再生醫學之前景和多元化潛力暨
2022年台灣再生醫學學會學術研討會

Prospects and Diverse Potential of Regenerative Medicine / 2022 Annual Meeting of FARM

台灣再生醫學學會
Formosa Association Regenerative Medicine
Since 2004

摘要集

2022 年 03 月 19 日

亞東紀念醫院14樓國際會議廳

主辦單位： 亞東紀念醫院骨科部、台灣再生醫學學會

協辦單位： 科技部生命科學研究推動中心、衛生福利部、國家衛生研究院

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再生醫學之前景和多元化潛力暨 2022 年台灣再生醫學學會學術研討會
Prospects and Diverse Potential of Regenerative Medicine / 2022 Annual Meeting of FARM

Scientific Program

Time	Topic	Speaker	Institute	Moderator
08:30	**Registration 報 到**			
Session 1				
09:00	Opening Remark 亞東紀念醫院 邱冠明院長			
I-01 09:30~10:00	從再生醫療發展法談台灣再生醫療的前瞻與挑戰	石崇良常務次長	行政院衛生福利部	陳耀昌教授 /亞東醫院 張至宏副院長
10:00~10:30 **Group photo / Coffee Break**				
Session 2				
I-02 10:30~11:00	材料在眼科的應用	陳克華 主任	台北榮民總醫院眼科部	林泰元教授 方旭偉教授
I-03 11:00~11:30	Functional Porous Scaffolds and Biomimetic Matrices for Tissue Regeneration	Prof. Guoping Chen 陳國平 教授	Research Center for Functional Materials National Institute for Materials Science, Japan Faculty of Pure and Applied Sciences University of Tsukuba, Japan	張瑞根教授 何美泠教授
I-04 11:30~12:00	From Good to Great---The Important Revolutions that Shaped the Regenerative Medicine for Ocular Surface Diseases	陳偉勵 教授	臺大醫院眼科部	王至弘主任 /亞東醫院 張淑雯副院長
12:00 **會 員 大 會** 12:00~13:30 **Lunch Break**				
Session 3				
I-05 13:30~14:00	Polyplex Nanomicelle Delivery of Self-Amplifying RNA Vaccine	胡育誠 教授	國立清華大學化學工程學系	陳志華副院長 黃玲惠教授
I-06 14:00~14:30	Stimuli-Responsive Biomaterials for Engineering Spheroids	Prof. Masaya Yamamoto 山本 雅哉 教授	Department of Materials Processing, Graduate School of Engineering, Tohoku University, Sendai 980-8579, Japan	鄭乃禎教授 楊凱強教授

Time	Topic	Speaker	Institute	Moderator
I-07 14:30~15:00	Allogeneic Mesenchymal Stem Cell (MSC) Therapy for Immune & Inflammatory Diseases: Advances & Challenges	顏伶汝 教授	國家衛生研究院細胞及系統醫學研究所	嚴孟祿教授 /亞東醫院 邱彥霖部長
15:00~15:30 **Group photo / Coffee Break**				
Session 4				
I-08 15:30~16:00	牙科的再生醫療	陳敏慧 教授	臺灣大學臨床牙醫學研究所	黃義侑教授 楊榮森教授
I-09 16:00~16:30	3D Patterning of Growth Factor Incorporated Hydrogel Complex to Regulate Tissue Regeneration	Prof. Jeong Ok Lim	Department of Biomedical Science Kyungpook National University, School of Medicine Biomedical Research Institute, Kyungpook National University Hospital	孫瑞昇教授 沈家寧教授
I-10 16:30~17:00	Regenerative Medicine in Rhinology	黃琮瑋教授	亞東紀念醫院耳鼻喉科	楊台鴻教授 /亞東醫院 鄭博文主任
17:00 Closing Remarks & Poster Competition Award				

壁報 Poster

評審委員：曾靖孋教授、楊凱強教授、王禎麒醫師

壁報論文解說時段：13:00~14:00。

No.	Classification	Topic	Authors	Institute
P-01	Biomaterials	Hyaluronic Acid Nanoparticles with Novel Peptide Loading for Corneal Neovascularization	吳昱儀　曾靖孋	臺北醫學大學生醫材料暨組織工程研究所
P-02	Biomaterials	Injectable Hyaluronic Acid Gel with Epigallocatechin Gallate Addition for being Vitreous Substitutes	陳誼寧 [1]　謝昌倫 [2] 曾靖孋 [2]　林峯輝 [1]	國立臺灣大學醫學院暨工學院醫學工程研究所 [1] 臺北醫學大學生醫材料暨組織工程研究所 [2]
P-03	Biomaterials	The Synthesis of Europium-Doped Calcium Carbonate by an Eco-Method as Free Radical Generator Under Low-Intensity Ultrasonic Irradiation for Body Sculpture	張生龍 [2] 管哲雍 [1, 3]　林妤楹 [1, 4] 楊易軒 [1, 3]　陳靖昀 [6] 杞至穎 [1, 4]　李奇翰 [1, 4] 陳緻宇 [1, 3]　林利澤 [2] 楊鈞程 [5]　林峯輝 [1, 3]	國家衛生研究院生醫工程與奈米醫學研究所 [1] 國立聯合大學材料科學工程學系 [2] 國立臺灣大學醫學工程學系 [3] 國立中興大學組織工程與再生醫學博士學位學程 [4] 國立臺灣大學材料與工程學系 [5] 國立中央大學生醫科學與工程學系 [6]
P-04	Biomaterials	Platelet Derived-extracellular Vesicles as Nanocarriers for Carrying Anti-Angiogenetic Agent for Treating Vascular Endothelial Cells and its Mechanism Study	楊雅涵　張哲禕 陳盈汝　白台瑞 曾靖孋*	臺北醫學大學生醫材料暨組織工程研究所
P-05	Bone Marrow Stem Cells	The Roles of Src and PKCζ in Piezoelectric Stimulations of Chondrocyte Aggregation and Rearrangement	劉禹呈　林若梅 王兆麟	國立台灣大學醫學工程研究所
P-06	Others	Single-cell Transcriptomic Analysis of Cellular Heterogeneity and Interaction in Mouse Cornea	吳岳峰 [1]　黃裕文 [2] 劉欣瑜 [3,4]　張乃文 [1] 余有勝 [1]　陳宥亘 [1] 白韻翎 [5]　譚欣媛 [6] 林頌然 [1, 2, 3, 7, 8]	國立臺灣大學醫學工程學系 [1] 臺大醫院醫學研究部 [2] 國立臺灣大學臨床醫學研究所 [3] 臺大醫院眼科部 [4] 國立台灣大學生化科技學系 [5] 長庚醫院眼科部 [6] 臺大醫院皮膚部 [7] 國立臺灣大學發育生物學與再生醫學研究中心 [8]
P-07	Regenerative Medicine	Cell Morphological Responses to Mechanical Stress: Nucleus Pulposus cell in 3D-culture of TYPE I Collagen and Hydrogel	黃少湘　林若梅 王兆麟	國立臺灣大學醫學工程研究所

No.	Classification	Topic	Authors	Institute
P-08	Regenerative Medicine	Involvement of Conserved Pathways in 3-Dimensional (3D) Sphere Formation in Diverse Stem Cell Types	張家齊 [1, 2, 4] 江士昇 [3] 徐珮茹 [2] 顏伶汝 [2] 嚴孟祿 [4]	國防醫學院生命科學研究所 [1] 國家衛生研究院細胞及系統醫學所 [2] 國家衛生研究院癌症研究所 [3] 臺灣大學醫學院醫學系婦產科 [4]
P-09	Regenerative Medicine	Manipulation of Inherent Niches in 3D MSC Spheroids Improves Therapeutic Potential	施起進 陳立騏 王歆雯 黃玠誠*	國立清華大學生物醫學工程研究所
P-10	Regenerative Medicine	Rapid and Precise MSC Chondrogenesis is Achieved Through Increasing Adherens Junctional N-cadherin-β-catenin Interactions and Restricting Off-target Lineage Commitment	謝承展 [1,2] 張家齊 [2,3] 徐珮茹 [2] 王麗姿 [4] 林秀芳 [2] 陳令儀 [1] 顏伶汝 [2]* 嚴孟祿 [4]	國立清華大學分子醫學研究所 [1] 國家衛生研究院細胞及系統醫學研究所 [2] 國防醫學院生命科學研究所 [3] 臺大醫學院醫學系婦產科 [4]
P-11	Regenerative Medicine	The Effect and safety of Xenogenic-free Collagenase Assistant Cultivate Oral Mucosal Epithelial Tansplantation (CA-COMET) for the Treatment of Limbal Insufficiency	蔡佳穎 [1,2] 陳偉勵 [3]	輔大醫院眼科部 [1] 國立臺灣大學醫學院臨床醫學研究所 [2] 臺大醫院眼科部 [3]
P-12	Regenerative Medicine	The Effects of Cyclic Stretching on Chondrogenic Differentiation of Rat Adipose-derived Stem Cells	李慧瑩 [1] 朱惠君 [1] 金亭佑 [2] 李宏滿 [3] 謝明發 [1*]	中原大學生物醫學工程學系 [1] 中原大學生物科技學系 [2] 花蓮慈濟醫院骨科部 [3]
P-13	Regenerative Medicine	Using Rho-associated Protein Kinase (ROCK) Inhibitor to Develop Simplified Oral Mucosal Epithelium Transplantation (SOMET) for the Treatment of Limbal Stem Cell Deficiency (LSCD)	黃韋綸 [1,2,3] 蔡佳穎 [1,2,4] 吳若玄 [5] 陳偉勵 [2]	國立臺灣大學醫學院臨床醫學研究所 [1] 國立臺灣大學醫學院附設醫院眼科部 [2] 臺大醫院新竹臺大分院生醫醫院眼科部 [3] 天主教輔仁大學附設醫院眼科部 [4] Shiley Eye Institute and Viterbi Family Department of Ophthalmology, University of California, San Diego [5]
P-14	Tissue Engineering	Gelatin Scaffold with Lipid-PLGA Microparticles for Sustained Curcumin Release and Corneal Tissue Engineering	張均愷 [1] 陳思靜 [1] 李佩蓁 [1] 沈柍君 [1] 陳宏吉 [2*] 薛詒仁 [2] 黃玠誠 [1*]	國立清華大學生物醫學工程研究所 [1] 林口長庚醫院眼科部 [2]
P-15	Regenerative Medicine	ADSC-derived Exosomes Suppress Th17 Cell Differentiation in Inflammatory Arthritis	廖秀蓉 [1] 李華翊 [2] 江妮恩 [1] 沈宜珊 [3] 張至宏 [1,4]	亞東紀念醫院骨科部 [1] 臺灣大學醫學院附設醫院內科部 [2] 國立臺灣大學醫學工程學系 [3] 元智大學生物科技與工程研究研究所 [4]

No.	Classification	Topic	Authors	Institute
P-16	Regenerative Medicine	Infrapatellar Fat Pad MSCs Suppress Inflammation via Enhancing M2 Macrophage Differentiation in Knee Osteoarthritis	廖秀蓉[1] 江妮恩[1] 沈宜珊[3] 張至宏[1,4]	亞東紀念醫院骨科部[1] 臺灣大學醫學院附設醫院內科部[2] 國立台灣大學醫學工程學系[3] 元智大學生物科技與工程研究研究所[4]
P-17	Regenerative Medicine	Treatment with Non-selective Transient Receptor Potential Canonical Channels Inhibitor, Derinat Promotes Hair Regeneration in Female Pattern Hair Loss Patients	吳青穎[1,2] 陳偉喬[1] 許文俐[1,2,3]	高雄市立大同醫院皮膚科[1] 高雄醫學大學醫學系皮膚科[2] 高雄醫學大學再生醫學與細胞治療研究中心[3]
P-18	Regenerative Medicine	Adipose-derived Stem Cells Seeded Supercritical Carbon Dioxide Decellularized Bone Accelerated Bone Regeneration in Rat Bone Defect Model	劉耿帆[1] 陳榮富[1] 李昀庭[1] 林運男[1] 謝達仁[2] Periasamy Srinivasan[2] 林幸道[1,3] 郭耀仁[1,4,5,6]	高雄醫學大學附設醫院整形外科部[1] 亞果生醫股份有限公司研發部[2] 高雄市立小港醫院外科部[3] 高雄醫學大學再生醫學與細胞治療研究中心[4] 國立中山大學生物科學系[5] 新加坡杜克-新加坡國立大學醫學院 肌肉骨骼臨床研究計畫[6]
P-19	Regenerative Medicine	Supercritical Critical Carbon Dioxide Decellularized Porcine Bone Graft for Orbital Floor Reconstruction	黃昭心[1] 謝達仁[2] 吳益嘉[3,4,5] 顏克中[2] Periasamy Srinivasan[2] 李孝貞[3] 陳映哲[6] 李書欣[3,4,5,6]	高雄醫學大學學士後醫學系[1] 亞果生醫股份有限公司研發部[2] 高雄醫學大學附設醫院整形外科部[3] 高雄醫學大學再生醫學與細胞治療中心[4] 高雄醫學大學醫學院外科學系[5] 高雄市立小港醫院外科部[6]
P-20	Regenerative Medicine	Regenerative Role of Supercritical Carbon Dioxide Decellularized Porcine Cartilage Combine with Platelets Rich Plasma (PRP) Graft in Anterior Cruciate Ligament Transection Osteoarthritis Model	吳佳駿[1] 唐逸文[2] 許德榮[3] Periasamy Srinivasan[4] 葉怡君[4] 賴意苹[4] 謝達仁[4]	三軍總醫院骨科部[1] 高雄榮民總醫院骨科部[2] 國立成功大學醫學院工業衛生學科暨環境醫學研究所[3] 亞果生醫股份有限公司研發部[4]

灰底 未參加壁報競賽

Invited Lectures

Curriculum Vitae

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現職
2020/09 迄今　行政院衛生福利部常務次長

學歷
2008/5　部定助理教授
2006/1　台灣大學公共衛生學院健康政策與管理研究所博士
1991/6　私立高雄醫學大學醫學士

經歷
2016/08~2020/08 行政院衛生福利部醫事司司長
2015/02~2016/07 行政院衛生福利部主任秘書
2013/07~2015/01 行政院衛生福利部綜合規劃司司長
2012/08~2013/07 行政院衛生署企劃處處長
2008/06~2012/07 行政院衛生署醫事處處長
2013　美國聯邦文官學院(FEI)受訓結業
2010　新加坡李光耀學院受訓結業
2008　行政院國家政務研習班第一期結業
2007/07~2008/05 行政院衛生署桃園醫院醫務秘書
2005/03~2008/03 財團法人醫院評鑑暨醫療品質策進會副執行長
2002/01~2008/05 台灣大學附設醫院品質管理中心副執行長
1998/07~2007/06 台灣大學附設醫院急診醫學部主治醫師

專長領域
急診醫學、模擬分析、病人安全與醫療品質管理、醫事法律、公共衛生

09:30-10:00

I-01

從再生醫療發展法談台灣再生醫療的前瞻與挑戰

石崇良 常務次長
行政院衛生福利部

衛生福利部於 2018 年 9 月發布「特定醫療技術檢查檢驗醫療儀器施行或使用管理辦法」(以下簡稱特管辦法),開放風險較低之自體免疫細胞、自體脂肪幹細胞、自體骨髓間質幹細胞、自體纖維母細胞及自體軟骨細胞等六類細胞治療技術可於國內核准之醫療機構施行。2021 年 2 月 9 日再度修正發布特管辦法,將細胞保存庫納管,並強化病人治療成果登錄及其後續追蹤。

