2018年度台灣再生醫學學會學術研討會暨會員大會

2018 Annual Meeting of Formosa Association of Regenerative Medicine



論文摘要&大會手冊

2018年03月03日 台大醫學院103講堂 台北市仁愛路一段一號

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2018 年度台灣再生醫學學會學術研討會暨會員大會 2018 Annual Meeting of Formosa Association of Regenerative Medicine

Scientific Program

Time	Topic	Speakers & Authors		Institute	Moderator	
08:00	Re		到			
	08:40~10:00 Oral Pr	開幕致 esentation (<u> </u>	ition (I)		
S-1 08:40~08:50	Differentiation of MSCs from Human iPSCs Results in Downregulation of c-Myc & DNA Replication Pathways with Immunomodulation Towards CD4 & CD8 T cells	王麗姿*,1,2 江士昇 ³ 丁僑 徐珮茹 ² 張家 司徒惠康 ^{1,4} 劉柯俊 ³ 顏伶	萱 ² 齊 ^{1,2}	國防醫學院生命科學研究所 ¹ 國家衛生研究院細胞及系 統醫學研究所 ² 國家衛生研究院癌症研究所 ³ 國防醫學院微生物及免疫 學研究所 ⁴		
S-2 08:50~09:00	Neuroepithelial Regeneration in an Anosmic Animal Model Scarless Healing in Adult Mice is Achieved by Delayed Collagen Network		瑋 2,3	國立台灣大學醫學工程學 研究所 ¹ 亞東紀念醫院耳鼻喉科 ² 元智大學電機工程學系 ³		
S-3 09:00~09:10			.儀3	台大臨醫所 ¹ 台大醫院外科部 ² 台大醫工所 ³ 台大醫院皮膚部 ⁴		
S-4 09:10~09:20	Divergent Biological Consequences Of 3-Dimensional (3d) Sphere Formation for Stem Cells vs. and Somatic Cells	張家齊 1,2,4 江士昇 3 李雨 徐珮茹 ² 顏伶 嚴孟祿 ⁴	薇 ² 汝 ²	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 台灣大學醫學院醫學系婦 產科 ⁴	陳敏慧 黃玲惠	
S-5 09:20~09:30	Promoting the Maturation and Growth of Induced Pluripotent Stem Cell (iPSC)- Derived Retina Ganglion Cells Using Glutamate- Containing Biocompatible Scaffolds	游子毅 ¹		國立臺灣大學材料科學與 國立臺灣大學所 ¹ 國醫學學院附設 醫院婦產灣大學醫學院附設 醫院婦產灣大學分子生醫影 像研究學中心 ³ 國立臺灣大學基因體暨蛋 白體醫學研究所 ⁴ 國立臺灣大學醫學院附設 醫院眼科部 ⁵	張志豪	
S-6 09:30~09:40	The Customized Artificial Trachea with Elastic and Biodegradable Properties	謝政田 ¹ 鄭堃 廖昭仰 ² 戴念 曾清秀 ² 顏伶 陳晉興 ⁵ 徐善	·梓 ³ ·汝 ⁴	國立臺灣大學高分子科學 與工程學研究所 ¹ 國立中央大學機械工程學系 ² 國防醫學大學外科學系 ³ 國家衛生研究院細胞及系 統醫學研究所 ⁴ 國立台灣大學醫學院 ⁵		

Time Topic		Speakers & Authors	Institute	Moderator		
S-7 09:40~09:50	Role of Post-Translational & Epigenetic Regulation in Human Mesenchymal Stem Cell (MSC) Immunomodulatory Properties	顏伶汝 1 <u>李瑋</u> 1,2 徐珮茹 1 劉柯俊 3 江士昇 3 林佳樺 4 華筱玲 4.5 司徒惠康 6 嚴孟祿 4	國家衛生研究院細胞及系統醫學所1 國防醫學院生命科學研究所2 國家衛生研究院癌症研究所3 台灣大學醫學院醫學系婦產科4 台灣大學醫學院法醫學科研究所5 國防醫學院微生物及免疫研究所6	陳 黄 張 惠 豪		
S-8 09:50~10:00	A Rapid& Robust System for Selection of Osteogenic Phytoestrogens Using Mesenchymal Stem Cells (MSCs) & Osteogenic Transcription Factor/Co-Factor Reporter Screening	林佳樺 ¹ 謝承展 ^{1,2} 嚴孟祿 ¹	台灣大學醫學院醫學系婦 產科1 國立清華大學分子醫學研 究所2			
	10:00~10:	30 Coffee Break				
	10:30~12:00 Symposium: Ner	ve Regeneration: fro	om Basic to Clinics			
I-1 10:30~10:35	Peripheral Nerve Injury, Repair and Regeneration	張志豪副教授	台大醫院骨科部			
I-2 10:35~10:55	A Neural Stem/ Precursor Cell Monolayer for Treatment of Ischemic Stroke	楊台鴻教授	台灣大學醫學工程學研究所			
I-3 10:55~11:15	1-3 The Preclinical Studies of Cell Therapy		台大醫學院藥理學科暨研 究所	莊垂慶		
I-4 11:15~11:35	Experimental Researches for Nerve Transfers	張乃仁助理教授				
I-5 11:35~11:55	From Debates to Conclusion in Peripheral Nerve Injury and Reconstruction – A 30 Years' Experience	莊垂慶教授	林口長庚整形外科			
11:55~12:00 Discuss						
	12:00) 會員大會				
	12:00-13:	30 Lunch Break				

Time	Time Topic		Institute	Moderator			
13:30~15:10 Symposium: Multiple Organ and Tissue Regeneration							
I-6 13:30~13:50	Neural Regeneration of Brain Injury in Animal Models via Cellular Therapy	錢宗良教授	台大醫學院解剖學暨細胞 生物學研究所				
I-7 13:50~14:10	幹細胞組織工程於氣管再生醫學之應用	陳晉興教授	台大醫院外科部				
I-8 14:10~14:30	Extracellular Matrix as a Treatment Strategy for TM Joint Disorder	許明倫院長	國立陽明大學牙醫學院	嚴孟祿			
I-9 14:30~14:50	Possible Solutions for Keloid Prevention Therapy	黄玲惠教授	成大學生科院生物科技與 產業科學系 醫學院 臨床醫學研究所 再生醫學卓越研究中心	林泰元			
I-10 14:50~15:10	Soft Tissue Regeneration, Reconstruction and Neural Repair in ALS	翁仕明副教授	國立台北護理健康大學				
	15:10-15	:30 Coffee Break					
	15:30~16:20 Oral P	resentation Competi	tion (II)				
S-9 15:30~15:40	Development of Gelatin/Ascorbic Acid Cryogels for Potential Use in Corneal Stromal Tissue Engineering	<u>羅麗娟</u> ¹ 賴瑞陽 ^{2*}	長庚大學化工與材料工程 學系 長庚大學生化與生醫工程 研究所 ²				
S-10 15:40~15:50	Development of Gelatin-Graphene Oxide Hydrogel by Argon- Microplasma for Orthopedics Tissue Engineering Applications	Mantosh Kumar Sathapaty ¹ , Batzaya Nyambat ¹ , Er Yuan Chuang ¹ , Pei Chun Wong ² , Chih-Wei Chiang ³ , Chih Hwa Chen ^{2,3}	臺北醫學大學生醫材料暨 組織工程研究所 ¹ 臺北醫學大學生物醫學工 程學系 ² 臺北醫學大學附設醫院骨 科部 ³				
S-11 15:50~16:00	Development of the Genipin- Crosslinked Adipose Stem Cell Derived ECM Sponge Containing Graphene Oxide for Skin Tissue Engineering	Batzaya Nyambat ¹ , Chih Hwa Chen ^{2,3} Er Yuan Chuang ¹ , Pei Chun Wong ² , Mantosh Kumar Sathapaty ¹ , Chih-Wei Chiang ³	臺北醫學大學生醫材料暨 組織工程研究所 ¹ 臺北醫學大學生物醫學工 程學系 ² 臺北醫學大學附設醫院骨 科部 ³	陳敏慧 黄 張 志 豪			
S-12 16:00~16:10	Nanostrontium Ranelate Incorporated Photo-Sensitive Hydrogel Enhanced Bone Regeneration Supporting Spinal Fusion	黄紹展 莊爾元 姜智偉 陳志華	臺北醫學大學生醫材料暨 組織工程研究所				
S-13 16:10~16:20	The Effects of the Preservative-Free Contact Lens Care Solution on Cleansing and Bio-Tribology	<u>李冠儀</u> 1 施柏伍1 蘇真瑩1 方旭偉 1,2,*	國立台北科技大學化學工程系與生物科技系 ¹ 國家衛生研究院生醫工程與奈米醫學研究所 ²				

Time	Topic	Speakers & Authors	Institute	Moderator			
16:20~17:10 Oral Presentation							
O-1 16:20~16:30	Hyaluronan Microenvironment Enhances Simvastatin-Induced Chondrogenesis and Cartilage Defect Regeneration in Human Adipose Derived Stem Cells	<u>吳順成</u> ¹ 陳崇桓 1,2 陳振偉 ^{1,3} 陳建學 1,3 張瑞根 ^{1,2} 何美泠 ^{1,3*}	高雄醫學大學骨科學研究 中心1 高雄醫學大學附設中和紀 念醫院骨科 ² 高雄醫學大學醫學系生理 學科 ³				
O-2 16:30~16:40	Autologous Adipose-Derived Stem Cells Reduce Burn-Induced Neuropathic Pain in a Rat Model	黄書鴻 ^{1.2} 吳昇樺 ³ 林岑紘 ¹	高雄醫學大學附設中和紀 念醫院整形外科 ¹ 外科 ² 麻醉科 ³				
O-3 16:40~16:50	Parathyroid Hormone (1-34) Ameliorated Knee Osteoarthritis and Function in Rats Via Autophagy	<u>陳崇桓</u> 1,2,3 何美泠 ² 林怡珊 ² 林松彦 1,2,3 傅尹志 ^{2,3,4} 張瑞根 ^{1,2,3}	高雄市立大同醫院骨科1 高雄醫學大學骨科學研究 高雄醫學大學附設中和絕 醫院骨科3 高雄市立小港醫院骨科4	林頌然鄭乃禎			
O-4 16:50~17:00	Using Induced Pluripotent Stem Cells Derived Chondrocytes Culture in 3D Scaffold Combine with Factors to Test the Therapy Effect	林宗立 ¹ 王啟鴻 ² 蔡俊灝 ¹ 許弘昌 ¹ 洪士杰 ^{1,3} 劉詩平 ²	中國醫藥大學附設醫院 骨科部 ¹ 中國醫藥大學生物醫學 研究所 ² 中國醫藥大學新藥開發研 究所 ³				
O-5 17:00~17:10	An Injectable Oxidized Hyaluronic Acid/Adipic Acid Dihydrazide/ Tricalcium Phosphate Hydrogel as Bone Substitutes	馮品翔 甘如瑩	亞洲大學生物資訊與醫學 工程學系				
頒 獎 閉 幕							

Invited Lectures

10:30-10:35

I-1

Peripheral Nerve Injury, Repair and Regeneration

Chih-Hao Chang Department of Orthopedics, National Taiwan University Hospital

Abstract

Peripheral nerve injuries are common conditions with broad ranging groups of symptoms depending on the severity and nerves involved. Although much knowledge exists on the mechanisms of injury and regeneration, reliable treatments that ensure full functional recovery are scarce. This review aims to summarize various ways these injuries are classified in the light of decades of research on peripheral nerve injury and regeneration. In this section, we invited several specialists to present the topic about nerve regeneration and treatment. The topic include materials applying in nerve regeneration, cell therapy in nerve regeneration, nerve transfer clinically and basically, and peripheral nerve repair and regeneration clinically.

