in DM patients. We investigated the ability of AdMSCs from DM patients to modulate PMN responses compared to healthy donors (HD). The effects of PMN modulation by AdMSCs were evaluated *in vitro*, and a murine model of diabetic wounds was established to assess the therapeutic potential of AdMSCs from DM patients versus those from HD.

Results : Our preliminary findings revealed that elevated PMN responses in diabetic wounds, compared to healthy skin using transcriptomic data. Unexpectedly, AdMSCs from DM patients triggered PMN activation and increased reactive oxygen species (ROS) production *in vitro*. In the murine model of diabetic wounds, AdMSCs from HD significantly reduced PMN infiltration and activation in ulcerated tissues.

Discussion : Further studies are necessary to elucidate the complex mechanisms underlying the therapeutic effects of AdMSCs from DM patients compared to HD, particularly local PMN responses.

Conclusion : This research investigates the therapeutic potential of AdMSCs from DM patients compared to HD in diabetic ulcers. Our findings aim to clarify the limitations of DM-derived AdMSCs and suggest that allogeneic AdMSCs from HD may provide promising new strategies for managing chronic wounds.

開發煙醯胺單核苷酸搭載奈米顆粒應用於視網膜神經節細胞再生
Development of Nicotinamide Mononucleotide Loaded Nanoparticle Applied in
Retinal Ganglion Cell Regeneration

朱培欣¹ 楊添鈞² 曾靖嬋^{3*}
臺北醫學大學奈米醫學工程研究所¹ 臺北醫學大學解剖學暨細胞生物學科²
臺北醫學大學醫材材料暨組織工程研究所³

Introduction : Retinal ganglion cells (RGCs) and retinal pigment epithelium (RPE) are crucial cells for maintain retinal and vision function; however, they are highly susceptible to oxidative stress, leading to ROS accumulation, DNA damage, and inflammation. These could drive retinal cell senescence and apoptosis resulted in ocular diseases like aged-macular degeneration (AMD) and glaucoma. Nicotinamide mononucleotide (NMN), a NAD⁺ precursor, restores NAD⁺ levels and mitigates oxidative damage, but it faces delivery challenges due to ocular barriers. A NMN-nanoformulation was designed to overcome this issue. A NMN-loaded gelatin nanoparticles (NMN-GNPs) was prepared for efficiently intracellular uptake and provided control release property. And this NMN-GNPs are expected to reduce ROS accumulation, delay senescence, and offer a potential therapeutic strategy for retinal degeneration.

Materials and Methods : NMN-loaded gelatin nanoparticles (NMN-GNPs) were synthesized by ethanol titration of Type A gelatin with NMN addition, followed by EDC/NHS crosslinking for nanoparticles stabilization. hiPSC-derived retinal ganglion cells (RGCs) were differentiated through stepwise medium transitions, validated by staining, and subjected to oxidative stress-induced senescence and apoptosis assays. Also adult retinal pigment cells (RPE) was also tested for comparison.

Results : Results of dynamic light scattering (DLS) analysis showed NMN-GNPs had a larger particle size (303.4 ± 1.2 nm) than GNPs (247.7 ± 4.6 nm), with stable zeta potentials and PDI values. Nanoparticle tracking analysis (NTA) confirmed good dispersibility, while TEM revealed uniform spherical structures. NMN-GNPs exhibited sustained release, with only 15% released after 48 h. In the H₂O₂ treated RPE cells, NMN-GNPs significantly reduced ROS accumulation, and retarded apoptosis (40%), and SA- β -Gal staining (3.3%) for senescence when compared with NMN. In RGCs, NMN-GNPs further suppressed senescence-related genes p53, p21, and p16 expression and reduced SA- β -Gal staining rate (66%), enhancing neuroprotection and promoting cellular regeneration, demonstrating superior anti-senescence potential.

Discussion : NMN-GNP exhibited superior anti-senescence effects in RPE and RGCs, these included reducing SA- β -Gal positive staining, and suppressing p21, p16 expression. It enhanced neuroprotection and regeneration, demonstrating greater efficacy than NMN alone by improving drug delivery and cellular function recovery via the advantages as nanomedicine.

Conclusions : These findings indicate that NMN-GNP effectively mitigates oxidative stress-induced cellular senescence and holds significant potential for neuroprotection and regeneration, offering a promising strategy for the treatment of retinal degenerative diseases.

利用一步驟封閉式生物反應器增殖與活化免疫細胞應用於免疫細胞治療
Enhanced Expansion and Activation of Immune Cell Spheroids Using a One-Step Closed Bioreactor for Immunocellular Therapy

林智妮¹ 楊易軒² 管哲雍² 林峯輝^{1,2}

國立臺灣大學醫學工程研究所¹ 國家衛生研究院生醫工程與奈米醫學研究所²

Introduction : Immunocellular therapy harnesses immune cells to target cancer, with NK cells offering rapid, nonspecific tumor elimination. However, large-scale expansion and activation remain challenges. This study introduces a one-step closed bioreactor that enhances proliferation and activation under pseudostatic conditions, optimizing aggregate size and reducing apoptosis for scalable immunotherapy applications.

Materials and Methods : A one-step closed bioreactor was designed using a two-chamber system with a 50 mL centrifuge tube connected by a two-way valve. NK-92MI cells were cultured in the upper chamber under pseudostatic conditions, incorporating brief mechanical rotation (15 rpm for 15 min every 6 hours). On day 8, cells were transferred to the lower chamber for activation with IL-15 or IL-18. Cell proliferation was assessed via flow cytometry, while viability was determined using live/dead staining. Gene expression of cytotoxic markers, including IFN- γ , IL-10, and NKG2A, was analyzed using qPCR. Cytotoxic activity was evaluated using a calcein AM-labeled K562 assay, with fluorescence intensity serving as an indicator of target cell lysis.

Results : The bioreactor system facilitated a 144-fold expansion of immune cell spheroids over 14 days, significantly surpassing conventional static cultures. The optimized pseudostatic conditions maintained an aggregate size of 80–150 μm , reducing apoptosis and enhancing cell viability (>85%). qPCR analysis revealed increased expression of IFN- γ following IL-18 activation, with a corresponding decrease in inhibitory markers such as NKG2A. Functional assays confirmed enhanced cytotoxicity against K562 cells, with IL-18 activation leading to a 1.62-fold increase in tumor cell lysis compared to non-activated controls.

Discussion : Unlike traditional static cultures, which often lead to oversized aggregates and necrosis, the controlled rotation in our bioreactor promotes optimal spheroid formation and improves mass transfer efficiency. The one-step activation process further streamlines the culture workflow, reducing handling steps and minimizing contamination risks. Additionally, IL-18 activation significantly enhanced IFN- γ expression, aligning with previous studies on NK cell-mediated cytotoxicity. While IL-15 provided moderate activation, its transient effects suggest it may be more suitable for short-term stimulation. The versatility of this bioreactor system extends beyond NK cells, offering potential applications for other immune cell therapies requiring scalable expansion and activation.

Conclusions : This study demonstrated a one-step closed bioreactor for efficient immune cell proliferation and activation. The pseudostatic culture optimizes aggregate size, viability, and cytotoxicity. IL-18-activated cells show enhanced tumor-killing, highlighting clinical potential. The scalable, contamination-free design supports immunotherapy advancements.