截至 2021 年 12 月 31 日止,共接獲 299 件細胞治療申請案,並已核准 114 件,遍布於全國 39 家醫院及 22 家細胞製備場所(分屬 21 家機構),另,衛福部也已初步統治療成果。

2022 年 1 月,衛福部為配合「生技醫藥產業發展條例」已將再生醫療列入我國重要生技產業之一,並蒐集各方意見經兩年研議催生「再生醫療發展法」、「再生醫療施行管理條例」、「再生醫療製劑管理條例」,統稱再生醫療三法,期使我國再生醫療之發展更上一層樓,讓細胞治療走向異體化、自動化、量產化,以嘉惠更多國人,並建構台灣成為亞洲再生醫療中心。

《再生醫療發展法》立法目的係做為政府推動再生醫療之政策依據,引導產業投入,並奠定設立國家細胞庫之法源基礎,以加速再生醫療之發展與實現;《再生醫療施行管理條例》則為特管辦法之進階版,分別規範醫療機構使用及細胞製備業者產製過程之安全與品質管理,並嚴格規範異體細胞來源與保存,賦予細胞保存庫之法律基礎,同時也立法明文保障病人使用再生醫療之相關權益;至於,再生醫療製品方面則以《再生醫療製劑管理條例》進行管理,除傳統之藥品查驗登記程序外,為解決病人臨床治療需要(unmet medical need),對於特殊再生醫療製劑可依其臨床試驗成果及真實世界數據,給予附款許可,並搭配相關登錄、追蹤機制,以確保產品的安全性、有效性及病人權益,使法規更趨完善。

本次演講,將就目前國內細胞治療技術之執行現況進行報告,並探討面臨之問題與挑戰,提出未來之策進作為與政策方向,包括再生醫療三法草案的立法重點,以建構永續發展之健康照護體系與生技產業環境。

Curriculum Vitae

陳克華 主任 Ke-Hua Chen
眼科部一般眼科科主任

學歷
台北醫學院醫學系畢業 (June, 1986)
美國哈佛大學醫學院 (Harvard Medical School, Massachusetts, USA)
史蓋本眼科中心(Schepens Eye Research Institute)研究員
(1997-2000)

經歷
長庚紀念醫院實習醫師 (1985-1986)
台北榮民總醫院眼科部住院醫師，總醫師 (1988-1995)
台北榮民總醫院眼科部角膜科主治醫師 (1995-)
國立陽明大學眼科副教授 (2000-2007)
國立陽明大學眼科助理教授 (2000-2007)
輔仁大學兼任助理教授(2003-)

現職
台北榮民總醫院眼科部一般眼科 科主任 (2018-)
國立陽明大學眼科副教授 (2007-)
國立陽明大學眼科助理教授 (2001-2007)
國家衛生研究院醫學工程組兼任研究員 (2001-)
國防醫學院眼科臨床講師 (1988-2007)
國防醫學院醫學系臨床副教授 (2007.8-)
台北醫學大學醫學人文中心委員(2001,8─2003,7)
輔仁大學兼任助理教授(2003-)
醫學會中眼會訊總編輯 (2004,7-2005,12)

專長
白內障手術、角膜移植手術、近視屈光手術、隱形眼鏡配戴及併發症之治療、
乾眼症之治療

專利
人類角膜內皮細胞的生長培養液,Growth Medium for Human Corneal Endothelial Cells. (Patent No: US 6,541,256 B1, Date of Patent: Apr. 1, 2003) for culturing adult human corneal endothelium and cells from neuro-ectoderm (1998~)
促進人類成年人角膜內皮細胞生長的新方法，Promotion of Proliferation of Adult Corneal Endothelial Cells (Patent No. US 6,548,059 B1, Date of Patent:Apr 15, 2003)
利用紅外線熱像儀判斷眼睛疾病之裝置(Method of Using Infrared Imager to Diagnose Eye Diseases and The Device Thereof): 張歐，江惠華，陳克華(中華民國專利證書號碼:1272931, Duration: 2007.2.11 to 2025.9.6, 美國及世界專利申請中)
人造玻璃體運用於視網膜剝離手術

10:30-11:00

I-02

材料在眼科的應用

陳克華 主任
台北榮民總醫院眼科部

眼睛有如一架構造精密的照相機，角膜和水晶體有如鏡頭，瞳孔和虹膜有如光圈，視網膜有如底片，視神經和大腦枕葉皮質有如底片沖洗和顯像儀器。

在胚胎及組織學上，眼睛可視為大腦（中樞神經）的向外向前的延伸凸出物，因此在材料的眼睛運用上，首先必需考慮的是第一，它的神經特質（譬如神經細胞的高度分化及不可再生性）以及第二，光學特性（如屈光係數，防紫外線或紅外線）。和大腦一樣，眼球內細胞和血管之間存在特殊的屏障，可以隔離血流當中的白血球，使得免疫發炎反應不易發生，是身體諸多「血疫豁免」（immune privilege)的區域之一。這使得許多材料在眼球內的使用得到更多發揮，如取代白內障的人工水晶體（intraocular lens, IOL) 及玻璃體切除後灌入的矽油（silicone oil)等。第三，由於眼球的角膜上皮（epithelium),間質(stromatolites)及內皮(endothelium)皆在體表，且透明肉眼可見，猶如一扇窗戶，使其下的水晶體，玻璃體及視網膜的細胞治療較人體其他部位相對容易，為再生醫學的細胞治療提供了簡易可行的目標。

基於以上三點，在疾病（disease)與老化退化（degeneration)兩者界限日趨模糊的今天，由於人類壽命的延長及 3C 產品過度使用，造成視力問題成為這時代人的共業，突顯幹細胞移植以及細胞治療等再生醫學的治療手段，在眼科學上的運用尤為重要。

Curriculum Vitae

Dr. Guoping Chen
Group Leader
Research Center for Functional Materials
National Institute for Materials Science, Japan
Professor
Faculty of Pure and Applied Sciences
University of Tsukuba, Japan

Prof. Guoping Chen received his Ph.D. from Kyoto University in 1997 majoring in Biomaterials and did postdoctoral research until 2000. He became Researcher in 2000 and Senior Researcher in 2003 at Tissue Engineering Research Center, National Institute for Advanced Industrial Science and Technology, Japan. He moved to Biomaterials Center, National Institute for Materials Science (NIMS) as Senior Researcher in 2004 and was promoted to Group Leader in January, 2007. He was Principal Investigator and Unit Director of Tissue Regeneration Materials Unit from April, 2011 to March, 2015; Principal Investigator, Field Coordinator and Unit Director of International Center for Materials Nanoarchitectonics, NIMS from April, 2015 to March, 2017. He is also Professor of Department of Materials Science and Engineering, Graduate School of Pure and Applied Science, University of Tsukuba, Japan. His research interests include tissue engineering and regenerative medicine, polymeric porous scaffolds, photothermal scaffolds, nanobiomaterials, biomimetic biomaterials, nano/micro-patterning and surface modification. He has authored more than 300 publications and holds 18 issued patents. He has given more than 140 plenary and invited lectures at conferences. He is Associate Editor of Journal of Materials Chemistry B; Editorial Board of Bioactive Materials, Journal of Bioactive and Compatible Polymers, Journal of Tissue Engineering and Regenerative Medicine, Regenerative Biomaterials and Biomedical Materials**;** Advisory Board of Biomaterials Science. He has been selected Fellow of the Royal Society of Chemistry in 2015, Fellow of American Institute for Medical and Biological Engineering in 2017 and Fellow of International Union of Societies for Biomaterials Science and Engineering in 2020.

Some representative papers:

1). Biomaterials, 275, 120923, 2021. 2). Biomaterials, 271, 120751, 2021. 3). Acta Biomaterialia, 125, 100-111, 2021. 4). Biofabrication, 12, 025027, 2020. 5). Advanced Healthcare Materials, e200061, 2020. 6). Acta Biomaterialia. 114, 158-169, 2020. 7). Biomaterials, 197, 317-326, 2019. 8). ACS Appl Mater Interfaces, 11, 1932-1941, 2019. 9). Acta Biomaterialia, 67, 341-353, 2018. 10). ACS Appl Mater Interfaces, 9, 35683-35692, 2017. 11) Advanced Healthcare Materials, 2017, 1700317 (1-12), 2017. 12). Biomaterials, 133, 253-262, 2017. 13). Acta Biomaterialia, 35, 185-193 (2016). 14). Advanced Functional Materials, 10.1002/adfm.201601585 (2016). 15). Biomaterials, 73, 23-31 (2015). 16). Biomaterials, 52, 199-207 (2015). 17). Biomaterials, 54, 226-236 (2015). 18). Acta Biomaterialia, 10, 2005-2013 (2014). 19). Biomaterials, 34, 2472-2479 (2013). 20). Biomaterials, 33, 6140-46 (2012). 21). Biomaterials, 33, 2025-31 (2012). 22). Advanced Materials, 24, 4311-6 (2012). 23). Biomaterials, 32, 9658-66 (2011). 24). Biomaterials, 32, 2489-99 (2011). 25). Advanced Materials, 22, 3042-47 (2010). 26). Biomaterials, 31, 5825-35 (2010). 27). Tissue Engineering, 16, 329-38 (2010). 28). Biomaterials, 31, 2141-52 (2010). 29). Journal of Biological Chemistry, 284, 31164-73 (2009). 30). Biomaterials, 29, 3438-43 (2008). 31). Biomaterials, 29, 23-32 (2008). 32). Advanced Materials, 19, 3633-36 (2007). 33). Biomaterials, 26, 2559-66 (2005). 34). Tissue Engineering, 10(3/4), 323-330 (2004) 35). Biomaterials, 22, 2563-67 (2001). 36). Advanced Materials, 12, 455-7 (2000).

10:30-11:00

I-03

Functional Porous Scaffolds and Biomimetic Matrices for Tissue Regeneration

Guoping Chen
Research Center for Functional Materials, National Institute for Materials Science,
1-1 Namiki, Tsukuba, Japan,

Porous scaffolds of biodegradable polymers and biomimetic matrices play an important role in controlling cell functions and guiding new tissue regeneration. Many biodegradable synthetic polymers such as PLLA and PLGA and naturally derived polymers such as collagen and gelatin have been used to prepare porous scaffolds. Cell-derived extracellular matrices have also been frequently used to prepare biomimetic scaffolds. We have developed a few types of porous scaffolds by using biodegradable polymers and extracellular matrices. The first type is porous scaffolds prepared with ice particulates. Funnel-like porous scaffolds were prepared by using ice particulates as a template and had a unique pore structure with large open pores on the top surface that communicated with interconnected inner bulk small pores. The second type is composite scaffolds of synthetic polymers and naturally-derived polymers. The composite scaffolds were prepared by forming collagen sponge or microsponges in the openings of porous skeletons of mechanically strong synthetic polymers. PLGA-collagen composite mesh, PLGA-collagen composite sponge and cylinder-type PLLA-collagen composite scaffolds were prepared by this hybridization method and used for 3D culture of chondrocytes for cartilage tissue engineering. The composite scaffolds combined the advantages of both types of polymers. The third type is biomimetic ECM scaffolds prepared from cultured cells. The ECM scaffold composition was dependent on the cell type and cell phenotype that were used to prepare the scaffolds. Furthermore, multi-functional composite scaffolds of biodegradable polymers and photothermal nanoparticles such as black phosphorus nanosheets and gold nanoparticles were prepared by incorporating photothermal nanoparticles in the porous polymer matrices. The composite scaffolds showed high photothermal conversion efficiency. The excellent photothermal performance of composite scaffolds was used for photothermal ablation of breast tumor cells. *In vitro* cell culture and *in vivo* animal experiment showed that the composite scaffolds could effectively kill breast tumor cells. The composite scaffolds could also promote adhesion, proliferation and adipogenic differentiation of hMSCs. The results demonstrated that the composite photothermal scaffolds had multi-functions for both photothermal ablation of breast tumor and regeneration of adipose tissue.

Acknowledgments: The research was funded by Japan Society for the Promotion of Science (JSPS) KAKENHI Grant Number 19H04475.

Curriculum Vitae

Wei-Li Chen, MD, PhD

National Taiwan University Hospital

Department of Ophthalmology

Professor

BIOGRAPHICAL SKETCH

I am a MD, PhD, and a professor at the department of Ophthalmology, National Taiwan University Hospital. My research majors in the clinical work and basic research in cornea/cataract/ refractive surgery. I major in cataract surgeries, various corneal transplantation techniques, refractive surgeries and handle difficult corneal disease. I have special interests in ocular surface disorders, stem cell therapy, corneal NV/nerve, corneal imaging and various corneal surgeries. Currently, I am the leader of the "Advanced Ocular Surface and Corneal Nerve Research Center" at my hospital. Recently, I am developing submicron resolutional OCT for cornea and regenerative medicine, novel medicine for corneal nerve regeneration, and novel ocular surface regeneration methods. AI with deep learning is also my current research interests.

11:30-12:00

I-04

From Good to Great---The Important Revolutions that Shaped the Regenerative Medicine for Ocular Surface Diseases

陳偉勵 教授
臺大醫院眼科部

ABSTRACT

Corneal epithelial stem cells are responsible for the maintenance of a healthy corneal surface. A deficiency or lack of corneal epithelium renewal due to limbal stem cell deficiency (LSCD) syndrome, may lead to severe visual impairments. In LSCD, the unstable ocular surface causes recurrent corneal epithelial breakdown or nonhealing ulceration and vascularization associated with chronic inflammation. Logically, the definitive treatment for medically irreversible total and/or severe LSCD is the transplantation of limbal tissue or limbal epithelial cells. There are various novel techniques developed to treat LSCD with variable successful rate. However, no best strategies so far were found to treat all kinds of LSCD.

In this talk, I will first briefly introduce the published technique to treat LSCD, focusing on cultivated limbal epithelial transplantation (CLET), cultivated oral mucosal epithelial transplantation (COMET), Simple Limbal Epithelial Transplantation (SLET), etc. Later, I will introduce my experience of treating patients with COMET and CELT under the GTP regulation in Taiwan. Some interesting experience of autologous or allogenic SLET will also been presented. Finally, I will introduce the current developing technique of simple oral mucosal epithelial transplantation (SOMET), which combine the benefits of SLET and COMET. With the aid of Rho kinase inhibitor (rho-associated protein kinase inhibitor or ROCK inhibitor), the new developing technique may make the regenerative medicine for ocular surface diseases from good to great.