10:35-10:55

I-2

A Neural Stem/ Precursor Cell Monolayer for Treatment of Ischemic Stroke

楊台鴻教授 台灣大學醫學工程學研究所

Abstract

The purpose of this study was to prepare a monolayer of neural stem/precursor cells (NSPCs) for neural tissue engineering applications. Two components present in serum, fibronectin and epidermal growth factor (EGF) were added into DMEM/F12 medium (termed examine the effect of the migration-, proliferationdifferentiation-promoting potential on the cultured NSPCs, isolated from embryonic rat cerebral cortex. Compared with the serum effect, medium B also permitted neurosphere attachment onto the substrate surface and cell migration out of neurospheres extensively, but enhanced more extensive cell division and slowed down NSPC differentiation to generate a confluent NSPC monolayer. It was found the medium B-treated NSPCs possessed the capability to form typical neurospheres or to undergo differentiation into neuron-related cell types on various biomaterial surfaces. Therefore, we proposed a two-stage process for wound healing in vitro and tried to treat ischemic stroke in a rat animal model.

Keywords: neural stem/precursor cells (NSPCs), differentiation, monolayer, epidermal growth factor (EGF), fibronectin, ischemic stroke.

10:55-11:15

I-3

The preclinical studies of cell therapy for multiple sclerosis

林泰元; Thai-Yen Ling, PH.D. Institute of Pharmacology, College of Medicine, National Taiwan University

Abstract

Multiple sclerosis (MS) is an autoimmune disease of the central nervous system characterized by chronic inflammation, focal demyelination and widespread damage of axon. Although a wide variety of medicine have been approved by FDA today, there is no cure for MS. So far, many studies have demonstrate mesenchymal stromal cells (MSCs) as a promising source to treat MS, however, the mechanism for the therapeutic effect of MSCs in MS is still unclear. In this studies we demonstrated that MSCs from the maternal part of human termed placenta (placenta choriodecidual-derived mesenchymal stromal cells, pcMSCs) could be a potential cell source to treat MS. In order to understand the pathological mechanism of MS and therapeutic effects of pcMSCs, we used myelin oligodendrocyte glycoprotein (MOG)³⁵⁻⁵⁵-induced experimental autoimmune encephalomyelitis (EAE) in C57BL/6I mice as the animal model to revel the therapeutic mechanism of MSCs for MS treatment in this study. We first demonstrated that pcMSCs could ameliorate the disease progress of (MOG)³⁵⁻⁵⁵-induced EAE mice compared to control. In *in vitro* studies, the results showed that when co-culture of pcMSCs and monocyte, the progenitor cells of dendritic cells (DCs), pcMSCs could inhibit the progress of differentiation and maturation of DCs. In the experiments, both the expression of typical DCs costimulatory molecules (CD80 & CD86) and antigen-presenting molecule MHC class II peptides were strongly down regulated by co-culture with pcMSCs. Taken together, our findings suggest that pcMSCs was likely the regulatory to modulate the immune response in EAE animal model and pcMSCs may be a potential therapeutic option for the treatment of MS.

11:15-11:35

I-4

Experimental researches for nerve transfers

Tommy Nai-Jen Chang, M.D (Assistant Professor)

Department of Plastic and Reconstructive Surgery, Taipei-Linkou Chang Gung Memorial

Hospital, Chang Gung University, Taiwan

Abstract

Nerve transfer is a powerful tool in extremity reconstruction, but the neurophysiological effects have not been adequately investigated. As 81 % of nerve injuries and most nerve transfers occur in the upper extremity with its own neurophysiological properties, the standard rat hindlimb model may not be optimal in this paradigm.

In our institution we have performed the rat forelimb model in rat for years, mostly for brachial plexus injury studies. Some of the examples including the comparison of the outcome of proximal and distal nerve transfer, steal phenomenon, injured donor nerve, agonist and antagonist donor nerve. The result of these studies modified our strategies of clinical practice already.

The above-described rat model demonstrated a constant anatomy, suitable for nerve transfers that are accessible to standard neuromuscular analyses and behavioral testing. This model allows the study of both neurophysiologic properties and cognitive motor function after nerve transfers in the upper extremity clinically.

11:35-11:55

I-5

From Debates to Conclusion in Peripheral Nerve Injury and Reconstruction – a 30 years' experience

David Chwei-Chin Chuang, M.D(Professor)
Taipei-Linkou Chang Gung Memorial Hospital, Chang Gung University, Taiwan

Abstract

I have performed numerous reconstructions related to peripheralnerve injuries, including adult brachial plexus injuries (more than 2000 cases of brachial plexus exploration and reconstruction), obstetrical brachial plexus palsy (>200 cases for infant OBPP; and >400 for late child OBPP with deformity), facial paralysis (> 400 using functioning free muscle transplantation for facial reanimation), functioning free muscle transplantation (over 1000 cases in face, upper and lower limbs reconstruction), compression neuropathy (thoracic outlet syndrome, cubital tunnel syndrome, carpal tunnel syndrome, and others), and other numerous peripheral nerve injuries, tumor resection and reconstructions since 1985. I also performed numerous peripheral nerve-related researches during the 30 years.

There are many debates but few conclusion on peripheral nerve injury and reconstruction. I am today trying to make some conclusion related to peripheral nerve debates from present knowledge and techniques from my person point of views. These conclusions include

- 1. Classification-related, such as degree of nerve injury, level of brachial plexus injury, level of traction avulsion amputation of limbs and level of radial nerve injury;
- 2. Technique-related, such as timing of nerve exploration, carpal tunnel syndrome, cubital tunnel syndrome, thoracic outlet syndrome, Choice of neurotizer (CFNG vs. spinal accessory nerve vs masseter nerve) for facial paralysis reconstruction, postparalytic facial synkinesis; and
- 3. debates conclusion such as multiple nerve transfers vs functioning muscle transplantation to treat total root avulsion of the BPI; proximal nerve graft and/or transfer in incomplete BPI:
- 4. Evaluation system –related, such as result evaluation after functioning free muscle transplantation, facial paralysis reconstruction.

13:30-13:50

I-6

Neural Regeneration of Brain Injury in Animal Models via Cellular Therapy

錢宗良教授 Chung-Liang Chien, Ph.D.
Professor, Department of Anatomy and Cell Biology,
College of Medicine, National Taiwan University

Abstract

Neurogenesis by activation of endogenous neural progenitor cells is considered as a potential treatment strategy for brain injuries. Although several researches support the benefit of brain-derived neurotrophic factor (BDNF) on neurogenesis as well as Erythropoietin (EPO) for neuroprotection and neuronal survival, yet there are still some technical problems needed to be overcome, such as the delivery system. In our studies, cDNAs of mouse BDNF and EPO were transfected into cell lines of 3T3 fibroblasts. The expression and bioactivity for both BDNF and EPO were analyzed by immunocytochemistry, Western blot, Enzyme-Linked Immunosorbent Assay (ELISA), and functional assays.

The ICH mouse model was produced by collagenase injection. Hematoma area and brain tissue loss were assessed by magnetic resonance imaging (MRI). EdU (5-ethynyl-2'-deoxyuridine) was given intraperitoneally for 5 days after ICH induction. Either BDNF transfected 3T3 fibroblasts or 3T3 fibroblasts were implanted as a growth factor source in ICH mice. Neurogenesis and functional recovery was evaluated at 5 days post-ICH. BDNF treatment mice have enriched doublecortin (DCX) positive cells toward lesion and less brain tissue loss than the control. Both cell treatment groups have profound GFAP/EdU colocalizing cells and better functional improvement than the PBS control. Fibroblasts transplantation together with recombinant BDNF treatment has the potential benefit on neurogenesis in ICH mice. The early functional recovery may be due to growth factors provided or evoked by the implanted grafts. A potential approach could combine both gene and cell therapy for the treatment of brain injury.

In another study, we produced ischemic stroke in adult rats by the approach of middle cerebral artery occlusion (MCAO) and examined the infarct zone with MRI. The EPO-overexpressing NIH/3T3 (EPO-3T3-EGFP) cells were directly injected to the infarct zone. The brain function was assessed via modified Neurological Severity Score (mNSS). On day 14 after stroke induction, the infarct volume was measured again by MRI and the animal was euthanized for the study of angiogenesis and neurogenesis. The result of neurological assessment suggested that both 3T3-EGFP-treated and EPO-3T3-EGFP-treated groups showed significantly improvement of functional ability in both acute and chronic phase of ischemic stroke. In MRI examination, the recovery rate of the EPO-3T3-EGFP treated group could be up

to 62% and significantly higher than 3T3-treated group and MCAO control group. In immunohistochemistry, significant increase of cell proliferation in subventricular zone (SVZ) was demonstrated in EPO-3T3-EGFP treated group and 3T3-EGFP group, which may indicate implantation of EPO-3T3-EGFP cells and could further enhance the repairing process of infarct site in our MCAO animal model.

In summary, our data suggests that both BDNF-overexpressing and EPO-overexpressing NIH/3T3 cells treatments could provide stable release of BDNF/ EPO in the brain injury area, facilitate neurogenesis and neuroprotection ability that may contribute to the functional recovery of brain.