利用點擊化學工程化表達嵌合抗原受體的小型細胞外囊泡在急性肝衰竭中表現出增強的療效
Small Extracellular Vesicles Engineered Using Click Chemistry to Express Chimeric
Antigen Receptors Show Enhanced Efficacy in Acute Liver Failure

陳姿妤¹ 呂彥葶¹ 陳雅紋² 林郁修¹ Duy-Cuong Le^{3,4,8} 黃彥華^{3,5,6,7} 王惠鈞² 李政忠^{2,8} 林泰元¹

國立臺灣大學醫學院藥理學研究所¹ 臺北醫學大學醫學科技學院轉譯醫學博士學位學程²

臺北醫學大學醫學院國際博士學位學程（細胞治療與再生醫學）³

Vinmec 高科技中心，Vinmec 醫療系統，河內，越南⁴

臺北醫學大學醫學院醫學系生物化學與分子細胞生物學科⁵

臺北醫學大學醫學院醫學科學研究所⁶ 臺北醫學大學細胞治療與再生醫學研究中心⁷

臺北醫學大學醫學科技學院國際轉譯科學博士學位學程⁸

Introduction : APAP overdose causes acute liver failure (ALF), with NAC as the standard treatment, though often insufficient. MSC-derived extracellular vesicles (EVs) show promise but lack targeting specificity. This study employs click chemistry to engineer CAR-modified small EVs (CAR-sEVs) for targeted liver therapy.

Materials and Methods : MSC-derived sEVs were modified with azide groups and conjugated with DBCO-scFv targeting ASGR1 via click chemistry. ALF was induced in mice using APAP, followed by treatment with NAC, sEVs, or CAR-sEVs. Liver injury was assessed via ALT/AST levels, histology, and hepatocyte proliferation.

Results : CAR-sEVs showed higher liver accumulation, significantly reduced ALT/AST levels, improved liver histology, and enhanced hepatocyte proliferation compared to NAC and unmodified sEVs.

Discussion : CAR-sEVs effectively target ASGR1-expressing hepatocytes, improving therapeutic efficacy over NAC and standard sEVs. Click chemistry enhances specificity without affecting EV function. Further studies are needed to optimize dosing and assess long-term effects.

Conclusions : CAR-sEVs provide a targeted, cell-free therapy for ALF, reducing liver damage and promoting regeneration. This approach highlights the potential of precision-engineered EVs in liver disease treatment.

臍帶間質幹細胞通過調控肺部巨噬細胞治療 *Porphyromonas gingivalis* 介導
的致死性吸入性肺炎

**Umbilical Cord Mesenchymal Stem Cell Therapy in *Porphyromonas Gingivalis*-Mediated
Severe Aspiration Pneumonia Via Modulation of Lung Macrophages**

林妘霏¹ 莊漢英¹ 蔡孟勳² 陳漪紋² 王麗姿¹
臺北醫學大學醫學檢驗暨生物技術學系¹ 台灣大學臨床牙醫學研究所²

Introduction : *Porphyromonas gingivalis* (*Pg*)-induced aspiration pneumonia is a significant health concern. While human umbilical cord mesenchymal stem cells (UCMSCs) show promise in treating pneumonia, the impact of *Pg* lipopolysaccharide (LPS), a key virulence factor, on pulmonary macrophage (MΦ) subsets and the therapeutic mechanisms of UCMSCs remain unclear.

Materials and Methods : Bioinformatics analysis was used to elucidate the impact of *Pg*-LPS treatment on MΦ responses. *Pg*-LPS was added to murine lung-extracted cells to evaluate its influence on pulmonary MΦ responses through flow cytometric analysis. Moreover, to assess UCMSC therapy, we established two *in vivo* models: a clinically relevant aspiration pneumonia model induced by dental implants placed under *Pg* LPS conditions, and a model involving direct intratracheal *Pg* LPS injection.

Results : Transcriptomic analysis revealed that *Pg* LPS induces a cytokine storm-like response in human monocyte-derived MΦs (MoMΦs), increasing inflammatory mediators like IL-1β, IL-6, TNF-α, and iNOS and then exacerbating acute lung injury. Further, *Pg* LPS exposure significantly promoted inflammatory M1 rather than anti-inflammatory M2 polarization in recruited MoMΦs, resident interstitial MΦs, and resident alveolar MΦs. In the implant model, UCMSC treatment shifted alveolar MΦs from M1 to M2 polarization. In the intratracheal *Pg* LPS model, UCMSC therapy not only decreased M1 polarization in all lung MΦs but also significantly improved body weight loss caused by *Pg* LPS. Moreover, mitochondrial transfer from UCMSCs was demonstrated to M2-dominant MΦs.

Discussion : Further investigations are needed to unravel the intricate mechanisms underlying UCMSC therapy for *Pg*-LPS-mediated aspiration pneumonia, particularly regarding mitochondrial transfer and metabolism in specific pulmonary MΦ subsets.

Conclusion : The findings enhance our understanding of lung MΦ responses to *Pg* infection and provide valuable insights into the therapeutic application of UCMSCs for treating severe aspiration pneumonia.

幹細胞球體衍生三維去細胞基質作為腦源性神經營養因子遞送平台於創傷性腦損傷之應用
3D Stem Cell Spheroid-derived Decellularized Matrix as Platform for Loading Delivering
Brain-derived Neurotrophic Factor Delivery to Treat Traumatic Brain Injury

林鈺萍 高英淇 黃玠誠
國立清華大學生物醫學工程研究所

Introduction: 創傷性腦損傷(traumatic brain injury, TBI)為常見的神經損傷，且目前缺乏有效治療。研究指出，腦源性神經營養因子(brain-derived neurotrophic factor, BDNF)在細胞分化、神經元發育與存活、突觸形成及突觸可塑性等方面發揮關鍵作用，是一種具有潛力可用於治療 TBI 的神經營養因子。先前研究發現，三維幹細胞球體去細胞後所留存之去細胞支架(decellularized matrix, dECM)，保存幹細胞分泌的天然細胞外基質結構及生長因子，可作為搭仔生長因子之遞送平台。本研究利用三維間葉幹細胞(Mesenchymal stem cell, MSC)衍生的去細胞基質作為 BDNF 的遞送平台，以應用於 TBI 治療。體外實驗顯示，該基質能夠有效搭載 BDNF 並穩定釋放長達 14 天，釋放出之 BDNF 可促進神經突生長、降低麩氨酸誘導的細胞死亡，並促進血管新生。植入小鼠 TBI 動物模型中也發現可以提升小鼠行為功能並減少損傷大小，免疫螢光染色結果亦證實其促進神經再生與血管新生的效果，顯示釋放出之 BDNF 具有生物活性與治療潛力。

Materials and Methods: 本研究先將 dECM 浸泡於含有 BDNF 溶液中並於室溫搖晃五小時，以確保 BDNF 成功搭載至 dECM。製備完成後，分析 dECM 對 BDNF 的搭載量與效率，並測定其釋放曲線。隨後，進行功能性測試，包括：促神經突生長、降低麩氨酸誘導之興奮毒性以及促血管新生實驗。最後，利用小鼠 TBI 模型評估搭載至 dECM 之 BDNF 是否能有效促進體內損傷區域的神經再生與血管新生，以驗證其治療效果。

Results: 結果顯示，dECM 不僅能有效搭載並釋放 BDNF，還能促進神經突生長、提高細胞存活率，並具有顯著的神經保護效果。此外，dECM 能增強血管新生。動物實驗證實，dECM 與 BDNF 結合使用能有效縮小創傷區域，增加新生組織的厚度，促進神經與血管再生，同時減少膠質疤痕形成。