Curriculum Vitae

Prof. Yu-Chen (Andy) Hu

Fellow, American Institute for Medical and Biological Engineering
Fellow, Biomaterials Science and Engineering (FBSE)
Tsing Hua Chair Professor
Department of Chemical Engineering, National Tsing Hua University Hsinchu, Taiwan

學歷

University of Maryland / USA / Chemical Engineering 1999
University of Maryland / USA / Chemical Engineering 1996
國立台灣大學 / 台灣 / 化工系 1992

專長

1. genetic engineering of viral vectors、2. gene therapy 、3. tissue engineering
4. vaccine development、5. synthetic biology、6. Biorefinery

現職及與專長相關之經歷

2021/04–present	Co-Chair, Division of Tissue Engineering and Biomaterials，亞洲生物技術聯盟(AFOB)
2019/08–2020/12	國際組織工程與再生醫學學會 亞太分會 獎章委員會委員
2019/08–present	清華講座教授
2018/11–2020/11	台灣化工學會 學術委員會 主任委員
2018/01-2020/12	科技部化工學門召集人
2018/03–2020/07	台灣再生醫學學會 理事
2018/03–2020/07	中華民國生醫材料及藥物制放學會 理事暨學術委員會 主任委員

榮譽獎助獎

2021	李昭仁教授基金會「研究學者獎」
2021	Review Editor, Frontiers in Bioengineering and Biotechnology (IF 4.21)
2020	科技部工程司產學合作計畫成果發表優良獎
2020	台灣化工學會 毛高文教授獎
2020	國際生醫材料科學與工程學會聯盟 會士
2019	第 16 屆國家新創獎 學研新創獎
2019	台灣化工學會 金開英獎
2018	科技部特約研究計畫

2018	科技部 未來科技突破獎
2017	李長榮福聚教育基金會學術研究傑出教授獎

學術著作目錄

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2. Nguyen, TKN, Chang, Y.-H., Truong, A.V., Hsu, M.-N., Pham, NN, Chang, C.-W., Wu, Y.-H., Chang, Y.-H., Li, H., **Hu, Y.-C.***. 2021 Aug. CRISPR activation of long non-coding RNA DANCR promotes bone regeneration. Biomaterials. 275: 120965 **(IF 12.479).**
3. Klionsky, D., Abdel-Aziz, A.K., ..**Hu, Y.-C.**, et al. 2021 Feb. Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition). Autophagy. 17:1-382. **(IF 16.016)**.
4. Chang, Y.-H., Lin, M.-W., Chien, M.-C., Ke, G.-M., Wu, I.-E., Lin, R.-L., Lin, C.-Y., **Hu, Y.-C***. 2021 Oct. Polyplex nanomicelle delivery of self-amplifying RNA vaccine. Invited paper. Journal of Controlled Release. 338: 694-704. **(IF 9.776)**.
5. Lin, M.-W., Shen, C.-C., Lin, Y.-J., Chou, M.-Y., Pham, N.-N., Chang, Y.-H., Chang, C.-W., Hwu, J.-R., Nguyen, M.T.T., **Hu, Y.-C.***. 2021 April. Enhancing the yield and activity of defucosylated antibody produced by CHO-K1 cells using Cas13d-mediated multiplex gene targeting. Journal of the Taiwan Institute of Chemical Engineers.121: 38-47. **(IF 5.876)**.
6. Hwu, J.-R., Panja, A., Gupta, N.K., Huang, W.-C., **Hu, Y.-C.**, Lin, C.-C., Hwang, K.-C., Chan, W.-J., Tsay, S.-C. 2021 April. Asymmetric synthesis of 3-pyrrolines through an aryne-induced domino process. Asian Journal of Organic Chemistry. 10: 803-815 **(IF 3.319)**.
7. Hwu, J.-R., Panja, A., Gupta, N.K., **Hu, Y.-C**., Tan, K-T., Lin, C.-C., Hwang, K.-C., Hsu, M.-H., Huang, W.-C., Tsay, S.-C. 2021 Jan. Domino Processes of Arynes Reacting with Three Classes of Nucleophiles for Organic Syntheses. European Journal of Organic Chemistry 4: 683-693. **(IF 3.021)**.
8. Hsu, M.-N., Yu, F.-J., Chang, Y.-H., Huang, K-L., Pham, N. N., Troung, A.V., Lin, M.-W., Nguyen, N.T.K., Hwang, S.-M., **Hu, Y.-C.*** 2020 Sep. CRISPR interference-mediated Noggin knockdown promotes BMP2-induced osteogenesis and calvarial bone healing. Biomaterials. 252: 120094. **(IF 12.479).**
9. Hsu, M.-N, Huang, K-L., Yu, F.-J., Lai, P.-L., Troung, A.V., Lin, M.-W., Nguyen, N.T.K., Shen, C.-C., Hwang, S.-M., Chang, Y.-H., **Hu, Y.-C.*** 2020 Feb. Co-Activation of endogenous Wnt10b and Foxc2 by CRISPR activation enhances BMSCs osteogenesis and promotes calvarial bone regeneration. Molecular Therapy 28: 441-451 **(IF 11.454)**.
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12. Srinivaas, M., Wu, C.-Y., Duh, J.-G., **Hu, Y.-C.**, Wu, J.-M. 2020 Jan. Multi-walled carbon

nanotubes decorated tungsten ditelluride nanostars as anode material for lithium-ion batteries. Nanotechnology 31: 035406 **(IF 3.874).**

13. Hwu, J.-R., Panja, A. Jayakumar, S., Tsay, S-C., Tan, K.-T., Huang, W.-C., **Hu, Y.-C.**, Leyssen, P., Neyts, J. 2020 Aug. Enterovirus inhibition by hinged aromatic compounds with polynuclei. Molecules. 25: 3821. **(IF 4.411)**
14. Oh, M-K, Sakai, Y., **Hu, Y.-C.** 2020 June. Asian Congress on Biotechnology 2019. Biotechnology Journal. 2020, 15: 2000214. **(IF 4.677)**
15. Hwu, J.-R., Roy, A, Panja, A., Huang, W.-C., Hu, Y.-C., Tan, K.-T., Lin, C.-C., Hwang, K.-C., Hsu, M.-H., Tsay, S.-C. 2020 Aug. Domino reaction for the synthesis of polysubstituted pyrroles and Lamellarin R. Journal of Organic Chemistry. 85: 9835-9843. **(IF 4.354)**.
16. Hsu, M-N., Chang, Y.-H., Truong, V. A., Nguyen, N.T.K., **Hu, Y.-C.*** 2019 Dec. CRISPR technology for stem cell engineering and regenerative medicine. Biotechnology Advances 37:107447. **(IF 14.227)**.
17. Hsu, M.-N., **Hu, Y.-C.***. Local magnetic activation of CRISPR. 2019 Feb. Nature Biomedical Engineering. 3: 83-84. **(IF 25.671).**
18. Truong, V. A., Hsu, M-N., Nguyen, N.T.K., Lin, M-W., Shen, C.-C., Lin, C.-Y., **Hu, Y.-C.*** 2019. July. CRISPRai for simultaneous gene activation and inhibition to promote stem cell chondrogenesis and calvarial bone regeneration. Nucleic Acids Research. 47: e74 **(IF 16.971).**
19. Shen, C.-C., Hsu, M.-N., Chang, C.-W., Lin, M.-W., **Hu, Y.-C***. 2019 Feb. Synthetic switch to minimize CRISPR off-target effects by self-restricting Cas9 transcription and translation. Nucleic Acids Research. 47: e13 **(IF 16.971).**
20. Hsu, M-N., Liao, H.-T., Truong, V. A., Huang, K.-L., Yu, F.-J., Chen, H.-H., Nguyen, N.T.K., Makarevich P., Parfyonova, Y., **Hu, Y.-C.*** 2019 Aug. CRISPR-based activation of endogenous neurotrophic genes in adipose stem cell sheets to stimulate peripheral nerve regeneration. Theranostics 9: 6099-6111 **(IF 11.556)**.
21. Wang, S.-Y., Chen, C.-L., **Hu, Y.-C.**, Chi, Y., Huang, Y.-H., Su, C.-W., Jeng, W.-J., Liang, Y.-J., Wu, J.-C*. 2019 Oct. High expression of microRNA-196a is associated with progression of hepatocellular carcinoma in younger patients. Cancers. 11: 1549 **(IF 6.639).**
22. Sung, L.-Y., Wu, M.-Y., Lin, M.-W., Hsu, M.-N., Troung, V. A., Shen, C.-C., Tu, Y., Hwang, K.-Y., Tu, A. P., Chang, Y.-H., **Hu, Y.-C.***. 2019 May. Combining orthogonal CRISPR and CRISPRi systems for genome engineering and metabolic pathway modulation in *E. coli*. Biotechnology and Bioengineering. 116: 1066-1079 **(IF 4.53).**
23. Hwu, J.-R., Huang, W.-C., Lin, S.-Y., Tan, K.-T., **Hu, Y.C**., Shieh, F.-K., Bachurin, S.O., Ustyugov A, Tsay, S.-C. 2019 March. Chikungunya virus inhibition by synthetic coumarin-guanosine conjugates. Eur J Med Chem 166: 136-143. **(IF 6.514).**
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13:30-14:00

I-05

Polyplex Nanomicelle Delivery of Self-Amplifying RNA Vaccine

Yi-Hao Chang[1], Mei-Wei Lin[1,2], Ming-Chen Chien[1], Guan-Ming Ke[3], I-En Wu[1], Ren-Li Lin[1], Chin-Yu Lin[4,*] and **Yu-Chen Hu**[1,5,*]
國立清華大學化學工程學系

Abstract

Self-amplifying RNA (SaRNA) is a burgeoning platform that exploits the replication machinery of alphaviruses such as Venezuelan equine encephalitis (VEE) virus or Sindbis virus (SIN). SaRNA has been used for development of human vaccines, but has not been evaluated for porcine vaccine development. Porcine reproductive and respiratory syndrome virus (PRRSV) causes tremendous economic losses to the worldwide pork industry, but current vaccines trigger delayed neutralizing antibody response and confer only partial protection. Here we first compared two SaRNA systems based on VEE and SIN, and demonstrated that in vitro transcribed VEE-based SaRNA conferred prolonged reporter gene expression and RNA amplification in pig cells with low cytotoxicity, but SIN-based SaRNA imparted evident cytotoxicity and limited gene expression in pig cells. Transfection of VEE-based SaRNA that encodes the major PRRSV antigen dNGP5 (SaRNA-dNGP5) conferred persistent expression for at least 28 days in pig cells. We next complexed SaRNA-dNGP5 with the polyaspartamide block copolymer PEG-PAsp(TEP) to form polyplex nanomicelle with high packaging efficiency and narrow size distribution. The polyplex nanomicelle enabled sustained dNGP5 expression and secretion in vitro. Compared with the commercial PRRS vaccine, nanomicelle delivery of SaRNA-dNGP5 into animal models accelerated the induction of potent neutralizing antibodies with minimal side effects, and elicited stronger IL-4 and IFN-γ responses against homologous and heterologous PRRSV. These properties tackle the problems of current vaccines and implicate the potential of SaRNA-dNGP5 nanomicelle as an effective PRRS vaccine.

Keywords: Self-amplifying RNA, polyplex nanomicelle, vaccine, PRRSV, neutralizing antibody

Curriculum Vitae

Masaya YAMAMOTO

Professor
Department of Materials Processing, Graduate School of Engineering, Tohoku University
Division of Biomedical Engineering for Diagnosis and Treatment, Graduate School of Biomedical Engineering, Tohoku University

Education and Training

1994B.Eng.	Dept. Polym. Chem.	Kyoto University
1999PhD	Dept. Polym. Chem.	Kyoto University
	(Mentor: Professor Yoshito Ikada)	
1999Post doc	Institute for Polymer Research, Dresden, Germany	
2000Post doc	Institute for Frontier Medical Sciences, Kyoto University	

Professional Experiences

2000Assistant Professor	Inst. for Frontier Med. Sci., Kyoto University
2002PRESTO Researcher	Japan Science and Technology Agency
2007Visiting Fellow	Weill Medical College of Cornell University
2011Associate Professor	Inst. for Frontier Med. Sci., Kyoto University
2017Professor	Graduate School of Engineering, Tohoku University
2018Adjunct Professor	The University of Tokyo
2020Adjunct Professor	Inst. for Mater. Chem. and Eng., Kyushu University
2021Project Officer	Japan Agency for Medical Research and Development
2021CREST PI	Japan Science and Technology Agency

Selected Awards and Distinctions

2010Young Investigator Award: Japanese Society for Regenerative Medicine
2010Young Investigator Award: Japanese Society for Biomaterials
2014The 2nd Nakatsuji Award, Kyoto SMI, Japan

Major Professional Service Activities

2012Editorial Board	Tissue Engineering
2013Academic Editor	PLoS ONE
2015Auditor	TERMIS-AP
2020Board Member	Japanese Society for Biomaterials

Achievements

Scopus h-index 38, 122 Research Articles and Reviews on Biomaterials and Tissue Engineering

14:00-14:30

I-06

Stimuli-Responsive Biomaterials for Engineering Spheroids

Masaya Yamamoto
Department of Materials Processing, Graduate School of Engineering, Tohoku University, Sendai 980-8579, Japan
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Stimuli-responsive polymeric biomaterials have been widely investigated not only as a drug carrier to enhance the efficacy of drugs in the body, but also as a material to be utilized for stem cell culture as a tunable substrate. The physicochemical properties of the stimuli-responsive polymeric biomaterials could be altered in response to an external stimulus without cytotoxicity, such as temperature, light, magnetic field, chemical compounds.

In this presentation, I will touch on two stimuli-responsive polymeric biomaterials for engineering spheroids as a carrier for cancer drug delivery and a scaffold for tissue engineering, respectively. One is a thermo-responsive nanoparticle of sulfobetain polymers as an intracellular carrier being capable of cell membrane translocation for anti-tumor drugs. Recently we found that the nanoparticle could also function as a tissue penetrating carrier for anti-tumor drugs, which can suppress the growth of tumor spheroids. The other is a sugar-responsive hydrogel scaffold that has been developed as a sacrificial template to maintain spheroids in culture. Growth factors could be incorporated in the scaffold and released in response to sugar-stimulation.

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2. K. Inoo, M. Yamamoto, Y. Tabata, J. Tissue Eng. Regen. Med, 2020, 14, 1050-1062.