13:50-14:10

I-7

幹細胞組織工程於氣管再生醫學之應用

陳晉興 教授 台大醫學系外科 教授 台大醫院胸腔外科 主任 台大醫院醫療事務室 主任

摘要

以氣管植體行氣管重建手術至今仍是胸腔醫學最困難的挑戰,此乃肇因於氣管構造複 雜,而植體無論是來自死後捐贈者或以傳統人工合成均難以實現氣管再生。近年來隨著結合 幹細胞之組織工程的進展以及積層製造等工程科技的進步,足以模擬人體氣管構造並兼具生 理功能的人工氣管成為解決此項難題的新選項。本計畫擬結合自動化培養、生物反應器及智 慧型載體,大量培養幹細胞應用於氣管組織工程與氣管再生醫學。研究分為六個部分,第一 部分建置自動化智慧化細胞培養系統,可智慧分析幹細胞培養狀況,自動以機器手臂進行拿 取、放置、搖晃及敲打培養盤等細胞培養步驟,以利細胞量產。目前正在開發培養基專用影 像分析軟體,與建構影像分析環境控制箱。再結合第二部分研發含超音波強化刺激之生物反 應器系統,在懸浮式生物反應器中提供流體剪切、輔以超音波來刺激幹細胞生長分化成所需 之氣管相關細胞。目前已順利開發出小型化超音波刺激設備,並著手設計生物反應器雛型。 第三部份製作含幹細胞之 3D 列印氣管並建立智慧型細胞培養材料。目前已有初步 3D 列印氣 管供動物手術測試之用。第四部分負責建立兔子誘導性多能幹細胞、確立該細胞之品管指標 及其監測方法,並將其活體外分化潛能測試方法標準化,作為氣管組織工程所需之細胞來源。 目前已在固定培養該幹細胞中,並逐步建立品管指標及其監測方法。第五部分進行 3D 列印 氣管組織工程動物實驗,發展氣管再生技術。目前數次移植 3D 列印氣管至兔子,並將所得 經驗回饋,以最佳化列印氣管之設計。第六部分探討倫理與法規之相關問題,目前已完成全 球先進國家的幹細胞治療相關法規整理與比較,即將進入台灣民意調查階段,做為日後建立 適用於台灣相關法規的基礎。經由本計畫之執行不僅可提升相關生技產業之進展,也可成功 培育出跨領域人才,並透過倫理法規研究,促進本計畫成果之早日臨床應用。

14:10-14:30

I-8

Extracellular Matrix as a Treatment Strategy for TM Joint Disorder

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Abstract

Temporomandibular joint disorder (TMDs) is a common disorder in dental clinic including joint or muscles pain, joint clicking as well as limitation of jaw movement (chewing or opening). Based on previous studies, up to 75% of the population suffer from at least one sign of joint disorder. Approximately 33% have at least one symptom, such as facial pain and joint pain. In some basic research, the parts of structure in TMJ was damaged during joint inflammation including its fibrocartilage layer which containing extracellular matrix (ECM). The component of ECM include aggrecan, collagen, hyaluronic acid et al. For clinical therapy, besides splint therapy, hyaluronic acid is one of the methods which has been used for treatment of TMDs. It can provide lubrication and nutrition as well as to increase joint space and provide shock absorption. However, there is another ECM component named link protein which is a stabilizer to maintain the interaction between aggrecan and hyaluronic acid. The inflammatory response can damage the link protein resulting in the loss of the N-terminal 16 amino acid which is named as link N. It has ability to regulate inflammation and tissue repair in the fibrocartilage tissue of intervertebral disc (IVD) which is similar in the TMJ. Therefore, Link N supposed to be another potential material for joint repair in the future.

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14:30-14:50

I-9

預防蟹足腫的可能治療方案 Possible Solutions for Keloid Prevention Therapy

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Introduction: Keloids are claw-like fibrous scars that expand beyond the borders of the original wound after a skin injury. The etiology of keloid disease is believed to be genetically relevant but no single gene mutation has been detected so far. The interaction between multifactorial inheritance genes and environmental factors has been implicated. Keloid treatment remains a big challenge to medical doctors. Steroid injections and surgical revision are two best treatment options nowadays. Steroid treatment can cause tissue atrophy but surgical removal has a risk of keloid recurrence. Since extracellular matrices are key environmental factors, we prepared four groups of keloid wound (KW) gels and investigated their effects on keloid fibroblasts.

Materials and Methods

- 1. Harvest of normal (NF) and keloid fibroblasts (KF): NF and KF were harvested from patients' skin under the approval by the Institutional Review Board of the National Cheng Kung University Hospital.
- 2. Preparation of KW gels: Four groups of KW gels were prepared according to our patent application.
- 3. Cumulative population doubling of cells: NF and KF were cultured and passaged for 12 times after sub-confluence. The cumulative population doublings were calculated as Log(Nf/N0)/Log2.
- 4. Migration assay: NF and KF on cell inserts with 0.8 μ m membrane in DMEM-1% FBS were placed in a 24-well plate with DMEM-10% FBS. The number of cells migrated onto the reverse side of membrane was scanned by a high throughput screening Microscope. In another study, the migration areas of NF and KF on various KW gels coated surface were compared.
- 5. Matix contraction assay: NF and KF were mixed with collagen or various KW gels respectively and placed in a 24-well plate. The percentage of matrix contraction by cells after 48 hrs of incubation was calculated and compared.
- 6. Expression of keloid-related mRNA: The mRNAs from NF and KF at passages 3 and 6 cultured in various KW gels were extracted and expressions of SP-1, PAI-1, PAI-2, Cyr 61, TGF- β 1, TGF- β 2, TGF- β 3, Col, Fn, α -SMA, CTGF were quantified by real-time PCR.

Results: KF were larger than NF. The cumulative population doublings of KF were significantly faster than NF. KF also migrated faster than NF. The contraction capacity of KF in collagen matrix was higher than NF. Migration area and contraction percentage of KF cultured in KW3 and KW4 gels were similar to NF.

The mRNA expression of PAI-1, PAI-2, Collagen-I, Fibronectin, α -SMA, CTGF, and TGF- β 2 in KF were significantly higher than NF. However, when KF were cultured in KW3 and KW4 gels, the above mRNA expression were similar to NF.

Conclusions: Four groups of KW gels were prepared and their effects on the cellular functions and expression of KF and NF were studied. KW gels have the potential to become a clinical therapy to prevent keloid formation during wound healing.

14:50-15:10

I-10

Soft Tissue Regeneration, Reconstruction and Neural Repair in Amyotrophic Lateral Sclerosis (ALS)

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Abstract

Recent advances in pluripotent stem cell (PSC) research have facilitated the generation of human induced pluripotent stem cells (human iPSCs) from skin fibroblasts, thus offering an source of patient-specific disease-relevant neuronal cells neurodegenerative diseases, such as ALS. Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive neurodegenerative disorder. Typical symptoms and signs are caused by muscle weakness and atrophy throughout the whole body due to the degeneration of the upper and lower motor neurons. Individuals affected by the disorder may ultimately lose the ability to initiate and control all voluntary movement, except those in eyes, bladder, and bowel, etc. Human PSCs offer a unique tool in new drug discovery of ALS or other neurodegenerative diseases as high-throughput screening platforms. Human PSCs can also derive various subtypes of neurons or glial cells for supporting and reorganizing the intact nervous system. Here I will give a review of how human ALS in vitro models have been used so far, what discoveries they have led to since 2008, and how the recent advances in technology combined with the genetic discoveries, have widened the horizon of ALS research, especially for either new drugs or new therapies development.

Oral Presentations

16:20-16:30

0-1

玻尿酸微環境強化辛伐化汀所誘導之脂肪幹細胞軟骨化及軟骨缺損重建 Hyaluronan Microenvironment Enhances Simvastatin-induced Chondrogenesis and Cartilage Defect Regeneration in Human Adipose Derived Stem Cells

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Introduction: Simvastatin (SIM) increases bone morphogenetic protein-2 (BMP-2), which is shown to contribute to chondrogenesis and osteogenesis of mesenchymal stem cell. Hyaluronan (HA) is one of the main extra cellular matrices during the early stage of chondrogenesis, and we previous found that HA microenvironment initiates and promotes chondrogenesis of adipose derived stem cells (ADSCs). In this study, we hypothesize that HA could promote the chondrogenic effect and reduce osteogenic effect of SIM on ADSCs, and this can be applied for ADSC-based articular cartilage defect regeneration.

Materials and Methods: The hADSCs were cultured in HA-coated well, and treated with SIM. The gene expression of BMP-2 by hADSCs was tested. Chondrogenesis of hADSCs was tested by cell aggregations, and chondrogenic genes (SOX-9, collagen type II: COL-II and aggrecan) and sulphated glycosaminoglycan (sGAG) synthesis. Osteogenesis including osteogenic gene (osteocakin) expression and calcium deposition by hADSCs were also tested. The chondral defect created in explants of osteochondral disc were used as the ex-vivo model. The ADSCs cultured in HA-encapsulated fibrin hydrogels (HA/Fibrin) implanted into the chondral defect then treated SIM was used to test cartilage defect regeneration. The cartilage regeneration was evaluated by neo-formation of cartilaginous tissue and sGAG content in the surrounding tissue.

Results: The SIM treatments enhanced BMP-2 gene expression of ADSCs and the combination of SIM with HA shows more enhanced BMP-2 expression. The combination of HA with SIM also showed higher chondrogenesis on ADSCs including cell aggregation, chondrogenic genes expressions (SOX-9, collagen type II and aggrecan) and sulphated glycosaminoglycan (sGAG) synthesis. HA also reduced SIM-induced osteogenic gene (osteocalcin) expression and calcium deposition by ADSCs. Blocking the BMP-2 function by Noggin reduced the chondrogenic genes expression of ADSCs. The ADSCs cultured in HA/Fibrin-implanted defect treated with SIM showed the highest neo-formation of cartilaginous tissue in comparison to Fibrin- or HA/Fibrin-implanted defects.

Discussion : Our result shows that the synergic effect of HA with SIM-induced BMP-2 promote chondrogenesis of ADSCs, and can be applied for ADSC-based articular cartilage defect regeneration. This result shows the local cue (HA microenvironment) on affecting chondrogenesis and cartilage regeneration of BMP-2 in ADSCs induced by SIM.

16:30-16:40

0-2

自體脂源性幹細胞治療燙傷神經性疼痛

Autologous Adipose-Derived Stem Cells Reduce Burn-Induced Neuropathic Pain in a Rat Model

黄書鴻 1.2 吳昇樺 3 林岑紘 1

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Introduction: Burn scar pain is considered as neuropathic pain. The anti-inflammation and anti-neuroinflammation effects of adipose-derived stem cells (ASCs) were observed in several studies. We designed a study using a murine model involving the transplantation of autologous ASCs in rats subjected to burn injuries. The aim was to detect the anti-neuroinflammation effect of ASC transplantation and clarify the relationships between ASCs, scar pain, apoptosis and autophagy.

Materials and Methods: We randomized 24 rats into 4 groups as followings: Group A and B, received saline injections and autologous transplantation of ASCs 4 weeks after sham burn, respectively; Group C and D, received saline injections and autologous transplantation 4 weeks after burn injuries. A designed behavior test was applied for pain evaluation. Skin tissues and dorsal horn of lumbar spinal cords were removed for biochemical analysis.

Results: ASC transplantation significantly restored the mechanical threshold reduced by burn injury. It also attenuated local inflammation and central neuroinflammation and ameliorated apoptosis and autophagy in the spinal cord after the burn injury.

Discussion: The differentiation of ASCs and their paracrine effect both contribute to their therapeutic efficacy, which can also be affected by the route and the cell amount administered. Compared to systemic injection and its direct homing effect, local injection results in lower survival of engrafted ASCs, especially in damaged sites [23,24]. Therefore, the paracrine effect is considered to play a major role in treatment by local injection

Conclusions: Conclusion: In a rat model, autologous ASC subcutaneous transplantation in post-burn scars elicited anti-neuroinflammation effects locally and in the spinal cord that might be related to the relief of post-burn neuropathic pain and attenuated cell apoptosis. Thus, ASC transplantation post-burn scars shows the potential promising clinical benefits.