Discussion: 本研究利用三維間葉幹細胞球體衍生的細胞外基質(dECM)作為 BDNF 的遞送載體，避免其快速降解並提升穩定性。此外，實驗顯示 dECM 可攜帶 25-100 ng/mL BDNF 並具劑量依賴性，且未達飽和，未來可進一步測試更高濃度的負載極限。

Conclusions: 本研究利用三維 MSC 球體去細胞衍生的 dECM 作為生長因子載體，攜帶 BDNF 以促進小鼠 TBI 模型的神經再生與血管新生。結果顯示，dECM 可有效攜帶並釋放 BDNF，提升神經突生長、細胞存活率與神經保護效果，並增強血管新生。動物實驗證實，dECM + BDNF 可減少創傷區域、增加新生組織厚度、促進神經與血管再生，並降低膠質疤痕，展現 TBI 治療潛力。

含骨形態發生蛋白-2 靜電紡絲薄膜於骨分化的應用
Bone Morphogenetic Protein-2 Hybrid Electrospinning Membranes
for Applications in Bone Differentiation

謝孟昀² 陳映彤² 李亦宸^{2,*} 姚俊旭^{1,*}

中國醫藥大學醫學院生物醫學影像暨放射科學系¹ 逢甲大學化學工程學系²

Introduction: 牙周病是一種常見的慢性疾病。目前，牙周手術治療方式在多數情況下，抗生素是最佳的治療策略。然而抗生素在手術過程中容易被沖洗掉，因此不易提供足夠作用時間，近年來，靜電紡絲薄膜混合抗生素、蛋白質等藥物疾作為病變局部的輸送藥物系統已廣泛地被應用於組織工程中。而靜電紡絲薄膜除了具有相互連通的孔洞結構可達到藥物釋放的優點以外，同時也具有利於手術後細胞再生和牙組織重建的潛在優勢。

Materials and Methods: 本研究選用高生物相容性、可降解性的天然胺基酸聚合物作為材料，利用靜電紡絲技術製備含有骨形態發生蛋白-2 (BMP-2) 奈米纖維薄膜，並探討了該薄膜的物理化學性及生物相容性。進一步，我們將結合該薄膜與骨母細胞做體外培養測試，評估此奈米纖維膜對骨細胞分化的影響。

Results and Discussion: 此研究證明奈米纖維薄膜混合 BMP-2 薄膜具有良好的生物相容性及緩釋的效果。此外，與骨母細胞相培養後，奈米纖維結構與 BMP-2 的協同效應可以促使骨母細胞有更好的黏附性及相互連結作用。在長天期培養後，該薄膜提供的 BMP-2 緩釋效果對於骨母細胞分化後骨鈣素含量有明顯的提升。此結果表明我們的靜電紡絲奈米纖維膜對骨母細胞無毒，並有助於細胞黏附及骨分化促進的效果。

Conclusions: 本研究通過靜電紡絲技術成功製備了具有含 BMP-2 的天然胺基酸聚合物奈米纖維膜。該薄膜除了具有與牙周組織相似的機械性質外，也顯示這類的組合具有較高的生物相容性和骨細胞分化誘導的效果，為牙組織工程材料提供了一項新的選擇。

使用不同成熟度之軟骨前驅細胞製造多層軟骨移植體
**Fabrication of Multi-zonal Cartilage Graft with Chondrocyte Precursors of
Different Maturity**

蔡宜蓁¹ 劉彥良² 林峯輝³ 劉華昌⁴
中國醫藥大學生物醫學工程學系¹ 中國醫藥大學生物醫學工程碩士學位學程²
國立臺灣大學醫學工程學系³ 國立臺灣大學醫學院骨科部⁴

Introduction : Cartilage defects are a major cause of chronic pain and disability worldwide, with associated mobility impairments increasing mortality rates by approximately 11%. Given the promising differentiation potential and immunomodulatory properties of umbilical cord mesenchymal stem cells (UC-MSCs), this study aims to compare their effectiveness with bone marrow mesenchymal stem cells (BM-MSCs). By leveraging MSCs at different stages of differentiation, we constructed a multilayered structure that mimics the stratified organization of native cartilage. This approach seeks to develop allogeneic stem cell-based cartilage grafts for improved repair strategies.

Materials and Methods : Human BM-MSCs and UC-MSCs were induced to undergo chondrogenic differentiation, and spheroids were collected at 7, 14, and 21 days to assess their maturation. Composite spheroids were created to evaluate integration capacity, and multilayered constructs were assembled to mimic native cartilage structure. A porcine femoral condyle defect model was used to compare the repair efficacy of BM-MSC-derived, UC-MSC-derived, and autologous cartilage grafts, with recovery assessed six months post-transplantation.

Results : Histological analysis confirmed the chondrogenic differentiation potential of both BM-MSCs and UC-MSCs. Less mature spheroids exhibited superior integration, and encapsulating more mature spheroids within less differentiated ones improved overall cohesion. The stratified arrangement of spheroids successfully replicated the layered structure of native cartilage, with undifferentiated MSCs enhancing integration with bone substitutes. In vivo experiments demonstrated that MSC-derived spheroids achieved superior tissue integration and repair outcomes compared to autologous cartilage transplantation.

Discussion : The findings indicate that UC-MSCs exhibit strong chondrogenic potential and hold promise as an allogeneic cell source for cartilage repair. Future studies should focus on evaluating the immunological safety and long-term efficacy of this approach to enhance its clinical feasibility and expand treatment options for cartilage defects.

Conclusions : This study confirms that both BM-MSCs and UC-MSCs possess significant chondrogenic differentiation capacity. By employing a stratified arrangement of chondrogenic spheroids, we successfully mimicked the multilayered structure of native cartilage. Furthermore, the incorporation of undifferentiated MSCs improved graft integration, aligning with our objective of enhancing cartilage repair. Preliminary animal studies support the clinical potential of this strategy, paving the way for further translational research.

運用 *SOX9* mRNA 脂質微粒誘導骨間質幹細胞在多孔生物支架內分化為軟骨細胞，
以治療軟骨缺損

Integrated *SOX9* mRNA Lipid Nanoparticles and Porous Cell Carriers: A Novel Approach to *In situ* Chondrogenesis for Mesenchymal Stem Cell Therapy in Cartilage Defect Repair

陳詩妮¹ 劉華昌² 劉彥良³

中國醫藥大學醫學檢驗生物技術學系¹ 國立臺灣大學醫學院骨科部²

中國醫藥大學醫學工程學院生物醫學工程碩士學位學程³

Introduction : Osteoarthritis (OA) is one of the world's most investigated bone and cartilage disorders. OA is a critical degenerative joint condition related to cartilage defects' breakdown over time. Despite the limiting self-repairing ability of the cartilage and the lack of blood supply and nerves, cartilage defects and its repair have become significant challenges. Therefore, we aim to develop an innovative cell therapy approach to seek a better treatment for OA by combining *SOX9* mRNA lipid nanoparticles (LNPs) and porous cell carriers.

Materials and Methods : MSC-derived chondrocyte precursors were generated by delivering *SOX9* mRNA via lipid nanoparticles within a microfluidic-fabricated porous scaffold made of hyaluronic acid and gelatin. *In vitro* characterization confirmed chondrogenic differentiation and matrix formation, while *in vivo* implantation and histological analyses demonstrated cartilage-like tissue formation. This approach integrates gene delivery and biomaterials for enhanced cartilage regeneration.