Curriculum Vitae

一、基本資料（PERSONAL INFORMATION）

英文姓名： B. Linju Yen
中文姓名： 顏伶汝
國籍： 中華民國 性別： 女
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苗栗縣竹南鎮 35053 科研路 35 號

二、主要學歷（EDUCATION）

1991-96 加州大學舊金山分校 (UCSF) 醫學院，M.D.
1986-91 加州大學洛杉磯分校 (UCLA) 藝術學院，B.A.，Summa cum Laude，雙 主修音樂歷史及鋼琴演奏 (Music History & Performance)

三、專長學科（SPECIALIZED FIELD）：婦產科及幹細胞研究

四、現職及與專長相關之經歷（按時間先後順序由最近經歷開始填起）

2017/9-訖今 國家衛生研究院 (國衛院)，細胞及系統醫學研究所 (細研所)，副所長
2014-訖今 國衛院，細研所，再生醫學研究團隊(前 幹細胞研究中心)，研究員級主治醫師
2009-14 國衛院，細研所，再生醫學研究團隊，副研究員級主治醫師
2005-09 國衛院，細研所，再生醫學研究團隊，助研究員級主治醫師
2003 UCSF 胚胎幹細胞研究中心，訪問學者
2002-05 國家衛生研究院幹細胞研究中心，博士後研究員
1998-2001 台大醫院婦產部 (建教訓練名額) 住院醫師
1996-97 UCLA 婦產科第一年住院醫師

五、榮譽獎助獎（HONORS AND AWARDS）（依年份及事蹟順序填寫）

2015 國衛院 傑出學術成就獎
2013 國家生技醫療產業策進會 (生策會) 第十屆國家新創獎
2010 中央研究院 年輕學者研究著作獎
2010 國衛院 年輕學者學術成就獎
2009 科技部 吳大猷先生紀念獎
1997 UCLA 婦產科最佳住院醫師獎
1991 UCLA 傑出大學畢業生獎 & UCLA 校長服務獎

六、會員身分（MEMBERSHIPS）

台灣幹細胞學會(TSSCR；理事)
中華民國細胞及分子生物學學會(CSCMB；理事)
國際幹細胞學會(ISSCR)
中華民國免疫學會
台灣婦產科醫學會(TAOG)

七、學術著作目錄（**PUBLICATION LIST**）(since 2018; *, corresponding author)

1. Peng KY, Jiang SS, Lee YW, Tsai FY, Chang CC, Chen LT, Yen Yen BL*. Stromal Galectin-1 promotes colorectal cancer cancer-initiating cell features & disease dissemination through SOX9 and β-Catenin: development of niche-based biomarkers. Front Oncol 2021;11:716055 (*, corresponding author)
2. Wang LT, Liu KJ, Sytwu HK, Yen ML*, Yen BL*. Advances in mesenchymal stem cell (MSC) therapy for immune & inflammatory diseases: use of cell-free products & induced pluripotent stem cell (iPSC)-derived MSCs. Stem Cells Transl Med 2021;10:1288-1303. **Invited manuscript
3. Wang LT, Chiu SK, Lee W, Siu KL, Liu KJ, Yen ML*, Yen BL*. Protocol for human placental MSC therapy in a murine model of intra-abdominal infection of hypervirulent Klebsiella. STAR Protoc 2021;2:100337 **Invited manuscript
4. Lee W, Wang LT, Yen ML, Hsu PJ, Liu KJ, Lin KI, Su YW, Sytwu HK, Yen BL*. Resident vs. non-resident MSC interactions with B lymphocytes result in disparate outcomes. Stem Cells Transl Med 2021;10:711-24.
5. Wang LT, LeeYW, BaiCH, Chiang HC, Wang HH, Yen BL, Yen ML*. A rapid and highly predictive in vitro screening platform for osteogenic natural compounds using human Runx2 transcriptional activity in MSCs. Front Cell Dev Biol 2021;8:607383.
6. Wang LT, Wang HH, Chiang HC, Huang LY, Chiu SK, Siu LK, Liu KJ, Yen ML*, Yen BL*. Human placental MSC-secreted IL1b enhances neutrophil bactericidal functions during hypervirulent Klebsiella Infection. Cell Reports 2020;32:108188. **Selected by Bioworld (news outlet of Clarivate Analytics, parent company of JCR & Web of Science group) for highlighting
7. Huang CY, Li LH, Hsu WT, Cheng YC, Nicholson MW, Liu CL, Ting CY, Ko HW, Syu SH, Wen CH, Yan Z, Huang HP, Su HL, Chiang PM, Shen CN, Chen HF, Yen BL, Lu HE, Hwang SM, Chiou SH, Ho HN, Wu JY, Kamp TJ, Wu JC, Hsieh PCH, Copy number variant hotspots in Han Taiwanese population iPSC lines - lessons from establishing the Taiwan human disease iPSC Consortium Bank. J Biomed Sci 2020;27(1):92-106.
8. Yen BL*, Hwa HL, Hsu PJ, Chen PM, Wang LT, Jiang SS, Liu KJ, Sytwu HK, Yen ML*. HLA-G expression in human MSCs is related to unique methylation pattern in the proximal promoter as well as gene body DNA. Int J Mol Sci 2020;21:5074.
9. Yen BL*, Yen ML*, Wang LT, Liu KJ, Sytwu HK. Current status of MSC therapy for immune/inflammatory lung disorders:Gleaning insights for possible use in COVID19. Stem Cells Transl Med 2020;9:1163-73. **Invited manuscript
10. Wang LT, Jiang SS, Ting CH, Hsu PJ, Chang CC, Sytwu HK, Liu KJ, Yen BL*. Differentiation of MSCs from human iPSCs results in downregulation of c-Myc & DNA replication pathways with immunomodulation toward CD4 & CD8 cells. Stem Cells 2018;36:903-14.
11. Wu KJ, Yu SJ, Chiang CW, Lee YW, Yen BL, Hsu CS, Kuo LW, Wang Y. Wharton's Jelly MSC therapy for ischemic brain injury. Brain Circ 2018;4:124-7.
12. Wu KJ, Yu SJ, Chiang CW, Lee YW, Yen BL, Tseng PC, Hsu CS, Kuo LW, Wang Y. Neuroprotective action of human Wharton's Jelly-derived MSC transplants in a rodent model of stroke. Cell Transplant 2018;27:1603-12.

14:30-15:00

I-07

Allogeneic Mesenchymal Stem Cell (MSC) Therapy for Immune & Inflammatory Diseases: Advances & Challenges

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Deputy Director,
Investigator & Attending Physician,
Regenerative Medicine Research Group,
Institute of Cellular & System Medicine,
National Health Research Institutes (NHRI),
Zhunan, Taiwan

Abstract

Mesenchymal stem cell therapy (MSCT) for immune and inflammatory diseases continues to be popular based on progressive accumulation of preclinical mechanistic evidence. This has led to further expansion in clinical indications from graft rejection, autoimmune diseases, and osteoarthritis, to inflammatory liver and pulmonary diseases including COVID-19 [invited review: Yen et al, *Stem Cells Transl Med* 2020]. A clear trend is the shift from using autologous to allogeneic MSCs, which can be immediately available as off-the-shelf products, as well as a shift away from using bone marrow MSCs, the site of first isolation, to other tissue/organ sources of MSCs. In addition, new products such as cell-free extracellular vesicles/exosomes and human pluripotent stem cell (hPSC)-derived MSCs—including MSCs derived from induced pluripotent stem cells (iPSCs)—are exciting developments to further prevalent use [invited review: Wang et al, *Stem Cells Transl Med* 2021]. Increasing numbers of trials have now published results in which safety profile of MSCT has been excellent. While reports of therapeutic endpoints are still emerging, efficacy can be clearly seen for specific indications—including graft-vs-host-disease, strongly Th17-mediated autoimmune diseases, and osteoarthritis—which are more robustly supported by mechanistic preclinical evidence. Data is also emerging on functional differences found with different sources of MSCs [invited review: Yen et al, *FEBS J* in revision]. With its excellent safety profile, multilineage differentiation capacity, and strong immunomodulatory properties allowing for unmatched/3rd party use, MSCT is one of the most versatile cell types for therapeutic use.

Curriculum Vitae

一、基本資料（PERSONAL INFORMATION）

英文姓名： Min-Huey Chen
中文姓名： 陳 敏 慧
國籍： 台灣, 中華民國 性別： 女
服務機關：臺灣大學臨床牙醫學研究所

二、主要學歷（EDUCATION）

紐西蘭奧克蘭大學生物醫學材料工程學博士
(1996-2000)
臺大 EMBA 管理碩士(2011-2013)
臺大醫學院牙醫學士 (1976-1982)

三、專長學科（SPECIALIZED FIELD）

幹細胞組織再生與生醫材料研發
Stem cell tissue regeneration and development of biomaterials
牙體復形美容牙科學
Esthetic Restoration

四、現職及與專長相關之經歷（按時間先後順序由最近經歷開始填起）

起訖 職位 服務機構
臺灣大學醫學院副院長 (2019 till now)
臺灣大學醫學院學務分處主任 (2019 till now
臺灣大學臨床牙醫學研究所所長 (2015-2021)
臺灣大學臨床牙醫學研究所教授 (2009 till now)
臺大醫院牙體復形美容牙科住任 (2002-2021)
臺大醫院牙體復形美容牙科主治醫師(2000 till now)
台灣再生醫學會理事 (2015-till now)
中華民國牙體復形學會理事長（2013-2015, 2017-2019）

五、榮譽獎助獎（HONORS AND AWARDS）（依年份及事蹟順序填寫）

2000 Award from Bone and Mineral Research Society in Japan
2002 Research Award from National Science Council
2003 Best Service Doctor in the Campus Health Center of National Taiwan University
2005 Professor Tsungmin Tu Award
2007 Best Teaching Award in National Taiwan University Hospital
2008 Ellected as fellow of International College of Dentists (榮任國際牙醫學院院士)
2008 Best Teaching Award in National Taiwan University
2009 Special Contribution Copper Award in National Dental Association
2011 Excellent Research Group Award in National Taiwan University Hospital
2011 Special Contribution Silver Award in National Dental Association
2014 Excellent Tutor Award in National Taiwan University.
2021 Special Contribution Gold Award in National Dental Association

六、會員身分（MEMBERSHIPS）

國際牙醫學會會員
台灣再生醫學會會員
亞太保存學會會員
中華民國牙醫學會會員
中華民國牙體復形學會會員

七、學術著作目錄（PUBLICATION LIST）

1. Tsai, H.C., Chen. C.H., Mochly-Rosen D., Li, Y.C. E. and Chen M.H. The role of alcohol, LPS toxicity and ALDH2 in dental bony defects. Biomolecules 2021 accepted.
2. Chang P.C., Luo H.T., Lin Z.J., Tai W. C., Chang C.H., Chang Y. C., Cochran D.L, Chen M.H. Preclinical Regeneration of Critical-Sized Mandibular Defect Using a 3D-Printed Hydroxyapatite-Based Scaffold: An Exploratory Study J Periodontology 2021 Mar;92(3):428-435
3. Chang P.C., Luo H.T., Lin Z.J., Tai W. C., Chang C.H., Chang Y. C., Cochran D.L, Chen M.H Preclinical Evaluation of A 3D-Printed Hydroxyapatite/Poly(lactic-co-glycolic acid) Scaffold for Supracrestal Ridge Augmentation. JFMA 2021 Apr;120(4):1100-1107.
4. Hsiao D, Hsu SH, Chen RS, Chen MH. Characterization of designed directional polylactic acid 3D scaffolds for neural differentiation of human dental pulp stem cells. JFMA 2020 (1 Pt 2);119:268-275.
5. Lai T.T., Chiou J.Y., Lai T C., Chen T., Wang H.Y. and Chen M.H. Perceived pain for orthodontic patients with conventional brackets or self-ligating brackets over a 1-month period: A single-center, randomized controlled clinical trial. JFMA 2020 (1Pt2);119:282-289.
6. Wang J.L., Lin Y.C., Young T.H., Chen M.H. Far-infrared ray radiation promotes neurite outgrowth of neuron-like PC12 cells through AKT1 signaling JFMA 2019; 118(2):600-610
7. Chang K., Chang F.H., Chen M.H Developing a Novel Cholesterol-based Nanocarrier with High Transfection Efficiency and Serum Compatibility for Gene Therapy. JFMA 2019 118(4):766-775
8. Chang K., Chen R. S., Chang F.H., Chen M.H Promoting Dentinogenesis of Dental Pulp Stem Cells through Inhibiting microRNA-218 by Using Magnetic Nanocarrier Delivery. JFMA 2019; 118(6):1005-1013.
9. Chen M.H. Restorative and Esthetic Dentistry—A Special Issue of the Dentistry Journal. Dent. J. 2018, 6(1): 5. doi:10.3390/dj6010005
10. Chen J.T., Wang C.Y., Chen M.H. Curcumin inhibits TGF- 1 induced connective tissue growth factor expression through Smad2 mechanism in human gingival fibroblasts JFMA2018;117:1115-1123

15:30-16:00

I-08

Regenerative Medicine in Dentistry

Min-Huey Chen
1. Postgraduate Institute of Clinical Dentistry
School of Dentistry, National Taiwan University
2. Department of Dentistry, National Taiwan University Hospital

Due to the development of regenerative medicine, the application of stem cells, growth factors and biomaterials for tissue regeneration had been widely investigated. In our previous study, tooth regeneration with complete root formation including dental pulp, dentin, cementum and periodontal ligaments in mini pigs had been demonstrated by isolating and loading the tooth germ cells in gelatin-ch ondroitin-hyaluronan-tri-copolymer scaffolds. In addition, the interactions of tooth germ cells with biomaterials had also been investigated. We found that tooth germ cells were suspended and formed cell spheroids on polyvinyl alcohol (PVA). Our results indicated that spontaneous aggregation of three dimensional tooth germ cell spheroids on polyvinyl alcohol (PVA) were with higher differentiation potential. By comparing with/without dental pulp stem cells in 3D printed polylactic acid scaffolds had been tried for tooth regeneration in adult dogs. It was found that the mineralization effects with dental pulp stem cells were higher than the group without dental pulp stem cells.

Chjartacterization of designed directional polylactic acid 3D scaffolds for neural differentiation of human dental pulp stem cells had also been investigated. It was concluded that 3DP-PLASs with 150 μm gaps can induce cellular orientations more easily than those with 200 μm gaps. In addition, 3DP-PLASs seem to improve cell adhesion after being coated with poly-l-lysine or soaked with alcohol.

For salivary gland regeneration, by transplantation of bone marrow stem cells or acinar like cells into the irradiated mice with damaged salivary glands, the body weight, glands weight and saliva production of the mice were shown to be increased and closed to normal control. It was found that cell therapy with BMMSCs for salivary gland regeneration is possible.

Key words: dental pulp stem cells, tooth regeneration, neural regeneration, salivary glands regeneration

Curriculum Vitae

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Professor
Department of Biomedical Science
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Director, Joint Institute for Regenerative Medicine(www.jirm.org)
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Education

- B.S Keimyung University, Korea
- M.S Cornell University, USA
- Ph.D. University of Massachusetts Lowell, USA
- Post-doc Massachusetts Institute of Technology (MIT)
  Research area: Drug Delivery System
- Post-doc Harvard Medical School/Children's Hospital
  Research area: Formulation and Evaluation of drug delivery system

Professional Appointments

- 2001-2002 Visiting Scientist,
  Harvard-MIT Division of Health Sciences and Technology
- 2004-2006 Assistant Professor
  Wake Forest Institute for Regenerative Medicine (WFIRM), USA
- 2004-2006 Assistant Professor
  School of Biomedical Engineering and Sciences
  Virginia Tech-Wake Forest University, USA
- 2007~ Professor
  Kyungpook National University School of Medicine, Korea
  Adjunct Professor
  Wake Forest Institute for Regenerative Medicine (WFIRM), USA
- 2014 President
  Korea Tissue Engineering and Regenerative Medicine Society (KTERM
- 2014 Program Chair
  2014 Tissue Engineering and Regenerative Medicine International Society Asia-Pacific Chapter (TERMIS-AP) Conference
- 2016~ Director, Joint Institute for Regenerative Medicine (www.jirm.org)
- 2019 Visiting Scholar, Cornell University, USA

Area of research interests

- Formulation and engineering of biomaterials for clinical applications
- Controlled drug delivery systems, Regenerative Cellular Therapeutic
- Wound healing and Tissue engineering (Muscle, Skin, Bone)

16:00-16:30

I-09

3D Patterning of Growth Factor Incorporated Hydrogel Complex to Regulate Tissue Regeneration

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The effective treatment of both acute and chronic wounds remains a major clinical challenge. Thus, it is highly demanding to develop wound dressings that not only function as protective barriers but also facilitate rapid wound closure to promote wound healing, reduction of scar formation and acceleration of angiogenesis. Numerous innovative dressing materials such as alginate, collagen, and hydrogels that possess wound healing properties have been developed and used to prevent infection and promote skin regeneration. For acceleration of angiogenesis at wound sites for successful wound repair, the most potent pro-angiogenic agent, vascular endothelial growth factor (VEGF) is widely used for the therapeutic stimulation of blood vessel growth. As reported recently, a small peptide, VEGF-mimicking sequence, mimics the helical region of VEGF, simulating VEGF's biological activities. In addition, fast development of 3D structure printing is a promising new technology. The high precision in producing the desired size and porosity together with its relative ease of operation facilitates extensive application in tissue engineering and regenerative medicine owing to tremendous potential to print tissue constructs.