16:40-16:50

0-3

副甲狀腺素 1-34 藉由自噬作用改善大鼠膝關節炎及功能 Parathyroid Hormone (1-34) Ameliorated Knee Osteoarthritis and Function in Rats Via Autophagy

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Introduction: Anterior cruciate ligament (ACL) tear usually leads to osteoarthritis (OA). However, parathyroid hormone (PTH) (1-34) was found to alleviate OA progression in a papain-induced OA model. Autophagy is a protective mechanism in normal cartilage, and its aging-related loss is linked with chondrocyte death and OA. Thus, we examined the roles of autophagy in PTH treatment on OA after ACL transection (ACLT).

Materials and Methods: Thirty-six rats were randomized into three groups: control group, ACLT-induced OA (ACLT-OA) group, and OA with intra-articular PTH (1-34) treatment group. Knee function was evaluated by weight-bearing and treadmill tests. Cartilage matrix was determined by a histological evaluation of glycosaminoglycan (GAG), the OARSI score, chondrocyte apoptosis, and immunohistochemistry.

Results: Rats in the ACLT-OA group had significantly decreased weight-bearing and running tolerance. The histological results indicated that functional markers (GAG, collagen type II) and chondrocyte autophagy had decreased, but that the OARSI score, terminal differentiation markers (collagen type X, Indian hedgehog), and chondrocyte apoptosis had increased in the OA group. Additionally, PTH (1-34) treatment significantly improved weight-bearing and treadmill test scores, preserved functional markers, and reduced the OARSI score and terminal differentiation marker. Finally, PTH (1-34) ameliorated chondrocyte apoptosis by regulating the expressions of autophagy-related proteins, through reducing mTOR and p62, and enhancing LC3 and Beclin-1.

Discussion : In this study, we demonstrated that intra-articular PTH (1-34) treatment can alleviate ACLT-induced OA. Potential mechanisms of PTH's effects are the reduction of terminal differentiation of chondrocytes, through the reduction of Ihh and Col X expression and the maintenance of GAG and Col II expression. PTH may also decrease chondrocyte apoptosis and increase autophagy, increasing the expression of LC3 and Beclin-1 and decreasing the expression of mTOR and p62. Finally, PTH (1-34) may be active in the treatment of ACL injury by delaying the progression of OA. With the continuing unmet treatment needs of an ACL injury, regardless of ACL reconstruction, it is necessary study the effect of PTH (1-34) following ACL injury in an attempt to alleviate OA progression.

Conclusions: Reconstructive surgery after ACL rupture cannot prevent OA occurrence. Intra-articular PTH (1-34) treatment can alleviate OA progression after ACLT, and improve joint function and histological molecular changes. Possible mechanisms are reducing chondrocyte terminal differentiation and apoptosis, with increasing autophagy.

16:50-17:00

0-4

利用誘導性多能幹細胞分化為軟骨細胞並結合 3D 支架及誘導因子測試修補能力 Using Induced Pluripotent Stem Cells Derived Chondrocytes Culture in 3D Scaffold Combine with Factors to Test the Therapy Effect

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Introduction: Articular cartilage (AC) is composed of chondrocytes, responsible for abundant matrix synthesis and maintenance. When pathological or traumatic damaged happened, AC does not heal spontaneously and resulted in Osteoarthritis (OA). OA is the most common musculoskeletal disease in the elderly. However, cartilage defect and OA currently lack effective therapeutic methods. Stem cells provide hope for cell therapeutic methods for cartilage defect and OA. In all type of stem cells, embryonic stem (ES) cells and induced pluripotent stem (iPS) cells are the most powerful cells that could differentiate into all three-layer cells, including chondrocyte.

Materials and Methods: Previously, we generated a novel iPS-OSH cells that under hypoxic conditions in the absence of viral infection and oncogenic factors. In this study, we differentiated the iPS-OSH cells into chondrocyte and cultured on the 3D bioresorbable scaffold (polycaprolactone) to compare the proliferation and differentiation ability between different factors treatment, including transforming growth factor- β 1 (TGF- β 1) and/or Granulocyte Colony-Stimulating Factor (G-CSF). We evaluated the cell proliferation rates and chondrogenic markers with several approach including trypan blue exclusion assay, alcian blue staining, immunofluorescent staining and real-time RT-PCR.

Results : The results showed that the differentiation and proliferation rates of chondrocytes were accelerated in 3D culture environment compared to the conventional 2D culture system. Additional supplements with TGF- $\beta1$ and G-CSF also promoted the differentiation and proliferation rates of chondrocytes both in both culture systems. Overall, iPS-OSH cells exhibited the highest chondrogenic activities in the 3D culture environment supplied with TGF- $\beta1$ and G-CSF.

Discussion : Chondrocytes cultured in 3D culture environment could accelerate differentiation and proliferation rates with comparing to the conventional 2D culture system. Moreover, both TGF- $\beta1$ and G-CSF supplements could promote the differentiation and proliferation rates of chondrocytes in 2D and 3D culture systems. With TGF- $\beta1$ and G-CSF supplements, iPS-OSH cells exhibited the highest chondrogenic activities in the 3D culture environment.

Conclusions: The present study assessed the clinical application of iPS cells and suggested a novel therapeutic strategy to improve the cartilage defect which lacking effective therapeutic methods nowadays.

17:00-17:10

0-5

含三鈣磷酸鹽可注射式氧化透明質酸/己二酸二醯肼水膠做為骨填補物之應用 An Injectable Oxidized Hyaluronic Acid/Adipic Acid Dihydrazide/Tricalcium Phosphate Hydrogel as Bone Substitutes

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前言:在臨床上使用的骨填充物通常以顆粒狀或塊狀等不規則型為主,往往無法與缺損部位緊密契合。在本研究中我們以氧化透明質酸(oxidized hyaluronic acid, oxi-HA)/己二酸二醯肼(adipic acid dihydrazide, ADH)水膠加上具骨引導特性的三鈣磷酸鹽形成一個可注射且原位成型的骨填補物(oxi-HA/ADH/TCP, oxiHAT),能以注射方式填補骨缺損的位置,也可在缺損部位快速成型,避免骨髓腔血液流出造成骨填補物崩解,植入骨缺損位置後,隨著新生骨組織的形成,骨填補物可逐漸降解,完成骨組織再生重建。

材料與方法:可注射式骨填補物製備 利用氧化劑將透明質酸開環形成帶有醛基之氧化透明質酸(oxidized hyaluronic acid, oxi-HA),隨後以 PBS 溶解成 10%w/v oxi-HA 溶液,稱為solution A。另外,製備 5%w/v 已二酸二醯肼(ADH)溶液,分別與不同濃度的三鈣磷酸鹽 10%、20%、30%(w/v) 混合成為 solution B。骨填補物製備時,將 solution A 及 solution B 以等體積的方式混合,即可透過交聯反應形成固態的水膠(oxiHAT10,oxiHAT20,oxiHAT30)。骨填補物性質分析 以流變儀(Rheometer)評估 oxi-HA/ADH/TCP 骨填補物的流變性質,由 G'(elastic modulus)及 G"(viscous modulus)計算其成膠時間(gelation time)。同時評估骨填補物的膨潤度(swelling index)、體外降解性質(in-vitro degradation)、電子顯微鏡(SEM)觀察材料的內部結構及孔隙度,以及細胞毒性測試。

結果與討論:流變儀測試結果顯示,加入三鈣磷酸鹽,隨著三鈣磷酸鹽含量越高,其在室溫定的成膠時間隨之增加,oxiHAT30的成膠時間在室溫下約為30分鐘,而在37℃時成膠時間則縮短為5分鐘。 膨潤度測試結果顯示,在成膠初期膨潤指數(swelling index)會顯著下降在第7天時,oxiHAT10、oxiHAT20及 oxiHAT30膨潤指數分別為70%、78%及88%,隨後緩慢下降,四週後,其膨潤指數分別為44%、66%和70%。結果顯示三鈣磷酸鹽含量越高,樣品收縮率越低。在體外降解測試中,三組水膠在4周時降解率分別為16%、7%及4%,隨著TCP的含量增加,降解率越低。樣品經過臨界點乾燥後,在電子顯微鏡觀察下顯示 oxiHAT 骨填補物內部可形成相互連接的孔洞,有利骨組織或血管生長進材料中。在不同TCP含量下,其平均孔徑分別為26.3μm、16.2μm、14.9μm。另外也可以發現TCP粉末可均勻分布於水膠內,有助於骨組織再生。另外,在細胞毒性測試顯示無顯著細胞毒性產生。

結論:本研究中提出一種可注射式骨填補物(oxiHAT)。oxiHAT 可在室溫下混合且維持足夠的操作時間(約30分鐘),並可透過注射的方式填補缺損部位,使術後傷口最小化,降低傷口感染風險,且三鈣磷酸鹽具有骨引導特性,可幫助骨組織修復。未來也可應用於藥物釋放系統,做成含抗生素之可注射式骨填物,降低患者術後感染骨髓炎風險。

08:40-08:50

S-1

探討由誘導性多功能幹細胞分化出低癌化特質之間質幹細胞其免疫調節特性 Differentiation of MSCs from Human iPSCs Results in Downregulation of c-Myc & DNA Replication Pathways with Immunomodulation Towards CD4 & CD8 T cells

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Introduction: Multilineage tissue-source mesenchymal stem cells (MSCs) possess strong immunomodulatory properties and are excellent therapeutic agents, but require constant isolation from donors to combat replicative senescence. The differentiation of human induced pluripotent stem cells (iPSCs) into MSCs offers a renewable source of MSCs; however, reports on their immunomodulatory capacity have been discrepant.

Materials and Methods: Using MSCs differentiated from iPSCs reprogrammed using diverse cell types and protocols, and in comparison to human embryonic stem cell (ESC)-MSCs and bone marrow (BM)-MSCs, we performed transcriptome analyses and assessed for functional immunomodulatory properties.

Results: Differentiation of MSCs from iPSCs results in decreased c-Myc expression and its downstream pathway along with a concomitant downregulation in the DNA replication pathway. All 4 lines of iPSC-MSCs can significantly suppress *in vitro* activated human peripheral blood mononuclear cell (PBMC) proliferation to a similar degree as ESC-MSCs and BM-MSCs, and modulate CD4 T lymphocyte fate from a type 1 helper T cell (Th1) and IL-17A-expressing (Th17) cell fate to a regulatory T cell (Treg) phenotype. Moreover, iPSC-MSCs significantly suppress cytotoxic CD8 T proliferation, activation, and differentiation into type 1 cytotoxic T (Tc1) and IL-17-expressing CD8 T (Tc17) cells. Co-culture of activated PBMCs with human iPSC-MSCs results in an overall shift of secreted cytokine profile from a pro-inflammatory environment to a more immunotolerant milieu. iPSC-MSC immunomodulation was also validated *in vivo* in a mouse model of induced inflammation.

Discussion : MSCs from iPSCs reprogrammed from diverse cell types and protocols are multilineage and downregulate c-Myc and proliferative pathways compared to ESC cells. Moreover, all lines of iPSC-MSCs were strongly immunomodulatory *in vitro* as well as *in vivo*, shifting the cytokine milieu as well as effector CD4—and even CD8—T cells toward immunomodulatory populations, thereby supporting that iPSC-MSCs may be good therapeutic candidates.