Results : We inserted *SOX9*-LNPs into BM-MSCs to determine whether *SOX9* mRNA was going to enhance the chondrogenesis of BM-MSCs. *SOX9*, Collagen, type II, alpha 1 (*COL2A1*) and Aggrecan (*ACAN*) are the iconic indicators of human chondrocytes. qPCR analysis showed that *SOX9*-LNP transfection into BM-MSCs up-regulated the gene expression of *SOX9*, *COL2A1*, and *ACAN* by 160-fold, 20-fold, and 65-fold respectively. Western blot experiment was conducted to emphasize the high expression of *SOX9* and *COL2A1* protein in experiment group. Cytotoxicity of the scaffold was proved by CCK-8 and LDH tests. CCK-8 and LDH results showed no significant difference on cell viability and cell damage respectively between control and scaffold groups. Encouraged by the positive results obtained in *in vitro* experiments, we conducted a mice experiment with long-term observation periods of 1 month, 2 months, and 4 months. Mice were sacrificed and the implanted cell carriers were collected. BM-MSCs were observed to grow and undergo chondrogenesis in the microenvironment provided by porous scaffold. An obvious observation of lacunae and high cell density was performed with months. Lacunae is a small space, containing a chondrocyte in cartilage. Lacunae forms when a chondrocyte is mature enough.

Discussion : Throwback to current cell therapies such as ACI and MACI®, the two-stage procedures make the treatment a more extended period and contribute to additional donor morbidity of healthy cartilage. We aim to shorten the treatment period and achieve the long-term outcomes by providing customized gene-activated matrix (porous scaffold with *SOX9*-LNP) with microfracture procedure. Only once small open surgery is needed. The bone marrow leakage from the perforations contains BM-MSCs which are expected to fuse with the *SOX9*-LNP within the scaffold. Therefore differentiate into functional chondrocytes.

Conclusions : Our results show that *SOX9* mRNA induces the chondrogenesis of BM-MSCs and enhances the *SOX9* and *COL2A1* expression in the target cells. The porous scaffold provides a suitable and ideal environment for *in situ* mRNA-guided chondrogenesis. This combination is believed to have emerged as an effective and promising approach for cartilage defect repair.

明膠乙二胺與唾液酸的耦合反應成新複合型高分子,利用光譜鑑定做為新材料的物性鑑定,抗氧化性,抑制酪胺酸酶,細胞相容性與胞遷移測試作為創傷傷口癒合之功能性的評估

The Synthesis of Gelatin-ethylene-diamine Couple to Sialic Acid to Formed the Composed Polymer Based that the Physicochemical Characterization Identification, Antioxidant Effect, Cell Viability and Cell Migration Test Were Evaluated for Functional Property in Wound Healing

蕭淑敏 方旭偉

國立台北科技大學生化與生醫研究所

Introduction : The goal of this research is to synthesis two new protein–monosaccharides compound as the target therapeutic biopolymer that it can be apply in wound healing and skin repair. Due to the patient has saliva gland hypofunctional (SGH) symptom in the subjective sensation or he got Parotid gland tumor that he has to do the surgery or by radiation to cure and to recover his health. Even the people who has cracked lips because the hyposalivation cause the dry skin on mouth. As the patient has surfer the painful. They really need have some new biomaterials to cure or to have good therapeutic treatment on the surface of skin.

Materials and Methods : Gelatin (bloom 300G), N-hydroxy succinimide (NHS)(Alfa), tyrosinase, Sialic acid, L- tyrosine (Alfa), 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide HCl (EDC) (Alfa), Trinitrobenzene sulfonic acid (TNBS), DMEM (Dulbecco's modified minimal essential medium (Gibico), ethylene diamine (Adich), methyl alcohol, ethyl alcohol (99.8%), 2,2-diphenyl-1-picrylhydrazyl (DPPH), glycine, and D₂O, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), were purchased from Sigma-Aldrich Chemical Company and used without further purification.

Results : In this research, we have synthesis two new copolymer. The first new copolymer is sialic acid-ethylenediamine-gelatin (SA-NH(CH₂)₂NH₂-Gel) which is from gelatin-ethylenediamine (Gel-NH(CH₂)₂NH₂) couple to sialic acid (SA) by the crosslinking agent. The second is Sialyl-NH(CH₂)₂NH-Gel which there are no crosslinking agent in the reaction. The Gel-NH(CH₂)₂NH₂ is a cationic compound which synthesis is the gelatin (Gel) reaction to ethylenediamine NH₂(CH₂)₂NH₂ in PBS solution by the pH adjustment and coupling agent. The characteristically property of copolymer was identified by the instrument analysis. ¹H NMR spectra shown up the (CH₂CH₂) characteristic chemical shift of Gel-NH(CH₂)₂NH₂ cationic position is located around $\delta = 3.02$ and 3.37 ppm. We also comparison the different chemical shift of the of SA-NH(CH₂)₂NH₂-Gel with Sialyl- NH(CH₂)₂NH-Gel. The characteristic absorption bands of functional group from these copolymers on FTIR-ATR spectrum are shown up. We used three methods to give the alternative animal testing, the first is in vitro cytotoxicity assay (MTT%). For the critical evaluation the cell viability, we using the densities 1.0×10^4 of L929 cells were exposed to a serials conc. 25-200 (ug/mL) of both no crosslinking and cross-linking polymer that the result of the data of MTT assay were at the range 88.36% - 103.81% for Sialyl-NH(CH₂)₂NH-Gel and 120.83% - 90.69% for SA-NH(CH₂)₂NH₂-Gel, separately. It is proved that two copolymers all have higher cell biocompatibility and nontoxicity at the same time these copolymers are benefit endocytosis to enhance the cell growth in the trend. The second is SA-glycosyl-NH(CH₂)₂NH-Gel and Gel-NH(CH₂)₂NH₂ both polymers have free radical scavenging effect by the DPPH test. The third, both polymers have the same function of antioxidant effect that is using ascorbic acid (AA) for the standard to inhibit tyrosinase and the result of inhibit efficiency is 23.43% for Sialyl-NH(CH₂)₂NH-Gel and

24.53% for Gel-NH(CH₂)₂NH₂, respectively. It means that the Sialyl-NH(CH₂)₂NH-Gel and Gel-NH(CH₂)₂NH₂ copolymer can prevent the cell growth of melamine and also it is able to brightening on the skin. Cell migration test is evaluated for the wound healing.

Discussion : The new materials of Sialyl-NH(CH₂)₂NH-Gel and starting materials Gel-NH(CH₂)₂NH₂ both polymers have good free radical scavenging effect by the DPPH test. The conc. of Sialyl-NH(CH₂)₂NH-Gel and Gel-NH(CH₂)₂NH₂ both are 10ppm that these are have free radical scavenging rate 29.76% and 42.62%, respectively. But the SA-NH(CH₂)₂NH-Gel did not have the ability to catch the free radical. As we compare the effect of inhibit tyrosinase of AA at the same conc. 50ppm that the result shown up Sialyl-NH(CH₂)₂NH-Gel and Gel-NH(CH₂)₂NH₂ both copolymers have the efficiency of inhibit rate near to 50%. It is obviously, both two copolymers also have good antioxidant effect.

Conclusions : In this research, we have synthesis of two new copolymers SA-NH(CH₂)₂NH-Gel and other Sialyl-NH(CH₂)₂NH-Gel. The characteristic properties on free radical scavenging effect, antioxidant have been evaluated form two copolymer that the result show up two copolymers higher cell biocompatibility prove the nontoxicity that were evidence by MTT assay, and cell migration test with the negative control also evaluated. So that we suggest the two biopolymers can serves as the target therapeutic new materials that it can be apply in wound healing.