In this study, we formulated a novel hydrogel complex composed of GelMA, hyaluronic acid (HA), glycerol, and VEGF peptide and further fabricated the complex hydrogel to dressing patch using 3D printing technology, and investigated its potential as an effective wound dressing patch including its structural characteristics, morphological stability, water absorbency, porosity, mechanical properties, and biological properties. The wound healing capacity of the VEGF-hydrogel patch was evaluated in vitro and in vivo using a pig wound model. The 3D structure of the hydrogel patch had high porosity, interconnectivity and water absorption properties. VEGF peptide incorporated to hydrogel patch, which released for a prolonged period of weeks, promoted cell viability, proliferation, and tubular structure formation. The use of the 3D printed VEGF hydrogel accelerated wound repair and remodeling by promoting ECM synthesis and angiogenesis at the wound site. Therefore, these findings suggest that 3D patterned hydrogel patch containing the VEGF peptide is a promising wound dressing.

***Keywords*:** 3D printing, hydrogel, VEGF, wound dressing, skin regeneration

Curriculum Vitae

Tsung-Wei Huang, MD, PhD

Education:
M.D., College of Medicine, National Taiwan University
Ph.D., Institute of Biomedical Engineering, College of Medicine and College of Engineering, National Taiwan University

Professional Assignments: Attending doctor,
Department of Otolaryngology,
Far Eastern Memorial Hospital

Position: Professor
Department of Otolaryngology
Far Eastern Memorial Hospital
Department of Electrical Engineering
Yuan Ze University

Awards:
2010 Best paper awards, Taiwan Otolaryngological Society
2010 Outstanding Research of the Year, Gold Award, Far Eastern Memorial Hospital
2017 &2021 Best paper awards, Taiwan Society of Ultrasound Medicine
2021 Future Tech Awards, Ministry of Science and Technology

Selected Publications:

1. Yen CH, Young TH, Huang TW* (2021, Jun). Cell detachment ratio on pH-responsive chitosan: A useful biometric for prognostic judgment and drug efficacy assessment in oncology. Carbohydrate Polymers, 261:117911. (SCI, IF=9.381,2/57 CHEMISTRY ORGANIC).
2. Li ST, Young TH, Huang TW*. (2021, Apr). Regeneration of olfactory neuroepithelium in 3-ethylindole-induced anosmic rats treated with intranasal chitosan. Biomaterials, 271:120738. (SCI, IF=12.479,1/38 MATERIALS SCIENCE, BIOMATERIALS).
3. Huang CC, Cheng PW, Liao LJ, Huang TW* (2021, Feb). Reduction of postural nasal resistance following oropharyngeal surgery in patients with moderate-severe obstructive sleep apnea. Rhinology; 59(1):75-80. (SCI, IF=3.681, 4/42, OTORHINOLARYNGOLOGY).
4. Huang TW*, Li ST, Chen DY, Young TH (2019, Dec). Neuropeptide Y increases differentiation of human olfactory receptor neurons through the Y1 receptor. Neuropeptides, 78:101964. (SCI, IF=3.286, 88/145 ENDOCRINE&METABOLISM).
5. Huang TW*, Li ST, Young TH (2019, Dec). Chitosan-hyaluronan: Promotion of mucociliary differentiation of respiratory epithelial cells and development of olfactory receptor neurons. Artif Cells Nanomed Biotechnol, 47:564-570. (SCI, IF=5.678, 12/80 ENGINEERING, BIOMEDICAL). MOST 107-2314-B-418-009.
6. Yen CH, Young TH, Hsieh MC, Liao LJ, Huang TW* (2019, Nov). Increased Cell Detachment Ratio of Mesenchymal-Type Lung Cancer Cells on pH-Responsive Chitosan through the β3 Integrin. Marine Drugs, 23;17(12). (SCI, IF=5.118, 6/61 CHEMISTRY, MEDICINALEERING, BIOMEDICAL).

7. Huang TW*, Li ST, Wang YH, Young TH (2019, Oct). Regulation of chitosan-mediated differentiation of human olfactory receptor neurons by insulin-like growth factor binding protein-2. Acta Biomaterialia, 97:399-408. (SCI, IF=8.947, 5/80 ENGINEERING, BIOMEDICAL). MOST 108-2314-B-418-009-MY3.

16:30-17:00

I-10

Regenerative Medicine in Rhinology

黃琮瑋教授
亞東紀念醫院耳鼻喉科

The nasal epithelium of human comprises 90% respiratory epithelium and 10% olfactory epithelium. The respiratory epithelium, which is composed of the ciliated epithelial cells, the mucous blanket, and the mucus-producing glands, is an important defense component of the respiratory system. Clinically, patients suffering from extensive surgical defect of respiratory mucosa always have symptoms of mucus stagnation, persistent nasal crusting or an unpleasant odor. These problems are attributed to the absence of mucociliary clearance and would be fixed if the ciliated columnar epithelium could be regenerated. Regeneration of respiratory epithelium is an alternative strategy for these patients. Olfactory dysfunction significantly influences patients' life quality, inclusive of feeling of flavors, appetite and even ability to the around environmental hazards. The olfactory neuroepithelium, which comprises specialized olfactory glands and olfactory receptor neurons surrounded by their olfactory ensheathing cells, has the unique ability of continual neurogenesis in peripheral neuron system of adult mammals. Glycosaminoglycans are abundant in the native olfactory neuroepithelium of rats and given a role in cell differentiation and axon guidance. Chitosan has been demonstrated to promote differentiation of olfactory receptor neurons and the regulatory pathway is through increasing IGFBP2 to sequestrate the IGFs-type 1 receptor signaling. Chitosan also regenerates olfactory neuroepithelium in the olfactory dysfunctional rats induced with 3-MI. Chitosan not only promotes olfactory receptor neurons maturation, but also suppresses apoptosis of olfactory receptor neurons, which is a potential agent for treating olfactory dysfunction in the future.

Poster Paper

P-01

探討透明質酸搭載胜肽奈米顆粒應用於抗角膜血管新生之研究
Hyaluronic Acid Nanoparticles with Novel Peptide Loading for Corneal Neovascularization

吳昱儀　曾靖孋
臺北醫學大學生醫材料暨組織工程研究所

Introduction：Corneal is a transparent structure without blood vessel distribute that covered anterior surface of the eye. Corneal neovascularization (CNV) is one of the most common disease happened on the cornea surface causing by the proliferation of the blood vessels from the corneal edge. We had discovered a novel peptide (pep) that can distribute VEGF signaling to inhibit angiogenesis. Hyaluronic acid (HA) is a negatively charge material that normally presence in cornea and highly-biocompatibility. By self-assembling mechanism of HA to form positively charge nanoparticles (HA-pep NPs), we combined the advantage of its great capacity and retard the distribution of drug on the eye surface by surface charge attraction to investigate its efficiency.

Materials and Methods：HA-pep NPs had been characterized by DLS, TEM, NTA, FTIR, and DSC to make sure the size, intensity, zeta potential, functional group, and the strength of structure. The release ratio and encapsulation efficiency of peptide in nanoparticles had also been by drug release and protein assay. For the *in vitro* measurements, human umbilical vein endothelial cells (HUVECs) were used to observed the uptake of nanoparticles into cells in the beginning and the viability of cells were tests by CCK-8 assay. Then, the investigation of whether novel peptide has the anti-angiogenesis function of vessel cell growth was measured by cell migration and tube formation. In animal trial, C57BL/6J mice were used to construct the angiogenesis animal model by chemical burn and evaluate the treatment effectiveness by grading its neovascularization and burn stimulus. Moreover, we will test for the retention time by IVIS and the angiogenesis pathway by western blotting of HA-pep NPs. The histological examination had been observed by H&E staining.

Results：HA-pep NPs was prepared with the size of 268.433 ± 7.124nm, and zeta potential was 17.978 ± 0.776 mV. We also confirmed that the encapsulation rate of gp91 in the NPs was around 92.953 ± 0.718 % and TEM images showed that these particles had spherical morphology and peptide separate evenly in the nanoparticles. NTA result showed the concentration of nanoparticles was $1.39 * 10^{10} \pm 4.7 * 10^{8} / 1$ mL. The structure of the functional groups and the combination of HA-pep NPs were characterized by FTIR and DSC. Result of drug release test showed the slow and stable release ratio of HA-pep NPs. Moreover, by the uptake intensity and figure indicated that HA-pep NPs had good uptake property, than confirmed the most appropriate drug given concentration by cell viability test. The effect of blood vessel inhibition had been proved by cell migration and tube formation assays. At last, we combined FITC fluorescent on peptide to prepare HA-pep NPs on the mice eyeball surface to track the drug retention. Result of H&E staining showed the curation of HA-pep NPs.

Discussion：The diameter of HA-pep NPs showed similar in DLS, TEM, and NTA. It has highly encapsulation efficiency due to the self-assembling mechanism. The result of cell migration and tube formation showed the potential of HA-pep NPs in appropriate concentration of peptide loaded nanoparticles. At last, the result of *in vivo* neovascularization animal model echoes with *in vitro* tests. H&E staining of tissues also showed that the integrity of HA-gp91 NPs group was closest to normal cornea.
Conclusions：We had successfully prepared HA-pep NPs with stable properties. Both *in vivo* and *in vitro* results had shown a good angiogenesis inhibition. This study points out the therapeutic effect of HA-pep NPs on corneal angiogenesis.

P-02

合成可注射交聯透明質酸添加兒茶素應用於人工玻璃體置換
Injectable Hyaluronic Acid Gel with Epigallocatechin Gallate Addition for being Vitreous Substitutes

陳誼寧[1] 謝昌倫[2] 曾靖孋[2] 林峯輝[1]
國立臺灣大學醫學院暨工學院醫學工程研究所[1]
台北醫學大學生醫材料暨組織工程研究所[2]

Introduction：There are many eye diseases associated with vitreoretinopathy, such as retinal detachment, etc., which need to be treated by vitrectomy; hyaluronic acid (HA) hydrogel, the major component in vitreous was used as vitreous substitutes. However, inflammation after surgery usually causes complication or failure. Therefore, the natural tea extraction epigallocatechin gallate (EGCG), was added to the hydrogel as substitute for the inhibition of, inflammatory after vitrectomy. The butanediol diglycidyl ether (BDDE) was added to cross-linked HA to prepare vitreous substitute. This HA-BDDE cross-linked hydrogel with EGCG addition were designed and synthesized, and application as vitreous substitute were studied.

Materials and Methods：We used FTIR and 1H-NMR to test the change of hydrogel components change after cross-linking and EGCG addition. And detect the residual amount of cross-linking agent BDDE. The refractive index, viscoelasticity and osmotic pressure, and degradation rate of hydrogel were treated. For in vitro part, WST-1 and Live/Dead staining were used to determine the cytotoxicity and cell viability of the hydrogel, and then the cells were stimulated by lipopolysaccharide (LPS) induced inflammation condition for evaluating the anti-inflammatory effect of the hydrogel. Real-time quantitative reverse transcription polymerization (RT-qPCR) was used to determine changes of inflammatory genes in cells. For *in vivo* test part, vitrectomy was performed and the substitute for this experiment was injected into rabbit's vitreous; then, intraocular pressure and corneal thickness were measured. The electroretinogram (ERG) was used to test retinal function. And observe the structure and inflammation of the eye by histological examination.

Results：In this experiment, a transparent and easy-to-inject hydrogel was successfully prepared. The residual amount of BDDE met the safety standards. The physicochemical properties of the hydrogel were very similar to those of the native vitreous body. It has a long degradation time and can maintain the filling effect after surgery. *In vitro* experiments confirmed that the material has good biocompatibility, and the addition of 50 μM EGCG has the effect of inhibiting inflammation; In vivo experiments used 50 μM EGCG as the benchmark to mobilize three concentrations of low, medium and high doses. Complete excision of vitreous humor diluted EGCG can play an anti-inflammatory effect, and the results showed that injection of a substitute containing 50 μM EGCG had a better replacement effect. There was no significant change in intraocular pressure and corneal thickness after surgery, and the amplitude of retinal electrical signals was also similar as normal. No significant difference after surgery for week.

Discussion：In this experiment, we used BDDE to cross-link HA to solve the problem of premature degradation, and added EGCG to reduce the problem of possible inflammation after surgery, and confirmed that there is no residual cross-linking agent.

Conclusions：We have successfully prepared a transparent and easy-to-inject hydrogel, which is similar to the natural vitreous in physicochemical properties, and proved to have good biocompatibility in in vitro experiments and anti-inflammatory effects in in vivo experiments. An injectable BDDE crosslinked HA mixed with EGCG as a vitreous substitute with appropriate physical properties and inflammation inhibition for vitrectomy was proofed in this study.

P-03

透過生態法合成摻銪之碳酸鈣用於人體雕塑在低強度超聲波照射的自由基產生器
The Synthesis of Europium-Doped Calcium Carbonate by an Eco-Method as Free Radical Generator Under Low-Intensity Ultrasonic Irradiation for Body Sculpture

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Introduction：Over the last decade, ultrasound has been developed to a commercial set in plastic surgery as physical lipolysis for body sculpture by specific ultrasonic parameters to break down fat tissue around the patients' waist. The study was firstly to synthesize a high-sonoluminescent europium-doped calcium carbonate ($CaCO_3$: Eu) particles by a new developed method. The combination of sonoluminescent $CaCO_3$: Eu and low-power ultrasound would generate reactive oxygen species (ROS) to damage the adipo-tissue under the stress of free radicals.

Materials and Methods：In this research, a sonosensitizer of $CaCO_3$: Eu would be synthesized by an eco-method and combined with low-intensity ultrasound for lipolysis. The crystal structure of was identified by XRD. The particle size was determined by Zeta-sizer. WST-1 were used to evaluate the cell viability. CM-H_2DCFDA and Live/dead stain were used to evaluate feasibility in vitro. SD rat was used to evaluate the safety and efficacy in vivo.

Results：The crystal structure was identified by XRD, which was matched with the standard pattern of calcite CaCO3. The average particle size of CaCO3: Eu was 2.1 μm, which fall in the range of optimum particle size for cellular endocytosis (0.5–10 μm). CaCO3: Eu had good biocompatibility and could produce ROS after treated with low-intensity ultrasound. The animal experiments showed that the injection of acoustically sensitive materials in animals and the effects of ultrasound of the rats are safe, and does not affect the physiological condition and organs of the rats by the ultrasound effect. After 4-weeks, the CaCO3: Eu exposed to ultrasound irradiation on SD rats could significantly decrease body weight, waistline, and subcutaneous adipose tissue.

Discussion：we used Eu-doped calcium carbonate as sonodynamic reagent to combine with ultrasonic irradiation for body sculpture. Compared to Ca ions, the doped Eu ions can obtain additional electrons, which creates a new energy level near the conduction band to reduce the energy gap effectively. This makes the sonosensitizer more susceptible to ultrasonic irradiation and stimulates the generation of singlet oxygen and ROS in adipocytes for increasing the effective on lipolysis.