Conclusions: These findings support that iPSC-MSCs possess low oncogenicity and strong immunomodulatory properties regardless of cell-of-origin or reprogramming method, and are good potential candidates for therapeutic use.

08:50-09:00

S-2

幾丁聚醣在嗅覺失能之動物模式中對嗅覺上皮再生之影響 The Effect of Chitosan on the Olfactory Neuroepithelial Regeneration in an Anosmic Animal Model

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Introduction: The prevalence of olfactory dysfunction is 12.3% in Taiwan [1]. This dysfunction significantly affects quality of life, such as appetite and flavors. The first relay point of odor sensation is the olfactory neuroepithelium (ON), comprising basal cells and various stages of olfactory receptor neurons (ORNs). Clinically, this dysfunction commonly results from reductions in the number and/or degree of differentiation of ORNs and atrophy of the ON. Currently, clinical practice still has no adequate approach showing a good prognosis. Of note, chitosan has been widely studied for regenerative purposes, including neuroprotection following ischemic stroke. However, whether chitosan enhances the ORN differentiation and the ON regeneration remains unknown.

Materials and Methods: For an *in vitro* test, olfactory neuroepithelial cells (ONCs) were isolated from embryonic day 17 of rats, and then cultured with/without 0.1 mg/ml chitosan for 9 days. For an olfactory-lesioned animal model, 3-methylindole (3-MI) was used to destroy the ON and chitosan was intranasally administered twice a week. The effect of chitosan treatment is assessed with immunocytochemistry, immunohistochemistry, western blots, and food-finding test.

Results: In an *in vitro* test, the number of mature ORNs, expressing *olfactory marker protein* (OMP), rose with days in chitosan-treated groups, accompanied with a reduced number of immature ORNs, expressing β III tubulin. In the animal experiments, the duration of finding food after chitosan treatment decreased from exceeded 5 minutes to around 80 seconds on day 28 following 3-MI-induced lesions. Further, histological images showed that both the ON thickness and the OMP expression gradually recover after chitosan treatment at appropriate time point, whereas those without chitosan treatment may pause at the stage of immature ORNs owing to the highest β III tubulin expression among groups.

Discussion: Timing is a critical point in medication administration. In this study, we start treatment on day 10 following 3-MI-induced lesions since basal cells proliferate at the initial stages of regeneration, and insufficient amount of basal cells may cause incomplete recovery of olfactory function [2].

Conclusions: Consequently, chitosan would promote the ORN maturation and the ON regeneration, and be a promising clinical application in the future.

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09:00-09:10

S-3

成鼠的無疤癒合特色:膠原蛋白的延遲性生成及成肌纖維母細胞的啟動缺乏 Scarless Healing in Adult Mice is Achieved by Delayed Collagen Network Regeneration without Myofibroblast Activation

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Introduction: In contrast to fetal scarless healing, adult skin tends to repair with fibrosis when injured, leading to scar formation. Whether and how scarless healing in adults can be achieved is unclear

Methods and Results: We found that, in contrast to extensive scarring induced by macrothermal damage, adult mice could heal scarlessly when the thermal injury was divided into zones microthermal damage. Though the microthermal injury also induced epidermal necrosis with dermal collagen denaturation, there was no myofibroblast activation. The skin was reepithelialized within 24 hours through migration of surrounding keratinocytes but the restoration of dermal collagen network showed a distinct slow process, contrasting the quick myofibroblast-mediated collagen production in macrothermal damage. In vivo multiphoton microscopic imaging showed that the regeneration of dermal collagen network was not restored until 4-6 months later with deposition of newly-formed collagen fibers extending from the surrounding existing collagen network toward the wound center. The structure of new collagen fibers merged with and better mimicked the adjacent normal collagen network both in density and architecture

Conclusions: Our results showed that adult skin still preserves the potential to heal without scarring. Tilting fibrotic healing toward scarless healing can be a potential strategy to reduce scar formation in adult skin.

09:10-09:20

S-4

探究三維球體培養方式於幹細胞與體細胞之生物異同性 Divergent Biological Consequences of 3-Dimensional (3d) Sphere Formation for Stem Cells Vs. and Somatic Cells

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Introduction: 3-dimensional (3D) culture for spheroid formation is increasingly used as a method to better mimic physiological states. However, the biological consequences of 3D spheroid formation could be drastically differed 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 thus is known to 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 the biological differences in the starting cells, however, there still should be a "core process" governing the ability for 3D sphere formation.

Materials and Methods: We performed transcriptome analysis on conventionally 2D-cultured and 3D spheroid ESCs and SSCs to explore the "core process" for 3D spheroid formation.

Results: As expected, pluripotency markers such as Oct4, Sox2, Nanog, & Klf4 were significantly down-regulated in ESCs after 3D sphere formation. But, these four markers were not significantly upregulated in somatic cells after spheroid formation. Convergent processes for both ESCs and SSCs include hypoxia and cell cycle arrest. Our data also demonstrate the cell cycle arrest after sphere formation via flow cytometry. Other highly expressed pathways include metabolic pathways involved in metabolism and oxidative phosphorylation. We found a metabolism pathway can mediate cytoskeleton rearrangement to regulate spheroid formation across diverse cell types.

Discussion: 3D spheroid formation is a process for lineage differentiation on ESCs; but a strategy to maintain SSC stemness. While the mechanisms of spheroid formation involved in of these two types cell is not due to the pluripotency, but a metabolism pathway.

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.

09:20-09:30

S-5

含谷氨酸之電紡絲生物支架促進幹細胞衍生視網膜神經節細胞之成熟與生長 Promoting the Maturation and Growth of Induced Pluripotent Stem Cell (Ipsc)-Derived Retina Ganglion Cells Using Glutamate-Containing Biocompatible Scaffolds

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Introduction: The optic nerve, composed of more than 1 million retinal ganglion cells (RGCs), functions as the most important transmission of visual information from the retina to the brain. Progressive degeneration of RGCs leads to irreversible visual disturbance in advanced glaucoma and other optic neuropathies. Currently, there is no clinically effective treatment for RGC degeneration. However, the development of stem cell therapy provides us a potential cure for this problem. Several kinds of retinal neurons, including retinal pigment epithelium (RPE), photoreceptors, and RGCs, have reported to be successfully induced from embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs). Among them, the development of cell therapies for optic neuropathy remains challenging due to the need of long and functional neurites for stem cell-derived RGCs to survive and extend through the original optic nerve track. The purpose of this study is to develop a bioengineered scaffold system that promotes stem cell-derived RGC production and may serve as a supportive substrate for potential surgical transplantation in the future.

Materials and Methods: In the present study, we used the established iPSC cell line for all the experiments. The induction of hiPSC differentiation employs a procedure based on SFEB methods. After 27 days culture of retinal differentiation and maturation protocols, the adhesion culture starts when the aggregates are transferred to 3% Matrigel-coated biocompatible scaffolds or cover glasses. Different electrospun scaffolds were used for investigation. Cell characteristics were surveyed by cell morphology, real-time PCR, and immunofluorescence staining. The rate of neurite outgrowth, neurite lengths, and the interface between neurite and scaffolds were also analyzed and quantified.

Results: We can smoothly produce the electrospun scaffolds with good ocular biocompatibility and 3D fibrous structures. (Some of them are now under application of patent.) Glutamate-containing biocompatible scaffolds showed promising results in promoting the maturation and growth of induced pluripotent stem cell (iPSC)- derived retina ganglion cells. Cells in that group demonstrated much more robust growth of neurites as well as RGC-specific markers. Retinal organoid structure could also be observed soon after adhesion culture.

Discussion : Glutamate-containing biocompatible scaffolds showed promising results in promoting the maturation and growth of induced pluripotent stem cell (iPSC)- derived retina ganglion cells. Furthermore, the quick formation of retinal organoid structures demonstrated the simultaneous differentiation of photoreceptors under the RGC layer. For the first time, this kind of electrospun scaffold was used as a simulated substrate to investigate this mechanism.

We proposed that the surface properties and the slow-release glutamate may both facilitate the differentiation and maturation of iPSC- derived retina ganglion cells.

Conclusions: Glutamate-containing biocompatible scaffolds promotes the maturation and growth of induced pluripotent stem cell (iPSC)-derived retina ganglion cells and can potentially serve as an artificial RGC stem cell supporter.

09:30-09:40

S-6

客製化之生物可降解組織工程氣管 The Customized Artificial Trachea with Elastic and Biodegradable Properties

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Introduction: Tracheal repair and reconstruction is a big challenge in current medicine. The only way to treat patients with diseases such as tracheal stenosis is to resect the stenosis path. However, the method suffers from limited tracheal length and sources. Moreover, the currently available tracheal prosthesis has the problems of mechanical mismatch and foreign body reactions. Here we sought to develop a customized artificial trachea for possible applications in tracheal tissue engineering.

Materials and Methods: The waterborne biodegradable polyurethanes were synthesized in our laboratory. The customized artificial tracheas were fabricated by a self-designed three-dimensional printer. The mechanical characteristics of artificial trachea were measured by tensile tests and dynamic mechanical analyses. Adipose mesenchymal stem cells (ADSCs) derived from adult male New Zealand white rabbits were seeded on the artificial trachea and implanted to bridge the gap of rabbit trachea.

Results : The customized artificial trachea and native rabbit trachea demonstrated similar flexural moduli. The flexural moduli were ~ 10.2 and ~ 9.0 kPa for the artificial trachea and native rabbit trachea, respectively. The customized artificial trachea has higher tensile stress than the commercial tracheal stent. The customized artificial trachea and commercial tracheal stent showed tensile stresses of ~ 9.5 and ~ 3.8 N, respectively. The rabbit receiving the ADSC-seeded tracheal replacement could stay alive normally over a period of 4 weeks without any phenomenon of breathe difficulty.

Discussion: The customized artificial trachea has mechanical properties quite matched to those of native rabbit trachea. The chemical designs for the polymeric structure of polyurethanes and the structural stability of artificial trachea contributed to the proper mechanical function of the customized artificial trachea. The rabbit survival over a period of 4 weeks indicated the feasibility of the designed constructs in tracheal tissue engineering. The appropriate mechanical stability, biocompatibility, and biodegradation as well as the chondrogenic differentiation of ADSCs may have contributed to the biological performance of the tissue engineered artificial trachea.

Conclusions: A customized artificial trachea was successfully fabricated. The flexural modulus of customized artificial trachea (~ 10.2 kPa) is similar to that of native rabbit (~ 9.0 kPa). The rabbit can survive over a period of 4 weeks after implantation of the customized artificial trachea. The customized artificial trachea may have potential applications in tracheal reconstruction.

Acknowledgments: This work was supported by MOST 105-2218-E-002-007.