三維列印支架接枝兒茶素於骨母細胞再生之評估 Evaluation of 3-D printed Scaffolds Grafted with EGCG on Osteoblast Activity

陳秀敏¹ 姚俊旭² 程正鑫³

中國醫藥大學醫學工程學院生物醫學工程碩士學位學程¹

中國醫藥大學生物醫學影像暨放射科學學系² 臺南市立安南醫院委託中國醫藥大學興建經營³

Introduction: 目前已知通過 3D 列印製造的陶瓷和聚合物支架，在骨組織工程方面取得了良好的改進。在選擇的材料方面，矽酸鈣(calcium silicate, CS)及聚己內酯(polycaprolactone, PCL)已是常見的材料之一，兩者混合可使 CS 便於列印使用，並提高其生物相容性和生物降解性。然而，作為骨修復支架還有一個傷口感染的問題存在，表沒食子兒茶素沒食子酸酯(epigallocatechin-3-gallate, EGCG)具有抗氧化、抗菌和提升骨母細胞增生和礦化的功用，因此本研究擬將 EGCG 接枝於 CS/PCL 支架上，以達到改善支架對於骨組織再生的效果。

Materials and Methods: 以 1:1 比例配製 CS 與 PCL 作為印製支架基底材料，再依序將支架浸泡於聚多巴胺(polydopamine, PDA)以及 EGCG，製作出 CS/PCL-EGCG 支架。選用的 EGCG 濃度為其與骨母細胞共培養之最佳促進增生的濃度再放大 20 倍，並進行後續測試分析。

Results: 將細胞接種在各個不同濃度的 CS/PCL-EGCG 支架上，進行共培養後，以 MTT 與 ALP 測試測定支架對於細胞的影響。從 MTT 結果可以得知不同濃度之 CS/PCL-EGCG 支架皆有促進細胞增生的作用，其中濃度組別為 0.625 µg/mL 的支架具有顯著的細胞增生。由 ALP 活性測定結果可以得知，濃度組別為 1.25、2.5 及 5 µg/mL 的支架具有顯著的促進 ALP 上升的趨勢。

Discussion: 使用不同濃度之 EGCG 與細胞共培養，並使用 MTT 與 ALP 測試分析 EGCG 對於細胞之影響，其中濃度為 5 µg/mL 是促進細胞生長的最佳濃度，但各組別對於 ALP 活性皆無明顯促進的效果。然而在使用支架與細胞共培養後發現其中三組濃度組別具有顯著促進 ALP 上升的趨勢，於過去文獻有指出 CS/PCL 支架具有促進 ALP 上升的作用，因此推測此結果可能是受到支架基底材料 CS/PCL 的影響。

Conclusions: 本研究利用生物三維列印系統製作一個適合骨修復的輔助支架，以 CS 與 PCL 作為印製支架基底材料，再依序將支架浸泡於 PDA 以及 EGCG，最終製作出 CS/PCL-EGCG 支架。透過細胞毒性測試以及鹼性磷酸酶活性測試得到 EGCG 促進細胞生長的濃度範圍，從支架與細胞共同培養後的 MTT 與 ALP 測試得知支架具有促進生長與提升 ALP 活性的效果。

液態泡沫用於腹腔內免疫治療之免疫細胞與抗癌藥物載體研究

Liquid foam as Carrier of Immune Cells and Anti-cancer Agents for Intraperitoneal Immunotherapy

沈雅涵¹ 洪明奇² 林峯輝¹ 劉彥良³

國立台灣大學醫學工程學系¹ 中國醫藥大學生物醫學研究所²

中國醫藥大學生物醫學工程碩士學位學程³

Introduction : Peritoneal carcinomatosis (PC) refers to cancers that spread to the peritoneum from other organs, including ovarian, gastric, colorectal, appendicular, or pancreatic cancers. Patients with PC often present with highly dispersed tumors, leading to a poor prognosis with a short median survival of 3.1 months. Combining cytoreductive surgery and Hyperthermic IntraPERitoneal Chemotherapy (HIPEC) or pressurized intraperitoneal aerosol chemotherapy (PIPAC) marginally improves median survival to 6-12 months. However, the long operative time and invasive procedure of HIPEC make it only suitable for a few highly selected patients. Postoperative adhesions impact aerosol delivery and gradually diminish the efficacy of PIPAC treatment with an increasing number of treatments. To address these challenges, we developed “Immunofoam”—a minimally invasive, highly expandable, and rapidly filling injectable liquid foam-based drug delivery system.

Materials and Methods : Alginate/gelatin and F127-based hydrogel serve as both the drug carrier and foaming agent. The formulation is infused into a two-channel microfluidic device to generate microbubbles.

Results : The Immunofoam system supports immune cell proliferation while preserving their ability to target cancer cells. Its highly expandable feature enables efficient peritoneal cavity filling, ensuring uniform tumor immersion in drug-laden foam. By delivering combination therapies—including chemotherapy, immune cells, and other active agents—Immunofoam significantly extends the survival of ovarian and peritoneal carcinoma murine models.

Discussion : Compared to liquid (gel), foam offers higher viscosity to prolong drug-tissue contact time, more homogenous drug distribution, and better drug penetration into the interstitium. Therefore, the features of Immunofoam make it an ideal drug delivery system for intracavitary combination therapy.

Conclusions : This study successfully demonstrated an intraperitoneal administration of immune cells through a foaming device, and the results exhibited the Immunofoam’s biocompatibility and non-cytotoxicity during the foaming process. In addition, the combination of STING agonist and dendritic cells significantly improved cytotoxic T-cell immunity to cancer cells inoculated in the peritoneal cavity, which indicates that Immunofoam is a promising therapeutic innovation for intraperitoneal immunotherapy.

Regenerative efficacy of Supercritical Carbon Dioxide-Collagen Matrix on Gingival keratinization in Comparison with CTG Technique

Chou Yu Shang¹, Srinivasan Periasamy², Ko-Chung Yen², Dar-Jen Hsieh² *
School of Dentistry, Collage of Dental Medicine, Kaohsiung Medical University, Taiwan¹
R&D Center, ACRO Biomedical Co. Ltd, Kaohsiung City 82151, Taiwan²

Introduction : Soft tissue augmentation with autogenic grafts is a commonly used technique in many correctional surgeries in dental medicine. Dental implants need long-term support, therefore keratinized gingival tissue plays a vital role. Keratinized gingiva aids to maintain oral health, preventing gum recession, and in total esthetics. Thin gingiva needs to be keratinized to increase the thickness for fixing dental implants. In the present study supercritical carbon dioxide-collagen matrix derived from porcine skin was used to evaluate the gingival keratinization in comparison with the traditional CTG technique

Materials and Methods : Male and female patients enrolled were equal, 50% each. The average age of the patients was 45.8 ± 12.0 . Patients enrolled were screened for systemic disease and enrolled without any. All the patients enrolled were non-smokers. The surgical locations and sites in the patient's oral cavities are the arch maxilla and the arch mandible. The total number of surgical locations is 44, of which the arch maxilla is 22 and the arch mandible is 22. The surgical sites include anterior premolar 18 sites and molar 19 sites. The average surgical time is 79.7 ± 19.2 minutes. For the soft tissue augmentation, we used two techniques, the first one is the traditional connective tissue graft (CTG) as a predicate procedure and we used ABCcolla® Collagen Matrix (CMX) for gingival keratinization.