Conclusions：The combination of the developed Eu-doped $CaCO_3$ and low-intensity ultrasound could effectively inhibit the adipogenesis without skin burning and charred sounding tissue; that would be a mild and non-invasive treatment for the body sculpture.

P-04

探討血小板衍生囊泡搭載血管新生抑制藥物對血管內皮細胞之作用機制
Platelet Derived-extracellular Vesicles as Nanocarriers for Carrying Anti-Angiogenetic Agent for Treating Vascular Endothelial Cells and its Mechanism Study

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Introduction：The physiological nanoparticles, extracellular vehicles, are released from the cellular membrane when various types of cells undergo activation or apoptosis. Platelet–derived extracellular vehicles (P-EVs) are recently get attention as cargoes for drug delivery applications. Due to their lipid bilayer membrane and nano-sizes, they can be easily uptaken by cells, thereby increasing the bioavailability of therapeutic agents. However, vascular endothelium growth factor (VEGF) in the P-EVs may promote angiogenesis. This study uses P-EVs as a drug carrier for anti-angiogenesis application. Therefore, an anti-angiogenetic agent, kaempferol (K), with anti-angiogenetic and anti-inflammatory capacity was chosen for loading in P-EVs for drug delivery system.

Materials and Methods：P-EVs were separated and purified from blood. Then the P-EVs with or without K loading were examined by dynamic light scattering (DLS) to acquire their particle size and charge-ability. A transmission electron microscope (TEM) was used to observe the morphology of particles. The particle numbers in the solution were checked using nanoparticle tracking analysis (NTA). To confirm the drug release rate, high-performance liquid chromatography (HPLC) was utilized. The human umbilical vascular endothelial cells (HUVECs) were used for *in vitro* tests. After HUVECs were treated with P-EV and P-EV-K, the anti-angiogenesis/anti-inflammation gene expression was analyzed using reverse transcription real-time polymerase chain reaction (RT-PCR).

Results：When P-EV with K loading, the size is around 158.5 nm, with zeta potential at -13.0 mV. The morphology observation under TEM was spherical. The cell tube formation tests revealed that P-EV-K has the ability to inhibit the tube formation, and P-EV-K at 1% (P-EVs $4.85*10^{8}$ particles/mL + K at 6　g/mL) is the concentration with the highest inhibitory effect. Compared to free kaempferol, P-EV-K possesses a slower and more stable drug release rate during 24 hrs.

Discussion：The P-EV with/without K loading has no difference in size. P-EV-K at 1% P-EVs ($4.85*10^{8}$ particles/mL + K at 6　g /mL) is the concentration with the highest inhibitory effect of HUVECs cell functions. Compared to free kaempferol, P-EV-K has a more stable and slow-release rate. Subsequent analysis will determine gene expression by RT-qPCR and by western blot to identify protein expression as validation.

Conclusions：The P-EV with K loading can inhibit the cell functions of HUVECs. The detailed signaling pathway influenced by P-EV, free drug (K), and P-EV-K treated HUVECs will be studied in the future by using RT-PCR and western blot.

P-05

Src 和 PKCζ 在壓電刺激促使軟骨細胞聚合及重新排列中的角色
The Roles of Src and PKCζ in Piezoelectric Stimulations of Chondrocyte Aggregation and Rearrangement

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Introduction：The clinical use of ultrasound in bone fracture healing is FDA approved. Studies have shown that the use of low-intensity pulsed ultrasound can induce the regeneration of cartilage and tendon tissue. The skeletal system consists of aligned collagens, which are piezoelectric materials. Since ultrasound and piezoelectric effects are difficult to be separated in the *in vivo* experiments, the question of whether ultrasound therapy stimulates the regeneration by its own or by piezoelectric effects is never asked. We previously showed that piezoelectric stimulation (PE) can cause cell aggregation of bone marrow stem cells (ref), which is significantly different from the ultrasound stimulation (US) and the control. In this study, we demonstrate that PE stimulation causes a cell rearrangement through Src and PKCζ signaling.

Materials and Methods：In the experiment, the ultrasonic stimulation device (LIC) developed in our laboratory was used for ultrasonic and piezoelectric stimulation. Ultrasonic wave and piezoelectric stimulation are generated on glass and quartz slide respectively. Quartz is a piezoelectric material. Mechanical vibration on the quartz slide causes microscopic deformation, thus generates electric field. The similar vibration on a glass slide only results in lamb wave, providing acoustic field stimulation. Based on these understanding, we designed our experiments comparing the cell orientation, the ciliary positions and the cell sizes in the control chondrocytes to those stimulated by PE or US.

Results：In the control chondrocytes, the orientation and the ciliary positions were randomized. US stimulated cells showed no significant difference to the controls while PE stimulation polarized the ciliary positions and results in cell rearrangement. There was also a significant reduction in cell size.

Since the ultrasound stimulation of bone fracture healing is attributed to integrin signaling, and since Src kinase is a key regulator in integrin signaling, we asked whether Src kinase is required in the PE stimulated cell rearrangement of chondrocytes. Indeed, the inhibition of Src kinase activity disrupted the polarization of ciliary position relative to the front rear direction of the cells as well as disrupted the rearrangement of the cells. However, Src inhibition did not reverse the PE induced cell size reduction.

PKCζ is involved in the regulation of cell polarity. Hence, we tested whether PKCζ inhibition can also abolish the cell rearrangement induced by PE. As expected, the inhibition of PKCζ also abolish the cell rearrangement but not affecting the PE effects on cell size.

Discussion：Both Src inhibitor and PKCζ inhibitor can abolish chondrocytes rearrangement induced by PE, indicating the roles of Src and PKC　in the PE induced cell signaling. We will be interested to test whether these two molecules are acting in parallel or they are functioning in sequential manner. Thus, we will design experiments to test the relationship between Src and PKCζ in this context.

Conclusions：Piezoelectric stimulation induces a signaling event in the chondrocytes that leads to the regulation of polarized ciliary position and cell rearrangement. The signaling is most likely mediated by Src and PKCζ activities.　(ref：Ya-Cherng Chu et al., (2020). *JASA* 148, EL58.)

P-06

小鼠角膜異質性和交互作用之單細胞轉錄體學分析
Single-cell Transcriptomic Analysis of Cellular Heterogeneity and Interaction in Mouse Cornea

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Introduction：Reconstruction of single-cell transcriptional profiling has greatly advanced our understanding of cellular heterogeneity in recent years. Mouse cornea cellular heterogeneity remains unexplored at the single-cell level. In this study, we analyze diverse cell subtypes and their interaction in mouse cornea using the single-cell RNA-seq.
Materials and Methods：Corneas were harvested from eight-week-old C57BL/6J mice. To collect whole cell populations, corneal epithelium and corneal stroma/endothelium were isolated separately. After digestion buffer incubation, live single cells were sorted using FACSAriaIII (the Flow Cytometric Analyzing and Sorting Core Facility, NTUH). Corneal epithelium and corneal stroma/endothelium were then pooled together at the ratio of 1:1 before being loaded on the 10x chip. The gel bead-in-emulsion (GEMs) generation, barcoding, post-GEM-RT cleanup, cDNA amplification, library preparation, and sequencing were performed at the Sequencing and biochemistry core, NTUH. The bioinformatic analysis, including mapping, quality control, trajectory, and cell-cell interaction, was performed by R package through the Sequencing and biochemistry core, NTUH.
Results：scRNA-seq generated 18,912 cell profiles isolated from a total of 40 corneas. UMAP analysis revealed 12 distinct cell clusters. Further identification showed that these 12 cell clusters correspond to 4 main groups, including corneal epithelium, stroma, corneal endothelium and monocytes/macrophages. Trajectory inference allowed analysis of the differentiation direction in corneal epithelium, stroma and endothelium. We also mapped intercellular communication to decipher regulatory signaling in the physiological state.
Discussion：We provided comprehensively mouse corneal transcriptomics. We will integrate these data with 3D whole cornea images to explore the spatial distribution of cellular diversity.
Conclusions：Our data provide the single-cell transcriptional landscape and cell-cell interaction of the adult mouse cornea

P-07

Cell Morphological Responses to Mechanical Stress: Nucleus Pulposus cell in 3D-culture of TYPE I Collagen and Hydrogel

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Introduction：There is currently no effective therapy for the degeneration of intervertebral disc (IVD) and especially that of nucleus pulposus (NP). NP cell proliferates slowly and cannot be regenerated in the adult animals. When being seeded in traditional 2D cultures, NP cells demonstrate phenotypic transformations for not being surrounded by proper extracellular matrix or accurate arrays of cell types. To better understand the mechanobiology of the degeneration, we used TYPE I collagen and Hydrogel, to set up 3D cell cultures that resemble physiological conditions. In this study, we aim to generate an injury model to study the cell responses to compression and puncture. We also compare the responses to ultrasound stimulations. In addition, we characterize the difference between injury without treatment and with ultrasound stimulations.

Materials and Methods：In this study, the NP cells were cultured in 3D collagen or hydrogel. We characterized the morphological difference of NP cells in these cultures. Subsequently, we used the customized chamber to ultrasonically stimulate the NP cells, in order to compare the mechano-responses of the NP cells in 2D and 3D cultures. To set up an in vitro injury model for NP cells, we mimic the disc damage by creating wounds in the 3D cultures and characterize the responses of the cells by immunofluorescent stainings of cytoskeletal and ciliary markers.

Results：We successfully set up the 3D cell culture. NP cell is spherical in the 3D structure, resembling their original shape in the IVD rather than fibroblast-like in the 2D structure. We found that p-PKCz translocated to the cilia, labeled with K40 acetylated tubulin, 24hr after 1 minutes of ultrasound stimulation. The sub-cellular localization of p-PKCz in the 5-minute, 30-minute, 1-hour time points is not significantly different from the controls. On the other hand, we generated compressional and puncture wounds in the hydrogel culture. During the 7-day after injury, we found that the cells change from the original spherical shape to the elongated spindle shape, and the cells also aggregate tangentially to the force inflicted upon injury. However, the morphological changes only occur at the wound site. The cells remain spherical in the other areas.

Discussion：p-PKCz is involved in the regulation of cell polarity. Interestingly, the translocation of p-PKCz into cilia is not an immediate response. The immediate mechano-signaling remains to be discovered. In our *in vitro* injury model, NP cells undergo morphological changes. There are numerous studies showing NP cells undergo possibly similar morphological changes during IVD degeneration. This model can be used for further study of how NP cells degenerate and whether ultrasound stimulations can ameliorate the degeneration or even induce regeneration.

Conclusions：In this study, we successfully used hydrogel and collagen to generate a 3D cell model for NP cells. This model enables us to ask more questions concerning molecular mechanisms of NP degeneration to develop the beneficial mechanical stimulations using ultrasound settings to maintain the properties of healthy NP.

P-08

探究幹細胞形成三維球體之生物路徑
Involvement of Conserved Pathways in 3-Dimensional (3D) Sphere Formation in Diverse Stem Cell Types

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Introduction：3-dimensional (3D) culture for spheroid formation are a novel cell culture system used to better mimic physiological states. However, the biological consequences of 3D spheroid formation are significantly different for diverse cell type. For embryonic stem cells (ESCs) which are pluripotent stem cells, spheroid formation—termed embryoid bodies (EBs)—mimics the natural process of embryo development, and result in loss of pluripotency with a concomitant occurrence of differentiation and lineage commitment. In contrast, spheroid formation in somatic cell types may allow for selection of higher 'stemness' possessing cells, i.e. selection of somatic stem cell (SSC) population as has been done with neural stem cells and mammary stem cells. Despite these different biological outcomes, there may be a "core process" governing the ability for 3D sphere formation since all these diverse stem cell types are capable of 3D sphere formation.

Materials and Methods：We performed transcriptome analysis on conventionally 2D- and 3D-cultured spheroids ESCs and SSCs to elucidate conserved processes/pathways involved in 3D spheroid formation of diverse stem cell types.

Results：Pluripotency markers such as Oct4, Sox2, Nanog, & Klf4 were significantly down-regulated in ESCs after 3D sphere formation, as expected; however, these 4 markers were not significantly upregulated in somatic cells after spheroid formation. Convergent processes for both ESCs and SSCs include hypoxia and cell cycle arrest. Other highly convergent pathways include metabolism and oxidative phosphorylation.

Discussion：While 3D spheroid formation is a process for lineage differentiation in ESCs, for SSCs it is a strategy to maintain stemness. But we found a number of conserved processes/pathways involved in 3D formation of diverse stem cell types, including cell cycle arrest, hypoxia, metabolism, and oxidative phosphorylation.

Conclusions：Our data implicates pluripotency, hypoxia, and cell cycle arrest are not playing a vital role in 3D spheroid formation across diverse cell types. One metabolism pathway mediate spheroid formation via cytoskeleton rearrangement.

P-09

透過調控三維間葉幹細胞球體內部之區位以提升其治療潛力
Manipulation of Inherent Niches in 3D MSC Spheroids Improves Therapeutic Potential

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Introduction：Mesenchymal stem cells (MSCs) that derived from various human tissues have been widely used in cell therapy and regenerative medicine. Transplantation of MSCs not only serves as cell replenishment but also MSC secretome improves therapeutic potential during tissue regeneration. Compared to conventional culture, three dimensional (3D) multicellular spheroids configuration, MSCs exhibit native tissue-mimicking feature due to substantial cell-cell and cell-matrix interaction, thus considered as a potential implantable regenerative building blocks for stem cell therapy. Different inherent niches in 3D MSC spheroids will further improve their therapeutic potential.

Materials and Methods]：3D MSC spheroids were prepared by using 12 % methylcellulose (MC) hydrogel which was prepared in phosphate buffered saline (PBS). After autoclaving, the sterilized MC solution was coated at 96-well culture plate. Desired MSC cell densities are seeded on MC-coated plate and cultivated for 24 h. 3D MSC spheroids morphology and immune-stained extracellular matrix (ECM) components were imaged by using phase-contrast microscope and confocal laser scanning microscope, respectively. Cell viability was detected by SYTOX Green staining. Metabolic reconfiguration, pro-regenerative signaling molecules and immunomodulatory factors of related genes are detected by Real-Time Quantitative Polymerase Chain Reaction (qPCR).

Results：We found that 3D MSC spheroids size affect MSC paracrine molecules signaling and immunomodulatory enzyme level which have the most abundant level at 3D MSC spheroids prepared by 40,000 cells per well. Besides that, 3D MSC spheroids culture period affects their viability and therapeutic potential. After 3-day cultivation, 3D MSC spheroids lead to cell death in the spheroid core and metabolic reconfiguration and autophagy are activated. However, we found that hypoxic niche development in 3D MSC spheroid is not the major component for its enhanced therapeutic potential.

Discussion：It is important for MSCs to be cultivated in a 3D niche for significantly enhanced therapeutic potential in terms of paracrine signaling and immunomodulatory activity. By optimizing cultivation parameters of 3D MSC spheroids, inherent niches could be modulated and further promote therapeutic capacity by activating the expression of pro-regenerative paracrine molecules and immunomodulatory factors. In the present study, MSC spheroids that were assembled by 40,000 cells and cultivated for 2 days showed the best therapeutic potential.

Conclusions：We expect that our findings can serve as guidelines for the future design of 3D MSC spheroids for cell-based therapies by providing a new insight into the mechanisms for the enhanced therapeutic benefits.