09:40-09:50

S-7

後轉譯和表觀遺傳調控在人類間葉幹細胞之免疫調節功能 Role of Post-translational & Epigenetic Regulation in Human Mesenchymal Stem Cell (MSC) Immunomodulatory Properties

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Introduction: Human mesenchymal stromal cells (MSCs) are multipotent somatic progenitors with strong immunomodulatory properties. We and others have shown that human embryonic stem cell-derived (hE-), bone marrow- (BM), placenta-derived MSCs (P-MSCs) express HLA-G that impart immunomodulatory actions. HLA-G is a non-classical major histocompatibility complex (MHC) class I molecule known to be normally expressed only by placental cytotrophoblasts and in the thymus, which are both transient organs. Thus, understanding of regulatory mechanisms involved in expression of this elusive molecule has proven difficult, relying almost exclusively on cancer cell line data and overexpression studies.

Materials and Methods: Using human BM- and P-MSCs, as well as human term placental tissue, we investigated the molecular mechanisms involved in HLA-G expression in these normal cells/ tissue.

Results: We found that BM- and P-MSCs express several but not all HLA-G isoforms, with expression of unique glycosylated forms. Upon interferon- IFN- stimulation, HLA-G levels are upregulated in MSCs but not the JEG-3 choriocarcinoma cell line. Most interestingly, methylation patterns in the HLA-G proximal promoter of human BM- as well as P-MSCs are comparable to human placental tissue but not to JEG-3.

Discussion: Our study implicates the importance of using normal cells and tissues for physiologic understanding of tissue-specific transcriptional regulation, and the utility of human MSCs in understanding the transcriptional regulation of HLA-G, an important but elusive immunomodulatory molecule.

Conclusions: Regulation of the non-classical MHC class I molecule HLA-G expression in human MSCs recapitulate normal, physiologic processes which involve post-translational and epigenetic mechanisms.

09:50-10:00

S-8

利用間質幹細胞及成骨細胞特異的轉錄因子活性建立快速穩定的系統 以利篩選有益成骨的植物雌激素

A Rapid& Robust System for Selection of Osteogenic Phytoestrogens Using Mesenchymal Stem Cells (MSCs) & Osteogenic Transcription Factor/co-factor Reporter Screening

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Introduction: Rapid increases in the incidence of osteoporosis are due to the aging of worldwide populations. While multilineage mesenchymal stem cells (MSCs) appear to be excellent cellular agents to reverse the bone loss that occurs with this disease, actual implementation of cell therapy is not feasible due to the systemic nature of osteoporosis. On the other hand, the 'gold-standard' *in vitro* osteogenic assay of calcium mineralization for MSCs are well established but lengthy, taking up to 1 month for completion. We therefore took advantage of *in vitro* MSC osteogenic capacity and in combination with reporter assays for multiple relevant osteogenic transcription factors (TFs) and/or co-factors,andestablished a rapid and robust system of screening for osteogenic compounds.

Methods Materials We established select for a rapid systemto osteogenicphystoestrogens and compounds using the combination of MSC early-osteogenesis assay of alkaline phosphatase (ALP) expression, and anosteogenic TF/co-factor-luciferase reporter assay. Validation was performed with thematureosteoblast functional assay of mouse MSC calcium mineralization as well as assessing for expression of the osteogenic factor BMP-2.

Results: Using this combination screening system, we are able tonot only shorten the selection process for osteogenic phytoestrogens as well as other compoundsfrom the usual 3~4 weeks to just 3 days, but also perform screening of multiple compounds simultaneously for comparison ofosteogenic potency. To validate the robustness of our system, we verified that these compoundscan elicit calcium deposition in MSCs as well as induce high levels of BMP-2protein expression in a dose-dependent fashion.

Discussion: Results elicited from the osteogenicTF-luciferase reporter assay arein close alignment with ALP activity as well as more mature osteogenic functional assays ofMSC calcium deposition and BMP-2 expression. Therefore, the use of MSCs and early functional assays of osteogenesis provide rapid and robust results for *in vitro* screening of osteogenic compounds.

Conclusions: Our findings demonstrate the utility of MSCs in establishingrapid and robust platforms for drug screening, and in the translational use of these versatile stem cells in *in vitro* settings.

15:30-15:40

S-9

開發明膠/抗壞血酸凍膠應用於角膜基質組織工程 Development of Gelatin/Ascorbic Acid Cryogels for Potential Use in Corneal Stromal Tissue Engineering

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Introduction: To offer an ideal hospitable environment for corneal keratocyte growth, the carrier materials can be functionalized with incorporation of signaling molecules to regulate cell biological events. This study reports, for the first time, the development of gelatin/ascorbic acid (AA) cryogels for keratocyte carriers in vitro and in vivo.

Materials and Methods: The cryogel samples were fabricated by blending of gelatin with varying amounts of AA and carbodiimide cross-linking via cryogelation technique. The carriers were characterized to examine their structures and functions. The in vitro/vivo biocompatibilities and anti-oxidative stress effects of materials for tissue reconstruction applications were assessed.

Results: Hydrophilic AA content in the carriers was found to significantly affect cross-linking degree, pore size, mechanical, biological stability and AA release profile. The cryogel carriers with low-to-moderate AA loadings were well tolerated in vitro/vivo tissues. Although higher incorporated AA level contributed to enhanced metabolic activity and biosynthetic capacity of keratocytes grown on cryogel matrices, the presence of excessive amounts of AA molecules could lead to toxic effect and limit cell proliferation and matrix production. The cytoprotective activity against oxidative stress was shown to be strongly dependent on AA release, which further determined cell culture performance and tissue restoration efficacy.

Discussion: With the optimum AA content in carrier materials, intrastromally implanted cell/cryogel constructs exhibited better capability to enhance tissue matrix regeneration and transparency maintenance as well as to mitigate corneal damage in an alkali burn-induced animal model.

Conclusions: It is concluded that understanding of antioxidant molecule-mediated structure-property-function interrelationships in gelatin/AA cryogels is critical to designing carrier materials for potential use in corneal stromal tissue engineering.

15:40-15:50

S-10

Development of Gelatin-Graphene Oxide Hydrogel by Argon-Microplasma for Orthopedics Tissue Engineering Applications

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Introduction: Gelatin is a well known biocompatible denatured biopolymer and a potential material for pharmaceutical, biomedical and tissue engineering applications. However, the drawbacks such as poor mechanical properties, high solubility and contagious nature restrictits biomedical applications. Recently, graphene oxide is used as an additive in biopolymers used in tissue engineering and regenerative medicine due to it's non-toxicity at low concentrations with improved biomaterial scaffold properties such as cellular attachment and proliferation. Furthermore, nanocomposite biopolymeric hydrogels which have recently attracted significant attention in tissue engineering are generally synthesized by traditional toxic chemical cross-linking processes. To overcome these problems, in this present study we successfully report the first ever attempt to fabricate gelatin-graphene oxide nano-composite hydrogel scaffolds by using microplasma as an effective and nontoxic method of crosslinking for future orthopedics tissue engineering and clinical applications. Consequently, we aim to create a safe and favorable environment for efficient cellular and material interaction within tissue environment for tissue regeneration and repair.

Materials and Methods: Optimized Ar-microplasma conditions (2,500 V and 8.7 mA) for 15-30 min with a gas flow rate of 0.100 slpm was found to be most suitable for producing the desired gel-GO nanocomposite hydrogel. The developed hydrogel was characterized by SEM, confocal microscopy, water contact angle measurement and rheology. The cell viability, cytotoxicity and cellular proliferation were examined by MTT assay and live/dead assay on L929 and MG63 cell lines respectively.

Results: The pore size of the hydrogel was found to be $287 \pm 27 \, \mu m$ with water contact angle of $78^{\circ} \pm 3.7o$. Rheological data revealed the well maintained tunable viscoelasticity of the hydrogel even up to 37 oC (body physiological temperature). Results of the MTT assay, microscopy, and live/dead assay exhibited better cell viability at 1% (w/w) of high-functionality GO in 8% purified gelatin.

Discussion : The adequate pore size of the hydrogel scaffold from SEM data proved it to be an ideal scaffold for orthopedics tissue engineering in resonance with cellular adhesion,

attachment and proliferation. In addition, results have indicated that Ar-microplasma treated gel-GO nano-composite hydrogel meets standard qualities of hydrogels such as tunable mechanical strength and degradation kinetic. Thus fabricated gel-GO hydrogels can also be tailored and controlled as per the need through Ar-microplasma treatment. Hence, Ar-microplasma treated Gelatin-GO scaffolds are promising materials especially for biomedical applications with the ability to support cellular proliferation, adhesion, and differentiation with little or no cytotoxicity.

Conclusion : The Ar-microplasma treated tunable designed scaffold may be used to support cell growth without toxicity for both hard and soft tissue regeneration.2

15:50-16:00

S-11

Development of the Genipin-Crosslinked Adipose Stem Cell Derived ECM Sponge Containing Graphene Oxide for Skin Tissue Engineering

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Introduction: Healing of the deep and chronic wound fails due to poor dermal regeneration and it leads to scarring, amputations and death. The conventional treatment of the deep wound is the autologous skin split graft creating donor site morbidity. Therefore tissue engineering approaches using biological or synthetic scaffolds have been emerged to enhance wound healing. Recently, tissue and cell derived extracellular matrix (ECM) scaffold are gaining research interest among them due to natural preservation of bioactive compositions such as, collagen, growth factor and cytokines. In comparison with tissue derived bio-scaffold, cultured cell derived ECM scaffold has less risk of pathogen transfer and immune rejection. However, mechanical property of the cell derived ECM scaffold is relatively lower than tissue derived ECM scaffold. Therefore, we have tried to reinforce mechanical property of ECM sponge with graphene oxide (GO) and genipin-crosslinking. GO is two dimensional carbon sheets owing high mechanical property as well as it has positive effect on cell proliferation and differentiation. Genipin is a natural crosslinking agent for various scaffold fabrication in tissue engineering. The purpose of our study was to develop a biocompatible, biodegradable, and genipin- crosslinked ADSC derived ECM sponge containing suitable amount of GO for skin tissue engineering.

Materials and Methods: Rabbit adipose stem cell derived ECM sponge containing different amount (10, 20, 50 and 100 µg/ml) of GO was produced using cultures of the adipose stem cells, production of cell sheet, decellularization of the ADSC cell sheet and freeze-thawing method. Crosslinking was performed by immersing of the sponge in Genipin solution (1% w/v). Pore size and porosity of constructed ECM sponge were assessed by scanning electron microscope (SEM). Immunofluorescent staining was done to identify collagen distribution in Cytotoxicity of the sponge were evaluated using sponge. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide). To identify *in* biocompatibility and biodegradability, constructed pure ECM sponges, non-crosslinked and genipin- crosslinked ECM sponges containing different amount of GO were implanted subcutaneously in rats. Rats were sacrificed after 4 weeks, and then systemic and local inflammatory response after subcutaneous implantation were assessed by histological H&E

staining. The different groups were compared using the T test and One Way ANOVA (IBM SPSS statistics, 19 version).