Results : The gingival thickness at the subgingival margin of 1.5 mm in the CTG group was 0.6 ± 0.2 and 0.7 ± 0.3 in the CMX group. The surgical time in minutes in the CTG group is 95.2 ± 16.0 , a significant increase in the surgical time 72.6 ± 17.0 , was observed in the CMX group, relative to the CTG group. The postoperative pain score in 1st week was 0.9 ± 0.6 in the CTG group, a significant increase in the postoperative pain score 3.5 ± 2.8 , was observed in the CMX group, relative to the CTG group.

Discussion : In the collagen matrix (CMX), usage led to a significant reduction in surgical time was observed, which is a greater comforting factor for the patients. The collagen matrix (CMX) usage does not need secondary surgery or wound. However, the CTG procedure involves a secondary surgical procedure. Therefore, using a collagen matrix avoids the secondary wound. By using collagen matrix multiple surgical sites performed in a limited time. The collagen matrix improved periodontal parameters comparable with the CTG group.

Conclusions : Supercritical carbon dioxide- derived CMX depicted similar gingival keratinization as CTG and reduced surgical time.

幹細胞球體衍生基質以聚多巴胺奈米粒子修飾後
透過減輕免疫反應和氧化壓力達到腦損傷修復之潛能

Stem Cell Spheroid-derived 3D Decellularized Matrix with Polydopamine Nanoparticle Dressing Promotes Brain Tissue Repair by Antioxidative and Immunomodulatory Potential

楊蓓青 黃玠誠*

國立清華大學生物醫學工程研究所

Introduction : Traumatic Brain Injury (TBI) causes direct brain damage, but secondary injury from excessive immune responses and oxidative stress worsens tissue damage. This study aims to mitigate secondary injury by regulating inflammation and reducing oxidative stress for improved therapeutic outcomes. To achieve this, we developed 3D decellularized extracellular matrix (3D dECM) scaffolds from mesenchymal stem cell (MSC) spheroids to provide structural support and immunomodulatory functions. Polydopamine nanoparticles (PDANP) were incorporated to enhance antioxidative properties and enable dECM assembly into sheet-like structures.

Materials and Methods : PDANP was synthesized and characterized for its reactive oxygen species (ROS) scavenging ability. 3D dECM scaffolds were prepared from MSC spheroids and modified with PDANP to enhance their antioxidative and adhesive properties. *In vitro* studies evaluated 3D dECM-PDANP's biocompatibility with neural cells, its antioxidative effect through DCFDA ROS measurement, and its role in neural differentiation via Tuj-1 expression. Immunomodulatory properties were assessed by analyzing macrophage polarization toward the pro-inflammatory M1 phenotype. *In vivo* studies examined lesion size and behavioral recovery in a TBI mouse model.

Results : PDANP was successfully synthesized and demonstrated strong ROS scavenging ability. When incorporated into 3D dECM, PDANP enhanced the scaffold's antioxidative properties. Additionally, PDANP's strong adhesion facilitated the assembly of 3D dECM-PDANP into sheet-like structures, improving its applicability for TBI treatment. *In vitro* studies showed that 3D dECM-PDANP exhibited excellent biocompatibility. Furthermore, PDANP's antioxidative properties accelerated neural differentiation. Regarding immunomodulation, 3D dECM-PDANP reduced pro-inflammatory M1 macrophage polarization. *In vivo* studies showed tissue recovery and improvements in behavioral function.

Discussion : PDANP-decorated 3D dECM scaffolds effectively reduced oxidative stress and regulated inflammation, key factors in secondary brain injury. This combined approach offers a promising strategy for neural tissue repair in TBI by providing both structural and biochemical support.

Conclusions : 3D dECM-PDANP integrates structural support, immunomodulation, and antioxidative properties, making it a promising scaffold for TBI treatment. Its ability to scavenge ROS and regulate inflammation suggests potential for mitigating secondary injury and promoting neural tissue repair. Further research is needed to explore its clinical applications in TBI treatment.

Supercritical Carbon Dioxide-derived Acellular Dermal Matrix-Based Neuromorphic Device with Ultralow Voltage, Ion Channel Emulation, and Synaptic Forgetting Visualization Computation

Lei Li¹, Yihua Xu¹, Qunkai Peng¹, Pei Huang¹, Xinqing Duan¹, Mingqiang Wang¹, Yu Jiang¹, Jie Wang¹, Srinivasan Periasamy², Kuan-Chang Chang¹, Dar-Jen Hsieh^{2*}

Guangdong Provincial Key Laboratory of In-Memory Computing Chips, School of Electronic and Computer Engineering, Peking University, Shenzhen 518055, P. R. China¹
R&D Center, ACRO Biomedical Co. Ltd, Kaohsiung City 82151, Taiwan²

Introduction : Neuromorphic devices have achieved highly biomimetic functions by simulating the transmission and processing of neural signals, translating neural plasticity into mechanisms for perception, cognition, and action. Neuromorphic bioelectronics aims to integrate electronics with biological systems yet encounter challenges in biocompatibility, operating voltages, power consumption, and stability. In the present biocompatible neuromorphic devices fabricated from acellular dermal matrix (ADM) derived from porcine dermis using low-temperature supercritical CO₂ extraction.

Materials and Methods : Sliced porcine skin was subjected to supercritical carbon dioxide extraction technology for decellularization. The decellularized ADM scaffold was freeze-dried and freeze-milled to granules of 50–200 μm and subjected to enzymatic hydrolysis using pepsin in acidic conditions. The atelocollagen solution was filtered through a 0.2-μm filter for sterilization. The atelocollagen solution a concentration of 6 mg/mL, was doped with hydrochloric acid mixed with deionized water in a volume ratio of 1:100 to adjust its pH. After 100 nm-thick molybdenum was deposited on the cleaned glass by the DC magnetron sputtering, 0.135 mL of atelocollagen solution was uniformly dispensed onto the Mo electrode using a pipettor. The atelocollagen film was dried on a baking machine for 45 min at a temperature of 40 °C. Finally, the top electrodes were deposited using the DC magnetron sputter and patterned with a shadow mask to complete the fabrication of neuromorphic devices.

Results : The ADM preserves the natural scaffold structure of collagen and minimizes immunogenicity by eliminating cells, fats, and noncollagenous impurities, ensuring excellent biocompatibility. The ADM-based devices emulate biological ion channels with biphasic membrane current modulation, exhibiting temperature dependency and pH sensitivity.

Discussion : ADM-based devices operate at an ultralow voltage of 1 mV and demonstrate reliable synaptic modulation exceeding 4×10^4 endurance cycles. The activation voltage can be theoretically as low as 59 μV, comparable to brainwave signals with a power of merely 7 aJ/event. Furthermore, a brain-like forgetting visualization algorithm is developed, leveraging the synaptic forgetting plasticity of ADM-based devices to achieve complex computing tasks in a highly energy-efficient manner.

Conclusions : Neuromorphic devices based on ADM not only hold potential in implantable bio-interfaces due to their exceptional biocompatibility, ultralow voltage, and power but also provide a feasible way for energy-efficient computing paradigms through a synergistic hardware-software approach.

具有調節免疫微環境的植物衍生物胞外體可促進糖尿病傷口上皮新生
**An Immune Microenvironment-modulating Plants-derived EVs with re-epithelialization
for Diabetic Wound Therapy**

廖秀蓉^{1,2} 蔡維妮² 吳廣俠² 張至宏^{3,4*} 黃奇英^{2*}
亞東紀念醫院醫學研究部¹ 國立陽明交通大學生物藥學所² 亞東紀念醫院骨科部³
元智大學生物工程與技術研究所⁴

Introduction : Diabetic wounds exhibit prolonged inflammation during the remodeling stage, driven by immune cell infiltration, the release of inflammatory cytokines, and matrix metalloproteinases (MMPs), which subsequently trigger reactive oxygen species (ROS) production and further tissue damage. Understanding the regulatory mechanisms of chronic wound healing is essential for developing effective treatment strategies. However, no current approach effectively regulates the inflammatory wound microenvironment or promotes re-epithelialization.