P-10

間葉幹細胞快速精確的軟骨分化—透過增強細胞黏著與限縮脫靶效應

Rapid and Precise MSC Chondrogenesis is Achieved Through Increasing Adherens Junctional N-cadherin-β-catenin Interactions and Restricting Off-target Lineage Commitment

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Introduction：Human mesenchymal stem cells (MSCs) are easily accessible cell sources for tissue engineering of cartilage, a tissue without the capacity for regeneration or repair but often injured in activity and with aging. However, the most common molecules currently used for chondrogenic differentiation are TGFβ1 and TGFβ3, growth factors we found to induce off-target lineage specification towards smooth muscle and osteogenic lineages. In this study, we demonstrate a precise and efficient approach to induce chondrogenesis in human MSCs from multiple sources including induced pluripotent stem cell (iPSC)-derived MSCs, by antagonism of Wnt-β-catenin signaling and in the absence of TGFβ.

Materials and Methods：Small-molecule Wnt modulators were applied during MSC chondrogenic differentiation in the presence or absence of TGFβ. Expression of glycosaminoglycans and chondrogenic mRNAs/proteins were examined to evaluate chondrogenic capacity. Transcriptomic analyses of human primary MSCs, chondrocytes, and osteoblasts were used to validate the relevance of Wnt antagonism for MSC chondrogenesis.

Results：Compared to TGFβ, Wnt/β-catenin antagonism more rapidly induced MSC chondrogenesis without eliciting off-target lineage specification towards smooth muscle or hypertrophy; this was mediated through increasing N-cadherin levels and β-catenin interactions—key components of the adherens junctions (AJ)—as well as increasing cytoskeleton-mediated condensation. Validation by transcriptomic analysis of human chondrocytes compared to MSCs and osteoblasts showed significant downregulation of Wnt/β-catenin signaling along with upregulation of a-catenin-related processes and integral to the AJ.

Discussion：Our study revealed that off-target lineage specifications induced by TGFβ may contribute to a lower chondrogenic differentiation efficiency and be responsible for ossification and/or fibrosis. Expression of N-cadherin, and interactions between N-cadherin and β-catenin by Wnt antagonism imply that Wnt/β-catenin antagonism can increase N-cadherin levels and cell condensation, both critical processes for chondrogenesis.

Conclusions：Our findings underscore the importance of structural modification and understanding of developmental pathways along with use of small molecules in achieving precise and efficient MSC chondrogenesis for translational application.

P-11

以膠原酶輔助之口腔黏膜表皮細胞移植治療角膜輪部幹細胞缺損之效能與安全性

The Effect and safety of Xenogenic-free Collagenase Assistant Cultivate Oral Mucosal Epithelial Tansplantation (CA-COMET) for the Treatment of Limbal Insufficiency

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Introduction：Bilateral total limbal stem cell deficiency (LSCD) may cause poor visual outcome due to corneal conjunctivalization, fibrosis, and poor corneal epithelialization. COMET has been used to treat LSCD. In traditional COMET protocol, dispase II/trypsin-EDTA was used to isolate oral epithelial stem cells and degrade epithelial basement membrane. 3T3 mouse fibroblasts were required for further epithelial cell expansion as feeder cells. Collagenase, a replacement of dispase II/trypsin-EDTA in isolating epithelial stem cells, may preserve niche environment for epithelial stem cells, and provides a way of oral mucosal epithelial stem cell culturing without feeder cells.
To report the effect of collagenase assisted cultivate oral mucosal epithelial tansplantation (CA-COMET) for the treatment of limbal insufficiency
Materials and Methods：We used collagenase to replace dyspase II/Trypsin-EDTA in the culture of oral mucosa epithelial cell sheets on amniotic membrane without the need of feeder cells. The quality of CA-COMET cell products were verified by cell morphology, cell growth rate, infection and endotoxin tests. The successful cultured cell products were transplanted to patients' ocular surface after removal of abnormal fibrovascular tissue on corneal surface and release of symblephraon. Each patient was regularly followed-up for 20-28 months.
Results：The cell products of CA-COMET demonstrated satisfactory quality for transplantation in all four cases. After transplantation, clinical outcomes of four patients showed smooth post-operative results without recurrence of fibrosis or conjunctivalization. The visual acuity of the patients improved after single CA-COMET surgery or combined with other surgeries, such as penetrating keratoplasty (PKP) and cataract surgery.
Discussion：In our CA-COMET system, all the processes were xenogenic free. The use of autologous oral mucosa and autologous serum also prevented the possible complications related to allogenic transplantation, such as rejection and long-term use of steroid. The CA-COMET provided not only excellent epithelial stem cell growth, qualified epithelial characteristics and *ex vivo* stemness, but also the potential in clinical application.
Conclusions：Our study reported the safety, efficacy, and long-term surgical outcomes of xenogenic-free CA-COMET for the treatment of limbal insufficiency.

P-12

探討動態拉伸對大鼠脂肪幹細胞分化為軟骨細胞的影響
The Effects of Cyclic Stretching on Chondrogenic Differentiation of Rat Adipose-derived Stem Cells

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Introduction：健康正常軟骨的基質合成及降解維持平衡關係，當降解大於合成速率時即可能引發骨關節炎。先前實驗室已經使用豬的骨缺損模型進行了體內研究，評估仿生支架對膝軟骨再生的作用。循環動態拉伸在許多參考文獻中提到具有促進幹細胞分化的效果，然而過度的拉伸可能誘發細胞的凋亡。因此本研究希望藉由動態拉伸系統在不同拉伸頻率下，找到影響細胞凋亡的相關蛋白，並克服幹細胞分化成軟骨細胞的問題，藉此改善先前研究中所遇到的問題。

Materials and Methods：本研究利用 Wistar 大鼠初代脂肪幹細胞 (Rat adipose-derived stem cells, rADSCs) 進行實驗，並培養於 low-glucose DMEM。為探討動態拉伸是否影響 rADSCs，利用 TGF-β1 誘導分化成軟骨細胞，分為控制組、靜態培養分化組、動態拉伸分化組 (0.5 Hz 與 1 Hz)。將細胞以相同密度分別培養於培養皿及矽膠薄膜，動態拉伸利用動態拉伸系統 (BOXER-AQA 7, TAIHOYO) 進行。以顯微鏡觀察細胞型態、Glycosaminoglycan (GAG) Assay kit 分析細胞外 GAG 濃度、safranin O 染色及 western blotting 量化相關蛋白表現。

Results：rADSCs 培養於 low glucose DMEM，細胞形態為貼附型紡錘狀。由不同培養條件觀察得知：靜態培養分化組較對照組有明顯方向性細胞聚集，且靜態培養分化組有較高的 GAG 濃度及 safranin O 呈色分布；在 1 Hz 拉伸分化組，細胞可染上 safranin O 且呈現不規則碎片狀及凋亡小體(apoptotic bodies)出芽圓形分布，其 safranin O 呈色與 GAG 濃度均較靜態培養分化組為低。0.5 Hz 拉伸分化組，細胞可染上大量 safranin O 且呈現聚集團塊且 GAG 濃度均較靜態培養分化組及 1 Hz 拉伸分化組為高。由蛋白表現量化分析發現：動態拉伸分化組均會促進 cleaved caspase-9 及 phospho-NF-κB p65 蛋白表現；然 1 Hz 拉伸分化組促進 cleaved caspase-3 及 p53 蛋白表現，0.5 Hz 拉伸則否。

Discussion：rADSCs 在靜態與動態培養 3 天後細胞形態、GAG 濃度及 safranin O 有顯著差異。特別是比較高頻率 (1.0 Hz) 拉伸下細胞分泌的 GAG 濃度及 safranin O 呈色較低且有細胞凋亡體 (apoptosome) 的生成 (safranin O 染色)。較低頻率拉伸下 (0.5 Hz) 細胞分泌的 GAG 濃度比靜態培養及 1.0 Hz 拉伸高，代表其軟骨分化程度較高。由蛋白表現量化分析得知，動態拉伸均會促進 cleaved caspase-9 及 phospho-NF-κB p65 蛋白表現；1.0 Hz 拉伸可誘發 cleaved caspase-3 及 p53 蛋白表現，0.5 Hz 拉伸則否，推論 p53 為動態拉伸誘發細胞凋亡的關鍵蛋白。

Conclusions：在 TGF-β1 誘導 rADSCs 分化成軟骨細胞的狀態，動態拉伸是否誘發 p53 蛋白表現為細胞存活的關鍵。

P-013

運用 Rho 激酶抑制劑發展簡單口腔黏膜上皮移植以治療眼輪部幹細胞缺損疾病
Using Rho-associated Protein Kinase (ROCK) Inhibitor to Develop Simplified Oral Mucosal Epithelium Transplantation (SOMET) for the Treatment of Limbal Stem Cell Deficiency (LSCD)

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Introduction：The ocular surface is a delicate system that maintains the smoothness and transparency of the cornea. Limbal stem cells (LSCs) that reside at the conjunction of cornea and sclera are crucial for corneal epithelium renewal. Limbal stem cell deficiency (LSCD) due to injuries or inflammatory diseases could damage the equilibrium of corneal surface, resulting in blindness. In this study, we developed a novel oral epithelial cell-based therapy for LSCD using amniotic membrane (AM), collagenase and Rho-associated protein kinase (ROCK) inhibitor to aid niche regeneration and graft colonization.

Materials and Methods：Oral mucosal tissues harvested from New Zealand albino rabbits were rinsed in Dulbecco's modified Eagle's/Ham's F12 medium (DMEM/F12) with 5% fetal bovine serum (FBS) and antibiotics. After cutting into small pieces with 1-2 mm^2 each, the oral mucosal tissues were incubated with collagenase type I (1, 2, 5, 10 μg/ml) to separate the epithelial sheet from the underlying stroma. The epithelial sheet was then seeded onto a six-well tissue culture plate with or without AM in α-MEM media with 5% FBS, 1X L-Glutamine, and 1X NEAA. Different concentrations of ROCK inhibitor Y27632 (0, 1, 5, 10, 20 μM) was added into the medium. After up to 14 days of cultivation, light microscopy and immunofluorescence staining of cell markers K3, K4, K12, K13, ZO-1, p63 were performed.

Results：The application of AM and the addition of Y27632 both facilitated the growth of oral epithelial cells, showing a more compact cell morphology and an enhanced expression of epithelial cell markers. A dose-dependent effect of Y27632 (up to 10 μM) on cell growth was found. The cell viability did not differ between the different concentrations of collagenase type I being used.

Discussion：Current treatment strategies for LSCD include (1) direct transplantation of limbal epithelial tissue from donor eye (Simple Limbal Epithelium Transplantation, SLET), and (2) the Cultivated Oral Mucosal Epithelial Transplantation (COMET) that requires intensive and prolonged lab manipulation. Our study showed that ROCK inhibitor hastened the oral epithelial cell growth and may offer a more robust treatment that does not require allogenic limbal tissue.

Conclusions：Collagenase and ROCK inhibitor treatments provide a niche environment for oral mucosal epithelial cells. The treated oral epithelial cell sheet product enables the development of a promising "Simplified Oral Mucosal Epithelium Transplantation" (SOMET) therapy for the treatment of LSCD.

P-014

搭載 Lipid／PLGA 微球之明膠支架用於薑黃素緩釋與角膜組織
Gelatin Scaffold with Lipid-PLGA Microparticles for Sustained Curcumin Release and Corneal Tissue Engineering

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Introduction：由於人類角膜內皮細胞不具有再生能力，因此在角膜內皮受損後，目前臨床上能改善患者視力的方法唯有角膜移植一途。然而，因為角膜捐贈的數量尚不足滿足臨床上的需求缺口，且角膜也可能因其品質不佳或在移植後產生免疫排斥而導致移植移植後的結果不理想。故我們希望開發可用於培養角膜內皮細胞並支持其移植到前房的組織工程支架，做為角膜移植之替代方案。本研究開發了一種可緩釋薑黃素的 Lipid／PLGA 複合微球，並將其結合作為細胞移植骨架的明膠支架。我們期望藉由薑黃素之抗氧化、抗血管新生及促細胞增生等特性來配合做為角膜內皮細胞培養與移植骨架的明膠支架，改善細胞移植後的存活率，並進一步提升移植成功率。

Materials and Methods：我們利用單乳化法製備含有薑黃素的 Lipid/PLGA 微球（Cur@Lipid-PLGA MBs，此稱 MBs）。將製得的 MBs 與 20%的明膠水溶液混合均勻後倒入模具，於 4°C 下固化，最後以 EDC/NHS 交聯。在細胞實驗中，以人類角膜內皮細胞株 B4G12 分析支架之生物相容性及抗氧化特性，更以人類臍靜脈內皮細胞(HUVEC)和小鼠白血病巨噬細胞(Raw264.7)測試 MBs 之抗血管新生作用及抗炎症分析。在動物實驗部分建立了化學灼傷之兔眼模型來觀察 MBs 對傷口癒合之效用。

Results：首先，我們經由 CCK-8 測試結果可以得知薑黃素對 B4G12 細胞無明顯細胞毒性，接著製作 Cur@ Lipid-PLGA MBs，並確保 MBs 有確實將薑黃素包覆於其中。同時，量測 MBs 釋放薑黃素之情形，我們發現釋放情形較緩慢且曲線趨於線性。將 MBs 與明膠製成 Cur@MBs/Gelatin 後，其支架於可見光波段之穿透率雖略低於未包覆微球之支架，但其穿透率仍可達 90%。為了研究其生物相容性，將 B4G12 接種在 MBs/Gelatin 的表面上，根據螢光定量分析後，其存活率高於對照組，證實 Cur@MBs/Gelatin 具有良好的生物相容性及抗氧化的能力。在 HUVEC 管狀形成實驗中，可看到 MBs 在 24 小時內即具有明顯的抑制血管新生效果，而經由 Raw264.7 的炎症反應測試也證實了 MBs 能有效增強細胞的抗發炎能力。在角膜灼傷之動物實驗中，經由 Cur@MBs 治療之組別傷口癒合速度確實是優於對照組的。

Discussion：Cur@MBs/Gelatin 之複合結構具有良好的透明度。於型態分析中，發現 Cur@MBs/Gelatin 表面具有 MBs 之顆粒狀結構，進而推測我們有成功將 Cur@MBs 與 Gelatin 結合。細胞實驗結果中，可發現於 Cur@MB/Gelatin 中，當薑黃素濃度保持於 40 μM 以下時，B4G12 細胞的增生情形有上升的趨勢。並且在抗氧化實驗中也顯示了同樣的結果，而兩者實驗結果之細胞存活率均高於對照組。與 Cur@MBs 共培養後，HUVEC 的管狀生成及 Raw264.7 的炎症反應也有被抑制之效果。在角膜化學灼傷實驗中，由於 Cur@MBs 能控制炎症反應及抗血管新生，因此促進傷口的癒合。故本實驗之 Cur@MP/Gelatin 可做為細胞移植骨架，讓細胞良好貼附，亦能藉由薑黃素的持續緩釋，提升角膜內皮細胞的活性與增生能力，並減緩血管生成現象和降低發炎反應。

Conclusions：我們成功製備出包覆有薑黃素的 Lipid/PLGA 複合微球，並證明其可緩釋薑黃素，延長藥物在生理環境下的作用時間。由細胞實驗結果可知，由於 Cur@MBs 可使薑黃素緩慢釋放，其對於提升 B4G12 細胞增生的效果相較於未受 Lipid/PLGA 複合微球包裹的薑黃素有著更加明顯的提升。將 Cur@MBs 與明膠薄膜結合成為 Cur@MP/Gelatin 後，發現整體仍能保持良好的光線穿透能力。此外，B4G12 細胞可於明膠支架的表面進行細胞貼附與生長；而支架內部的 Cur@MBs 亦能透過持續釋放包封的薑黃素以提升細胞的抗氧化、抗血管新生及抗發炎能力，最後，在進一步的動物實驗中也證實了 Cur@MBs 確實能夠促進傷口區域的癒合能力。

P-015

發炎性關節炎中脂肪間質幹細胞之胞外泌體抑制 Th17 細胞分化
ADSC-derived Exosomes Suppress Th17 Cell Differentiation in Inflammatory Arthritis

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Introduction：Infrapatellar fat pad adipose-derived stem cells (IPFP-MSCs) have been studied to facilitate cartilage repair and relieve the pain caused by osteoarthritis (OA) due to anti-inflammatory and chondrogenesis capacity. However, little research has been conducted to elucidate how the IPFP-MSC exerts anti-inflammatory effects in OA. Serum IL-17 concentrations are significantly higher in OA patients, and articular joint injury induces IL-17 expression from T cells in the anterior cruciate ligament transection (ACLT)-generated OA mice. IL-17A rs2275913 and IL-17F rs763780 polymorphisms are possibly related to the high-risk knee OA occurrence. This study will first identify the potential capacity of anti-inflammation by IPFP-MSC and find out the possible genes in the Th17-mediated pathway.