Results: Macroscopic observation showed that the disc shaped sponges were 5mm in diameter with 2.5 mm thickness as well as with white (pure ECM), grey (non-crosslinked) and dark blue (genipin- crosslinked) appearance. SEM analysis demonstrated a highly porous microstructure with 71.22 \pm 19.52 μ m pore size, whereas porosity of the sponge was 63.45 \pm 6.40 % in crosslinked group. Immunofluorescent staining showed that evenly distribution of collagen type I. MTT analysis indicated that the ECM sponge with 10 and 20 μ g/ml concentration of the GO had significantly higher cell viability in comparison with the ECM sponge containing 50 μ g/ml and 100 μ g/ml amount of the GO (p>0.05). Histological examination revealed that there was no inflammatory response in heart, lung, liver, pancreas, spleen and kidney in pure ECM, non-crosslinked and genipin-crosslinked group. Moreover 4 weeks after implantation, smaller residual sponges with less inflammatory reaction was observed in both crosslinked and non-crosslinked ECM sponge containing 20 μ g/ml GO group in subcutaneous tissue compared with other groups. Further, the smallest residual sponge was found in pure ECM sponge which indicates lower mechanical property of the sponge.

Discussion: Ideal scaffold degradation should match host tissue regeneration without adverse efficacy. In our study, ECM sponge with $20~\mu g/ml$ of GO showed suitable degradation with less inflammatory reaction after 4 weeks implantation. Previous studies revealed that engineered scaffolds are degraded by activated macrophages. Therefore we assume that ECM sponge containing $20\mu g/ml$ GO might be activate host macrophages properly.

Conclusion: We have successfully developed a biocompatible, biodegradable and genipin-crosslinked ECM sponge containing GO using rabbit adipose derived stem cells. The ECM sponge could preserve uniform distribution of collagen. Furthermore, suitable degradation was found after 4 weeks implantation with no any systemic, local toxicity and undesired host responses in rat.

16:00-16:10

S-12

奈米雷納酸鍶納入光敏感性水膠可增加骨再生並幫助脊椎融合 Nanostrontium Ranelate Incorporated Photo-Sensitive Hydrogel Enhanced Bone Regeneration Supporting Spinal Fusion

黃紹展 莊爾元 姜智偉 陳志華 臺北醫學大學生醫材料暨組織工程研究所

Introduction: Spinal Fusion is a well-known surgery for patients with instability in spine or dislocations in spine. Current concerns of causing inflammation and discomfort for patients arise from the use of bone graft, bone screw and bone plate. Strontium Ranelate (SrR), an oral osteoporotic medicine with a dual mechanism on bone remodeling, can not only promote bone formation but also inhibit bone resorption. We aim to improve the absorbing efficiency of SrR compare to orally administered method by combining nanotechnology and photo-responsive hydrogel. The goal is to achieve not only sustained release of SrR but also supporting spinal fusion by promoting bone regeneration.

Materials and Methods: Nanostrontium ranelate (SrRNP) was formulated by electrostatic interaction. Strontium Ranelate (SrR) was mixed with Glycol Chitosan (positive charged) and Hyaluronic Acid (Negative charged). SrRNP was detected by Dynamic Light Scattering (DLS) to check the size and zeta potential. Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) were used to observe the morphology of SrRNP. Fourier Transform Infrared Spectroscopy (FTIR) was used to check if the peak of functional group from materials do exist in SrRNP. Rheology test was done by using Rheometer to check the viscoelasticity of SrRNP incorporated with hydrogel (SrRNP-H). Inductively Coupled Plasma Mass Spectrometry (ICP-MS) was used to calculate the concentration of SrR inside SrRNP-H. In vitro drug release study was carried out to check the release rate of SrRNP-H. MTT assay and LIVE/DEAD assay were done to check the cell viability in the condition of SrRNP-H. Calcium-ECM was carried out to check the osteoblastic proliferation. For animal study, 9 wistar rats (300-350g) were used. There are three groups for animal experiment including Decortication only, Decortication with hydrogel, Decortication with SrRNP-H. X-ray and micro-CT were used to check the imaging of bone growth. Histology was done to check the cytotoxicity in organ and bone formation.

Results: The particle size of SrRNP was found to be 419.13±6.48 nm. The loading efficiency values of SrRNP were found to be 77%. TEM and SEM showed the spherical shape and monodispersity of SrRNP. FTIR showed the functional peak of SrR, HA, GCS in SrRNP. The value of G' and G" increases as the time of UV exposure increases. The concentration of Sr in SrRNP-H was calculated to be around 40ppm. *In vitro* release study showing the sustained release of SrR in SrRNP-H compared to strontium ranelate solution. MTT assay and LIVE/DEAD assay suggested a good cell viability of SrRNP-H. Calcium-ECM showed the significant proliferation of osteoblast. The results of animal experiment suggested that over an observation period of 8 weeks, the group treated with SrRNP-H exhibit the highest level of bone regeneration under the non-invasive x-ray and uCT estimation compared to the group

treated with decortication or decortication with PEGDA hydrogel. Body weight study showed no significant change in body weight. Histology showed bone formation in spine without damage in organ.

Discussion: The size of nanoparticle for bone growth is suitable to be around 400nm. Negatively charged particle also has advantages such as less toxicity and higher tissue organ uptake. Spherical shape and monodispersity suggested the narrower size distribution of particle, which is also good for clinical use. As the rheology study shows, SrRNP-H becomes more rigid as the time of UV exposure increases. Sustained release of drug suggested to shorten recovery time for patients.

Conclusion: SrRNP-H can not only provide sustained and slow releasing rate of SrR but also increase bone regeneration both *in vitro* and *in vivo*. Last but not least, SrRNP-H is safe and will not cause cytotoxicity. As a result, SrRNP-H could be a promising biomaterial to support spinal fusion.

16:10-16:20

S-13

不含防腐劑隱形眼鏡保養液之清潔能力和生物摩擦潤滑特性 The Effects of the Preservative-Free Contact Lens Care Solution on Cleansing and Bio-Tribology

李冠儀1 施柏伍1 蘇真瑩1 方旭偉 1,2,*

國立台北科技大學化學工程系與生物科技系1國家衛生研究院生醫工程與奈米醫學研究所2

Introduction:利用自行研發且含多種生物材料、生物相容性佳之隱形眼鏡保養液,以及體外測試軟性隱形眼鏡摩擦潤滑的方法,測試不含防腐劑之隱形眼鏡保養液對不同材質軟性隱形眼鏡的摩擦係數,和保養液在含量最多之淚液蛋白質-溶菌酶的環境中之摩擦潤滑影響。另外藉由溶菌酶吸附和保養液清潔能力,提出不含防腐劑保養液可能造成某些隱形眼鏡材質在溶菌酶溶液中降低摩擦之機制。

Materials and Methods: 不含防腐劑隱形眼鏡保養液為 1.25 ppm 二氧化氯、1.5%聚麩胺酸、0.1%玻尿酸、10 μ g/ml 茶多酚、0.2%乙二胺四乙酸二鈉、0.05%界面活性劑 Poloxamer-407 溶於以 CaCl₂, KCl, NaCl, Na₂HPO₄ 製成的基底溶液。本實驗所使用之隱形眼鏡材質為: (1)高含水量之離子型水凝膠: Etafikon-A;(2)低含水量之非離子型水凝膠: Polymacon。本摩擦潤滑測試儀器設備為微摩擦磨損測試機(CETR universal micro-tribometer-2,UMT-2),主要分為上平台和下平台。上平台是利用 UMT-2 FVL Model 的感測器,再用機械式方法固定本團隊設計的軟性隱形眼鏡載具。下平台為旋轉式平台,以厚度 5 mm、直徑 60 mm 的石英玻璃當作隱形眼鏡的對磨表面。本研究之參數設定為正向力為 60 mN,旋轉速率為 1 rpm,摩擦時間為 900 秒。隱形眼鏡浸泡於 1.9 mg/ml 或 50 mg/ml 之溶菌酶 24 小時後,利用酵素免疫分析法測得溶菌酶吸附量。另外吸附溶菌酶之鏡片置於保養液中震盪 30 分鐘,測量溶菌酶殘留量以當作清潔能力之評估。

Results:由於觀察摩擦側向力發現摩擦 300 秒後趨向平穩,因此比較兩種材質隱形眼鏡之最後 600 秒所得到之摩擦係數平均,在溶菌酶溶液中,Polymacon 之摩擦係數較 Etafilcon-A 大。然而一旦加入不含防腐劑之隱形眼鏡保養液,Polymacon 在溶菌酶中的摩擦係數即大幅降低。另外在低濃度溶菌酶中,不易觀察到保養液有明顯的清潔能力,但若隱形眼鏡吸附高濃度溶菌酶,保養液即可有效清除附著之溶菌酶,尤其對於非離子型的 Polymacon,保養液之清潔能力效果最佳。

Discussion:綜合體外摩擦潤滑測試和清潔能力評估發現,不含防腐劑保養液對於低含水量非離子型之隱形眼鏡有較佳的清潔效果,並可降低因溶菌酶增高之摩擦係數,可能機制為溶菌酶大量吸附在非離子型鏡片之表面,因摩擦而使溶菌酶變性而增加其摩擦係數,但保養液可將溶菌酶帶離鏡片表面,不但有效清潔鏡片,更能降低摩擦。而高含水量離子型之隱形眼鏡利用電性相吸及其較大孔洞吸引溶菌酶吸附,因此溶菌酶親水端在外,不易因摩擦產生變性,故摩擦係數較不易受到溶菌酶濃度或保養液之影響,使得保養液對離子型隱形眼鏡較無潤滑效果。

Conclusions:由以上實驗結果發現不含防腐劑之隱形眼鏡保養液,對於吸附過多溶菌酶之低含水量非離子型隱形眼鏡有較佳的清潔能力和增加潤滑的特性。將來病患若因植入角膜或植入促進角膜細胞再生材料時而產生摩擦不適感,可應用此不含防腐劑保養液達到降低摩擦和增加潤滑之效果。

第八屆第一次會員大會

台灣再生醫學學會第七屆理、監事名單 (照筆劃順序排列)

理事長 洪士杰

秘書長 張至宏

常務理事 徐善慧、陳敏慧、楊榮森、嚴孟祿

理 事 方旭偉、王兆麟、王至弘、林峰輝、林泰元

林頌然、張志豪、陳耀昌、黄玲惠、蔡清霖

候補理事 江清泉、何美泠、林高田、楊俊佑

常務監事 楊台鴻

監 事 侯連團、孫瑞昇、黃義侑、鄭乃禎

候補監事 顏伶汝

第八屆第一次會員大會議程

時間:民國107年3月3日(星期六)12:00

地點:臺大醫學院103講堂(台北市仁愛路一段一號)

主席:洪士杰 理事長

一、大會開始

二、主席致詞

三、理、監事會工作報告

四、討論事項

- 1. 通過 106 年度工作報告、107 年度工作計劃
- 2. 通過 106 年度經費收支決算、107 年度收支預算

五、臨時動議

六、散會

106年度工作報告

理事會報告

- 一、召開理監事會議計三次。
- 二、會員實際人數一百八十一人。

監事會報告

- 一、理事會處理會務均係依據大會章程辦理,遇有重大事項召開理 監事聯席會議商討決定。
- 二、理事會所編財務報告,業經本監事會審核無誤。
- 三、本屆理事會竭盡全力推展會務。