Materials and Methods : Tangential flow filtration was utilized to obtain highly purified extracellular vesicles (EVs) from various plants. These plant-derived extracellular vesicles (P-EVs) were then applied to human keratinocytes to assess their potential in stimulating anti-inflammatory responses. To investigate the key components responsible for the effects of P-EVs on inflammation resolution and skin repair, liquid chromatography-tandem mass spectrometry (LC-MS/MS) was performed. Furthermore, to evaluate the inhibitory effects of P-EVs on keratinocyte function in both acute and chronic wounds, a diabetic mouse model was employed.

Results : Plant-derived extracellular vesicles (P-EVs) offer several advantages over animal cell-derived EVs, including superior biocompatibility, biodegradability, and abundant availability. By screening various P-EVs, purification methods, and plant culture conditions for their wound-healing potential, EVs from *Laurus nobilis* (LN) exhibited the most significant effects, notably enhancing anti-inflammatory cytokine levels in the skin microenvironment. IL-33 and thymic stromal lymphopoietin (TSLP), traditionally associated with allergies and helminth infections, have also been reported to promote wound healing. Our preliminary findings suggest that LN-EVs facilitate re-epithelialization, increase anti-inflammatory cytokines (TGF-beta, IL-33, TSLP), and regulate MMP family proteins in human keratinocytes under diabetic conditions.

Discussion : Diabetic wounds suffer from persistent inflammation due to immune cell infiltration, cytokine release, and excessive ROS production, leading to impaired healing. Currently, no effective strategy exists to regulate this inflammatory microenvironment and promote re-epithelialization. Our findings demonstrate that LN-EVs enhance re-epithelialization, increase anti-inflammatory cytokines (TGF-beta, IL-33, TSLP), and modulate MMPs in diabetic keratinocytes. This suggests that P-EVs target anti-inflammatory signaling to mitigate immune activation, offering a potential therapeutic approach for skin disorders with impaired healing.

Conclusions : LN-EVs promote re-epithelialization, enhance anti-inflammatory cytokines, and regulate MMPs in diabetic keratinocytes, offering a promising therapeutic strategy for chronic wound healing. Their immunomodulatory effects suggest potential applications in treating skin disorders characterized by excessive inflammation and impaired tissue repair.

類軟骨細胞外基質仿生支架促進人類滑液膜幹細胞軟骨分化
**Bioinspired Scaffold Biomimicking Native Cartilage Extracellular Matrix Enhances
Chondrogenesis of Human Synovium-Derived Stem Cells**

陳怡儒 楊雅婷 王禎麒
台北慈濟醫院骨科部

Introduction : The microenvironment determines the differentiation fate of stem cells, and using a scaffold that resembles the extracellular components found in native cartilage can enhance chondrogenesis. To create a suitable environment for chondrogenic differentiation of stem cells, we utilized components that closely resemble the extracellular matrix (ECM) of native hyaline cartilage. These components—collagen, gelatin, hyaluronic acid, and chondroitin sulfate—were used to fabricate a biomimetic scaffold aimed at promoting cartilage regeneration.

Materials and Methods : A collagen–gelatin–hyaluronic acid–chondroitin sulfate biomimetic scaffold with composition and architecture similar to those of hyaline cartilage was fabricated using a microfluidic technique. Synovial tissues collected from the human knee joints during total knee arthroplasty surgery were used for the isolation of synovium-derived stem cells (SDSCs). SDSCs were cultured in the biomimetic scaffold with chondrogenic induction and evaluated.

Results : SDSCs seeded into the biomimetic scaffold attached to the scaffold firmly and exhibited good mitochondrial activity and high cell survival with pronounced glycosaminoglycan production. SDSCs cultured on the scaffold with chondrogenic induction exhibited upregulated mRNA expression of COL2A1, ChM1, Nrf2, TGFB1, and BMP7. *Ex vivo* study revealed that the SDSC/scaffold regenerated cartilage-like tissue in SCID mice with abundant type II collagen and S-100 production. BMP7 and COL2A1 expression in the tetra-copolymer scaffold group was much higher than that in the gelatin scaffold group *ex vivo*.

Discussion : The microenvironment of stem cells influences their fate through biochemical induction and biophysical modulation. We designed a novel scaffold using a microfluidic technique, characterized by a highly organized honeycomb-like structure. Relative to the gelatin scaffold, the biomimetic scaffold facilitates chondrogenesis to SDSCs.

Conclusions : The biomimetic scaffold demonstrates strong abilities to promote cartilage formation, making it an effective niche for cartilage tissue engineering.

臍帶間質幹細胞分泌之細胞外囊泡可促進軟骨細胞之細胞增殖及減少其氧化壓力
Wharton's Jelly Mesenchymal Stem Cells Secrete Extracellular Vesicles Enhance Cell Proliferation and Reduce Oxidative Stress in Chondrocytes

伍哲緯^{1,2,3} 傅尹志^{1,3,4} 邵佩琳⁵ 張玲華^{1,3} 鄒亞璇^{1,3} 曹雲雅^{1,3} 吳順成^{1,3*}

高雄醫學大學再生醫學與細胞治療研究中心¹ 元培醫事科技大學食品科學系² 高雄醫學大學骨科學研究中心³ 高雄醫學大學骨科⁴ 亞洲大學護理學系⁵

Introduction : Chondrocyte-based articular cartilage tissue engineering (ACTE) has been studied for treating articular cartilage defects. However, obtaining enough chondrocytes for ACTE by monolayer expansion in vitro makes chondrocytes lose chondrogenic phenotype, which is indicated as the cause of fibrocartilage formation in vivo. Studies indicate that chondrocytes lose chondrogenic phenotype is due to oxidative stress caused senescence in these cells. Wharton's jelly mesenchymal stem cells (WJMSCs) are MSCs derived from Wharton's jelly. WJMSCs are considered as a cell source to replace chondrocytes in ACTE for the advantages of strong proliferation, chondrogenic differentiation, noninvasive acquisition procedures, and no ethical controversy. However, the storage and transportation conditions of the WJMSCs are stringent. It is suggested that the therapeutic effect of MSCs comes from extracellular vesicles (EVs) secreted by MSCs. Whether WJMSCs secreted EVs (WJMSCs-EVs) reduce oxidative stress of chondrocytes remains rarely investigated. We hypothesize that WJMSCs-EVs can be used for reducing oxidative stress of chondrocytes. We tested the effects of WJMSCs-EVs on proliferation, survival, and oxidative stress in chondrocytes.

Materials and Methods : The WJMSCs-EVs were provided by Kao-Ho hospital in Kaohsiung. To characterize WJMSCs-EVs, the number, size and biomarkers (CD9, CD63 and CD81) of WJMSCs-EVs were analyzed. The chondrocytes were divided into 2 groups: 1. Control group: chondrocytes without any WJMSCs-EVs treatment, 2. WJMSCs-EVs group: chondrocytes were treated with WJMSCs-EVs. The WJMSCs-EVs uptake by chondrocytes, survival, and oxidative stress (mitochondrial superoxide production and antioxidant enzyme Superoxide Dismutase 2: SOD2) in chondrocytes after WJMSCs-EVs treatment were analyzed.