Materials and Methods：

Research Ethics and Consent

Patients with OA (n = 30) between 50 and 75 years old undergoing joint replacement surgery will be recruited into this study, and the IPFP will be obtained and immediately processed. The Research Ethics Committee approved the study of Far Eastern Memorial Hospital, Taiwan (109146-F).

Gene Expression Profiles of Inflammation- Quantitative Real-Time PCR

The C20A4 human chondrocytes were collected and extracted to determine gene expression levels of cytokines and chondrogenic markers by using a LightCycler® (Roche Applied Science).

Results：We have reported that IPFP-MSC can improve cartilage repair and relieve pain in OA patients with inflamed joints. Moreover, our preliminary results showed that IPFP-MSC-derived exosomes significantly suppressed the differentiation and IL-17 production in Th17-skewing conditions. On the other hand, IPFP-MSCs play a critical role in injured cartilage healing.

Discussion：IPFP-MSC-Exos exerted a substantial stimulatory effect on anti-inflammation. IPFP-MSCs may represent a novel therapeutic approach for OA treatment in future clinical settings.

Conclusions：ADSC-based inhibition of inflammation in inflammatory arthritis could suppress Th17 cell differentiation. IL-17 has been reported to cause OA progression that may result from the Th17 cell responses. IPFP-MSC has the efficacy of reducing inflammation, enhancing chondrogenic differentiation, and resulting in cartilage repair.

P-016

髕骨下脂肪墊分離間葉幹細胞在退化性關節炎中透過促進 M2 巨噬細胞分化抑制發炎
Infrapatellar Fat Pad MSCs Suppress Inflammation via Enhancing M2 Macrophage Differentiation in Knee Osteoarthritis

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Introduction：Infrapatellar fat pad adipose-derived stem cells (IPFP-MSCs) can repair articular cartilage and relieve the pain caused by osteoarthritis (OA) due to solid differentiation and anti-inflammation. However, the mechanisms of IPFP-MSC are unknown, and challenges remain for clinical applications. Interestingly, the anti-inflammation in IPFP-MSC is more evident than subcutaneous adipose tissue (SC)-derived MSC. Therefore, in this study, we first identified the potential capacity in anti-inflammation between IPFP-MSC and SC-MSC and found out the possible mechanisms.

Materials and Methods：

Research Ethics and Consent

Patients with OA (n = 30) between 50 and 75 years old undergoing joint replacement surgery will be recruited into this study, and the IPFP will be obtained and immediately processed. The Research Ethics Committee approved the study of Far Eastern Memorial Hospital, Taiwan (109146-F).

Induction of Human M2-like Macrophages

$CD14^+$ cells from peripheral mononuclear cells were purified by magnetic cell sorting and cultured in complete RPMI-1640 medium supplemented with M-CSF to induce macrophages for 6 days.

Results：IPFP-MSCs can suppress *TNFA* and *IL1B* gene expressions in chondrocytes in response to IL-1β. An increase in CD103 and CD206 expressions were also noted in IPFP-MSC-M2 macrophage co-cultures compared to SC-MSC-M2 macrophage. As expected, the percentage of $CD103^+CD206^+$-expressing M2 macrophages co-cultured with IPFP-MSC/SC-MSC was significantly increased. The results showed that the induction of M2 macrophage capacity of IPFP-MSC is greater than SC-MSC.

Discussion：IPFP-MSC exhibited an extraordinary capacity toward chondrogenesis. We evaluate the gene differences between IPFP-MSC and SC-MSC and the M2 differentiation induced by each MSCs.

Conclusions：IPFP-MSC cell therapy indicated improved ability to bend and straighten knee joint and decreased inflammation via inducing M2 macrophage differentiation.

P-017

處理非選擇性瞬態感受器電位陽離子通道 C 型抑制劑 Derinat 促進毛髮再生於女性型態落髮病人

Treatment with Non-selective Transient Receptor Potential Canonical Channels Inhibitor, Derinat Promotes Hair Regeneration in Female Pattern Hair Loss Patients

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Introduction：Female pattern hair loss (FPHL), a potential age-related disease, the most common alopecia in adult women starts development by age 30 years and becomes more common when reaching menopause. FPHL is characterized by chronic inflammation, and inflammatory infiltrates in the scalp have been observed as the pathogenesis of FPHL. The disorder also results in huge physiological problems and psychological stress that profoundly influence the quality of life of the patients, but there is no efficient treatment to deal with FPHL to date. Transient receptor potential canonical channels (TRPCs) are reportedly involved in regulating the skin aging process. TRPCs-mediated increase of the intracellular Ca^{2+} signaling initiates the skin aging process, causing Ca^{2+}-overloaded mitochondria reactive oxygen species (ROS) increase, the activation of DNA damage response (DDR), senescence inflammatory response (SIR), and senescence-associated secretory phenotype (SASP) activity. Blockage of TRPCs activity by Derinat restrains skin damage and aging according to our previous study. Thus, we hypothesized that treatment with TRPCs inhibitor, Derinat potentiates inhibition of FPHL pathogenesis.

Materials and Methods：*Caenorhabditis elegans* (*C. elegans*) was firstly utilized to screen the feasible concentration of Derinat for further application to murine and clinical experiments. BALB/c-nu mice were daily treated with the Derinat-containing hydrogel forms a 3-cm diameter circular chip for 3 h; after 7 days, the mice were sacrificed and identified their skin biopsies by H&E and immunohistological staining. Dihydroethidium (DHE) and PCNA were stained to detect intracellular ROS production and hair follicle stem cell (HFST) activation respectively. A total of 37 FPHL patients without nutrient deficiencies are daily received Derinat or control (placebo) for 8 weeks; hair growth, hair density, and hair diameter were detected by Scalp Analyzer.

Results：In this research, our results revealed that Derinat application in *C. elegans* extends the lifespan with anti-aging efficacy. We also found that treatment with Derinat in BALB/c-nu mice promoted hair growth, accelerated the number of hair, and attenuated intracellular ROS production. Proliferation marker PCNA and HFSCs markers CD49f and CD34 also co-localized along the HFSCs. Further application of Derinat and control (placebo) to FPHL patients, the clinical data indicated that FPHL patients with Derinat treatment reveal a significant improvement in hair density and hair diameter, enhancing hair regeneration.

Discussion：TRPCs-mediated Ca^{2+} signaling is potentially involved in FPHL pathogenesis, contributing to intracellular ROS production, DDR, SIR, and SASP activity. Hair cycle and HFSC niche may be influenced by TRPCs activation.

Conclusions：Blockage of TRPCs activity by TRPCs inhibitor, Derinat restrains FPHL pathogenesis, providing a new therapeutic approach for treating FPHL.

P-018

超臨界二氧化碳脫細胞豬骨支架結合脂肪幹細胞加速骨缺損大鼠骨骼再生
Adipose-derived Stem Cells Seeded Supercritical Carbon Dioxide Decellularized Bone Accelerated Bone Regeneration in Rat Bone Defect Model

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Introduction：Bone has the ability to regenerate and restore itself. However, the regenerative ability may be diminished based on the size of the defect. Currently, the use of decellularized xenogenic bone is a new trend in tissue engineering and regenerative medicine (TERM). Adipose-derived stem cells (ASC) are a perfect stem cell population for practical regenerative medicine. In the present study, we used supercritical carbon dioxide ($scCO_2$) decellularized porcine bone (scDPB) seeded with ASC for the restoration of rat model segmental defect.
Materials and Methods：Bio-scaffold produced by seeding ADSC to scDBM was evaluated by scanning electron microscopy (SEM). Bio-scaffold was implanted in rat segmental femoral defect model to investigate the callus formation *in vivo* at 12 and 24 weeks post-surgery.
Results：ADSC is firmly attached to scDBM bioscaffold in a dose-dependent manner. X-ray bone imaging revealed callus formation in both scDBM seeded with $2x10^6$ and $5x10^6$ ASCs groups. H&E staining revealed ASCs accelerated bone formation. The expression of Ki-67, BMP-2, and osteocalcin was elevated in scDBM seeded with $5x10^6$ ASCs group at 12 weeks after surgery, relative to other experimental groups. scDBM combined with $5x10^6$ ASCs promotes cell proliferation of bone defects in the early stage of bone regeneration and new bone formation.
Discussion：In the current investigation, scDBM seeded with ASC depicted increased expression of Ki 67, BMP 2 and osteocalcin thus leading to accelerated cell proliferation, bone regeneration and new bone formation in a rat segmental femoral defect model. Thus, the scDBM scaffold is an excellent biomaterial for bone tissue repair. This study is a biomimetic bone tissue engineering approach that features the natural endochondral cascade involving endochondral ossification in bone defect regeneration.
Conclusions：The scDBM is an excellent bioscaffold that enhanced the attachment and recruitment of mesenchymal stem cells. scDBM seeded with ASCs accelerated new bone formation [1].

P-019

超臨界二氧化碳脫細胞豬骨移植物應用於臨床眼窩骨折研究
Supercritical Critical Carbon Dioxide Decellularized Porcine Bone Graft for Orbital Floor Reconstruction

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Introduction：Orbital fractures are the result of a traumatic accident leading to impaired alignment and integrity of facial bones, with the symptoms of periorbital oedema, enophthalmos and diplopia. Thus, restoring symmetry of the orbital framework is critical to improving clinical outcomes. Numerous graft materials are used in orbital floor fractures varied from autografts to alloplastic grafts, which possess certain limitations. In the present study, a novel porcine bone matrix decellularized by supercritical carbon dioxide ($scCO_2$), ABCcolla® Collagen Bone Graft, was used for the reconstruction of the orbital framework.

Materials and Methods：This study was approved by the institutional review board (IRB) of Kaohsiung Medical University Chung-Ho Memorial Hospital (KMUH). Ten cases underwent orbital floor reconstruction in KMUH. The orbital defects were fixed by the implantation of the ABCcolla® Collagen Bone Graft. Nine out of ten cases used 1 piece of customized ABCcolla® Collagen Bone Graft in each defect. The other case used 2 pieces of customized ABCcolla® Collagen Bone Graft in one defect area due to the curved outline of the defect.

Results：In the outpatient clinic, all 10 cases showed improvement of enophthalmos on CT (computerized tomography) at week 8 follow-up. No replacement of implants was needed during follow-ups.

Discussion：Reconstruction of the orbital floor fracture has been a challenge in plastic surgery due to the fragility and complexity of bone arrangements in the orbital cavity. Since each kind of graft material has unique properties, there is no conclusive treatment plan for orbital wall reconstruction. Therefore, this study provides evidence and proves that the xenograft decellular framework, ABCcolla® Collagen Bone Graft is a new alternative to other graft material for orbital floor reconstruction. The result of this study proved ABCcolla® Collagen Bone Graft is a suitable graft material with optimal clinical outcomes in orbital floor reconstruction.

Conclusions：The $scCO_2$ decellularized, ABCcolla® Collagen Bone Graft proved to be safe and effective in the reconstruction of the orbital floor with high accessibility, high stability, good biocompatibility, low infection rate and low complication rate [1].

P-020

超臨界二氧化碳脫細胞豬軟骨結合高濃度血小板血漿促進大鼠軟骨修復與再生
Regenerative Role of Supercritical Carbon Dioxide Decellularized Porcine Cartilage Combine with Platelets Rich Plasma (PRP) Graft in Anterior Cruciate Ligament Transection Osteoarthritis Model

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Introduction：Osteoarthritis (OA), is a degenerative joint disease and the most common type of arthritis. In OA, the cartilage within a joint break down and the bone is subsequently altered. Inflammation and injury of the OA cause pain and swelling, leading to reduced function and disability. In the present study, we decellularized the porcine articular cartilage using the supercritical carbon dioxide ($scCO_2$) technique. Intraarticular administration of the decellularized porcine cartilage graft (dPCG) with and/or without PRP after ACLT- induced OA to evaluate the cartilage regenerative efficacy in rats.

Materials and Methods：The dPCG was produced by proprietary $scCO_2$ (100-350 bar carbon dioxide pressure, 20-40°C) extraction technology from porcine articular cartilage. The dPCG was characterized by hematoxylin and eosin, DAPI staining, scanning electron microscopy (SEM) and residual DNA quantification. The regenerative efficacy dPCG was evaluated by pain assessment by capacitance meter, X-ray and micro-CT. In addition, articular knee cartilage damage was explored by safranin-O, type II collagen, aggrecan and SOX-9 immuno-staining.

Results：The $scCO_2$ technology completely decellularized the porcine cartilage. The dPCG with or without PRP significantly reduced the ACLT-induced OA symptoms and attenuated the OA progression. The dPCG alleviated pain with or without PRP and attenuated articular cartilage damage in the rat knee as revealed by X-ray and micro-CT. . In addition, dPCG protected the knee cartilage as evidenced by the histological analysis. The safranin-O, type II collagen, aggrecan and SOX-9 immuno-staining depicted repair and attenuation effect by dPCG with or without PRP in the articular knee cartilage damage.

Discussion：The triads of cartilage regenerative medicine are the scaffolds (dPCG), signal (PRP) and the cells (resident chondrocytes). Therefore, our approach is direct and we provide a mixture of scaffold and signal (dPCG +PRP) so that the resident chondrocyte gets the structural support and nourishment for its proliferation. This study can be extrapolated to OA patients and patients with cartilage defects caused by sport-related injury.

Conclusions：The intra-articular administration of dPCG with or without PRP can attenuate ACLT-induced OA progression by elevating the expression of type II collagen, aggrecan and SOX-9 [1].

台灣再生醫學學會 （個人、贊助、準）會員入會申請書

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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)：					行動電話：		
準會員申請者	推薦人簽名 會員一		**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。** 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) 2.贊助會員：贊助本會工作之團體或個人。(設立證明、身分證) 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)						
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