Results : The results shows that the mean diameters of WJMSCs-EVs are $79.8 \pm 19.05\text{nm}$. The WJMSCs-EVs are positive for CD9, CD63 and CD81. The WJMSCs-EVs were uptake by chondrocytes. The cell proliferation of chondrocyte was increased by WJMSCs-EVs treatment. The WJMSCs-EVs treatment does not alter cell survival of chondrocytes. The WJMSCs-EVs decrease oxidative stress in chondrocytes. After WJMSCs-EVs treatment, the SOD2 protein level was increased in chondrocytes, and the level of mitochondrial superoxide production in chondrocytes was decreased.

Discussion : We show that WJMSCs-EVs promote proliferation of chondrocytes. WJMSCs-EVs do not alter cell survival of chondrocytes. Moreover, WJMSCs-EVs decreases oxidative stress via increasing protein levels of SOD2 and decreasing superoxide synthesis protein level.

Conclusions] WJMSCs-EVs promotes proliferation and reduces oxidative stress in chondrocytes. This may be applied for more effective chondrocyte-based ACTE.

台灣再生醫學學會 (個人、贊助、準) 會員入會申請書

姓名	性別	出生 年 月 日	出生地	身分證 ID or 統編		
學歷	民國 年 月 畢業於					
戶籍住址						
現任職務	醫院/單位：	科部：	職稱：			
通訊地址	專科醫師證書字號： (無者免填)					
電話	(公)	(宅)	傳真：			
其他連絡 方式	(e-mail)：					
準會員申請者	推薦人簽名 會員一	<p>入會申請敬請附上相關證明，經理事會審查通過後始得為本會會員。</p> <p>1.個人會員：有醫師執照者或取得與再生醫學、組織工程學相關博士學位者。(醫師證書、學位證明)</p> <p>2.贊助會員：贊助本會工作之團體或個人。(設立證明、身分證)</p> <p>3.準會員：碩、博士班學生、博士後研究員、住院醫師、研究助理或等同資格者，須會員二人推薦。(學生證、在職證明)</p>				
	推薦人簽名 會員二					
審查結果 (由學會填寫)	會員類別 (由學會填寫)	會員證號碼 (由學會填寫)				
本人贊同貴會宗旨，擬加入為會員，嗣後並願意遵守會章，共圖發展						
此致			申請人：	(簽章)		
中	華	民	國	年	月	日

感謝下列廠商對本次學術研討會之贊助 & 支持
謹 在此致上十二萬分的謝意！

大江基因醫學股份有限公司

弘晉有限公司

百達醫療產品股份有限公司

亞果生醫股份有限公司

冠亞生技股份有限公司

茂士榮再生科技有限公司

海昌生化科技股份有限公司

博晟生醫股份有限公司

歐強國際有限公司

潤霈生技股份有限公司

醫晟生醫股份有限公司

(以字首筆畫數順序排列)

史坦賽爾生醫股份有限公司 STEMCELL BioTech CO., LTD.



更多TZX4研究結果
請見官方網站

神經退化性疾病新希望，遇見更清晰的自己

New hope for neurodegenerative diseases: discovering a clearer self.

• 神經再生 精準修復

史坦賽爾與花蓮慈濟神經外科權威林欣榮院長團隊合作，技術轉移TZX4幹細胞製程專利及授權商業化技術！史坦賽爾的研究專注於如何利用間質幹細胞來治療神經系統疾病，包括帕金森氏症、腦中風、創傷性腦傷和脊椎損傷等疾病。同時更關注患者的實際需求，期盼能為受神經系統疾病困擾的患者與家屬，帶來更好的修復方案。

• Start from Neuroscience Research

STEMCELL BioTech has partnered with the renowned neurosurgeon Dr. Shinn-Zhong Lin and his team at Hualien Tzu Chi Hospital to commercialize the TZX4 stem cell culture technology through patented innovations. STEMCELL BioTech focuses on how to use mesenchymal stem cells to treat neurological disorders, including Parkinson's disease, stroke, traumatic brain injury, and spinal cord injuries. Additionally, STEMCELL BioTech is dedicated to addressing the practical needs of its clients, aiming to provide better repair solutions for individuals and families affected by these disorders. By doing so, STEMCELL BioTech seeks to enhance their quality of life and restore for a healthier future.

獨家 8Rs 全能修復系統 感受新生，重現活力！

Exclusive 8Rs Total Solution
Experience Renewal Restore Your Vitality!



Amnion Membrane Allograft



Amnion is the inner membrane of tissue closest to the fetus throughout development in the womb.

Amnion is composed of structural extracellular matrix (ECM) and it contains specialized proteins and natural growth factors.¹

Because of its natural microstructure and biological characteristics, amnion has in recent years gained popularity in North America and Europe for treating all sorts of wounds. From Ophthalmology to wound management, amnion has shown to be an excellent source to promote healing and reduce scarring.²

Product No. (AGCS : Single Layer / AGCD : Double Layer / AGCT : Triple Layer)

AGCS016 1.6 cm disc	AGCS024 AGCD024 AGCT024	AGCS046 AGCD046	AGCT011 1X1 cm	AGCT023 2X3 cm	AGCD033 AGCT033 3X3 cm
AGCS022 AGCD022 AGCT022 2X2 cm	2X4 cm	4X6 cm	AGCT025 2X5 cm		

*Actual size

¹ Silini, Antonietta R. et al. "The Long Path of Human Placenta, and Its Derivatives, in Regenerative Medicine." *Frontiers in Bioengineering and Biotechnology* 3 (2015): 162. PMC. Web.
² ElHeneidy, Hossam et al. "Amniotic Membrane Can Be a Valid Source for Wound Healing." *International Journal of Women's Health* 8 (2016): 225-231. PMC. Web.



醫晟生醫股份有限公司

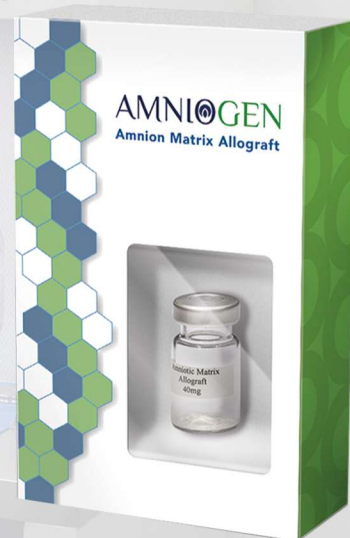
American Association of Tissue Banks(AATB) accredited institution.

Amnion Matrix Allograft

Because of its biological characteristics, amnion matrix allografts have been clinically utilized to treat orthopedic sport injuries, such as refractory plantar fasciitis*, tendinopathy or arthritis.** In a clinical study, significant improvement in plantar fasciitis symptoms was observed in patients receiving amnion matrix allografts.



Product No.	Size
AGBM020	20mg
AGBM040	40mg
AGBM100	100mg



* C. Zelen et al., "Prospective, Randomized, Blinded, Comparative Study of Injectable Micronized Dehydrated Amniotic/Chorionic Membrane Allograft for Plantar Fasciitis - A Feasibility Study." *Foot & Ankle International*. 34 (2013):1332-1339

** A. Gellhorn et al., "The Use of Dehydrated Human Amnion/Chorion Membrane Allograft Injection for the Treatment of Tendinopathy or Arthritis: A Case Series Involving 40 Patients.

" *American Academy of Physical Medicine and Rehabilitation* 9 (2017): 1236-1243