107年度工作計劃

- 一、招收會員
- 二、舉行三次理監事會議。
- 三、舉辦學術交流研討會。
- 四、隨時通知會員學會相關訊息。

召開年會、相關研討會所能之費用 依收入總額提列 5%作為準備基金 雷 廣告聯位收入、贊助捐款等 犯 中華民國 106年1月1日至106年12月31日止 会入會費、常年會費 員工薪資及加班費 郵局、銀行利息 召開理監事會 7,886 4 台灣再生醫學學會收支決算表 決算與預算比較數 城 1,211,916 1,313,447 53,116 2,293 73,612 853 4,950 1,008,751 1,350,833 2,195 22,083 65,672 pp 常務監事: 歌 500,000 000'009 80,000 8,000 000'009 20,000 200,000 4,000 10,000 5,000 58,000 70,000 25,000 000'061 預算數 1,850,833 253,116 12,114 系統 50,500 6293 83,612 5,853 10,195 92,083 29,950 229'56 1,811,916 101,531 1,913,447 36,391 ,198,751 決算數 物書長: 其他業務費 会费收入 提權基金 捐款收入 利息收入 本原統 4个支出 全体费 交通費 人事費 印刷學 業務費 卸电费 報項 本 w 理事長: 2 3 4 野 4 2 0 7 7 本 裁 N

台灣再生醫學學會 收支預算表 中華民國 107 年 1月 1日至 107 年 12 月 31 日止

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227	2		含人全費、常年全費	廣告掛位收入、贊助捐款等	邮局、銀行利息		員工薪資及加班費						召附理監事會		年會、相關研討會所能之費用	依收入總額提列5%作為準備基金	
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科目名稱	全額	科目名稱	全額
上期結餘	\$1,934,438	本期支出	\$1,716,244
本期收入	1,913,447	本期結除	2,131,641
合計	\$3,847,885	合計	\$3,847,885
理事長:末洲和春長:	金河	作務監事: 186 M Wat: 開表圖	勝息副
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科目	金額	4 目	金額
库存現金	\$1,131,641	累計基金	\$276,162
定期存款	1,000,000	本期捐益	101,531
	:	累積餘組	1,753,948
各計	\$2,131,641	合計	\$2,131,641

台灣再生醫學學會章程

第一章 總 則

- 第一條本會名稱為台灣再生醫學學會(以下簡稱本會)。
- 第 二 條 本會以國內外人士共同發揚再生醫學之研究、教學及應用為宗旨。
- 第 三 條 本會以全國行政區域為組織區域。
- 第 四 條 本會會址設於主管機關所在地區。本會得視會員人數及分配與會務進行之需要設分會與各種委員會,其組織簡則由理事會擬訂,報請主管機關核准後實施, 變更時亦同。
- 第 五 條 本會之任務如左:
 - 一、提倡再生醫學之研究並發揚醫學倫理道德。
 - 二、調查國內外再生醫學之發展,徵集有關圖書資訊以供各學術團體之參考及 交流。
 - 三、舉辦學術演講及討論會。
 - 四、出版會誌及有關書刊。
 - 五、獎助再生醫學及組織工程學人才及舉辦其他有關事宜。
 - 六、與有關公司、廠商及機構合作,共求再生醫學及組織工程學之發展與應用。
- 第 六 條 本會之主管機關為內政部。

本會之目的事業應受各該事業主管機關之指導、監督。

第二章 會 員

- 第 七 條 本會會員申請資格如下:
 - 一、個人會員:凡贊同本會宗旨、取得中華民國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並經理事會通過後得申請為本會個人會員。
 - 二、贊助會員:贊助本會工作之團體或個人。 申請時應填具入會申請書,經 理事會通過,並繳納會費後,始得為本會贊助會員。
 - 三、準 會 員:凡贊同本會宗旨的碩、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,由會員二人推薦,經理監事會審查通過,得為本 會準會員。
- 第 八 條 會員(會員代表)有表決權、選舉權、被選舉權與罷免權。每一會員(會員代表) 為一權。贊助會員、準會員無前項權利。
 - 個人會員另享有 1. 參加本會年會及本會所舉辦之其他集會之權利。
 - 2. 參加本會所舉辦各種活動或事業之權利。
 - 3. 本會各種書刊訂閱優待之權利。

贊助會員享有 1. 參加本會年會及本會所舉辦之其他集會之權利。

2. 本會出版之資訊及刊物贈閱之權利。

準會員享有 1. 參加本會年會及本會所舉辦之其他集會之權利。

2. 本會出版之資訊及刊物贈閱之權利。

第 九 條 會員有遵守本會章程、決議及繳納會費之義務。

會員每年年初需繳納會費,以利本會之運作。未繳納會費者,不得享有會員權利;連續二年未繳納會費者,視為自動退會。會員經出會、退會或停權處分,如欲申請復會或復權時,除有正當理由經理事會審核通過者外,應繳清前所積欠之會費。

第 十 條 會員(會員代表)有違反法令,章程或不遵守會員大會決議時,得經理事會決議, 予以警告或停權處分,其危害團體情節重大者,得經會員(會員代表)大會決議 予以除名。

第 十一 條 會員喪失會員資格或經會員大會決議除名者,即為出會。

第 十二 條 會員得以書面敘明理由向本會聲明退會。

第三章 組織及職權

第 十三 條 本會以會員大會為最高權力機構。

會員人數超過三百人以上時得分區比例選出會員代表,再召開會員代表大會,行使會員大會職權。會員代表任期二年,其名額及選舉辦法由理事會擬訂,報請主管機關核備後行之。

第 十四 條 會員大會之職權如左:

- 一、訂定與變更章程。
- 二、選舉及罷免理事、監事。
- 三、議決入會費、常年會費、事業費及會員捐款之數額及方式。
- 四、議決年度工作計畫、報告及預算、決算。
- 五、議決會員(會員代表)之除名處分。
- 六、議決財產之處分。
- 七、議決本會之解散。
- 八、議決與會員權利義務有關之其他重大事項。前項第八款重大事項之範圍由 理事會定之。
- 第 十五 條 本會置理事十五人、監事五人,由會員(會員代表)選舉之,分別成立 理事會、監事會。 選舉前項理事、監事時,依計票情形得同時選出候補理事五 人,候補監事一人,遇理事、監事出缺時,分別依序遞補之。本屆理事會得提

出下屆理事、監事候選人參考名單。

理事、監事得採用通訊選舉,但不得連續辦理。通訊選舉 辦法由理事會通過,報請主管機關核備後行之。

- 第十六條 理事會之職權如左:
 - 一、審定會員(會員代表)之資格。
 - 二、選舉及罷免常務理事、理事長。
 - 三、議決理事、常務理事及理事長之辭職。
 - 四、聘免工作人員。
 - 五、擬訂年度工作計畫、報告及預算、決算。
 - 六、其他應執行事項。
- 第十七條 理事會置常務理事五人,由理事互選之,並由理事就常務理事中選舉一人為理事長。理事長對內綜理督導會務,對外代表本會,並擔任會員大會、理事會主席。理事長因事不能執行職務時,應指定常務理事一人代理之,未指定或不能指定時,由常務理事互推一人代理之。理事長、常務理事出缺時,應於一個月內補選之。
- 第十八條 監事會之職權如左:
 - 一、監察理事會工作之執行。
 - 二、審核年度決算。
 - 三、選舉及罷免常務監事。
 - 四、議決監事及常務監事之辭職。
 - 五、其他應監察事項。
- 第 十九 條 監事會置常務監事一人,由監事互選之,監察日常會務,並擔任監事會主席。 常務監事因事不能執行職務時,應指定監事一人代理之,未指定或不能指定時, 由監事互推一人代理之。

監事會主席(常務監事)出缺時,應於一個月內補選之。

- 第 二十 條 理事、監事均為無給職,任期二年,連選得連任。理事長之連任,以一次為限。 第二十一條 理事、監事有左列情事之一者,應即解任:
 - 一、喪失會員(會員代表)資格者。
 - 二、因故辭職經理事會或監事會決議通過者。
 - 三、被罷免或撤免者。
 - 四、受停權處分期間逾任期二分之一者。
- 第二十二條 本會置秘書長一人,承理事長之命處理本會事務,其他工作人員若干人,由理 事長提名經理事會通過聘免之,並報主管機關備查。但秘書長之解聘應先報主 管機關核備。前項工作人員不得由選任之職員擔任。工作人員權責及分層負責 事項由理事會另定之。

- 第二十三條 本會得設各種委員會、小組或其他內部作業組織,其組織簡則經理事會通過後 施行,變更時亦同。
- 第二十四條 本會得由理事會聘請名譽理事長一人,名譽理事、顧問各若干人,其聘期與理 事、監事之任期同。

第四章 會 議

- 第二十五條 會員大會分定期會議與臨時會議二種,由理事長召集,召集時除緊急事故之臨時會議外應於十五日前以書面通知之。定期會議每年召開一次,臨時會議於理事會認為必要,或經會員(會員代表)五分之一以上之請求,或監事會函請召集時召開之。本會辦理法人登記後,臨時會議經會員(會員代表)十分之一以上之請求召開之。
- 第二十六條 會員(會員代表)不能親自出席會員大會時,得以書面委託其他會員(會員代表) 代理,每一會員(會員代表)以代理一人為限。
- 第二十七條 會員(會員代表)大會之決議,以會員(會員代表)過半數之出席,出席人數較多數 之同意行之。但章程之訂定與變更、會員(會員代表)之除名、理事及監事之罷 免、財產之處分、本會之解散及其他與會員權利義務有關之重大事項應有出席 人數三分之二以上同意。

本會辦理法人登記後,章程之變更以出席人數四分之三以上之同意或全體會員三分之二以上書面之同意行之。本會之解散,得隨時以全體會員三分之二以上之可決解散之。

- 第二十八條 理事會、監事會至少每六個月各舉行會議一次,必要時得召開聯席 會議或臨時會議。前項會議召集時除臨時會議外,應於七日前以書面通知,會 議之決議,各以理事、監事過半數之出席,出席人數較多數之同意行之。
- 第二十九條 理事應出席理事會議,監事應出席監事會議,不得委託出席。 理事、監事連續 二次無故缺席理事會、監事會者,視同辭職。

第五章 經費及會計

第三十 條 本會經費來源如左:

一、入會費:個人會員新台幣壹仟元,於會員入會時繳納。 贊助會員新台幣壹仟元,於會員入會時繳納。 準會員新台幣五百元,於會員入會時繳納。

二、常年會費:個人會員新台幣壹仟元。

贊助會員新台幣貳仟元。 準會員新台幣五百元。

三、事業費。

四、會員捐款。

五、委託收益。

六、基金及其孳息。

七、其他收入。

第三十一條 本會會計年度以曆年為準,自每年一月一日起至十二月三十一日止。

第三十二條 本會每年於會計年度開始前二個月由理事會編造年度工作計畫、收支預算表、 員工待遇表,提會員大會通過(會員大會因故未能如期召開者,先提理監事聯席 會議通過),於會計年度開始前報主管機關核備。並於會計年度終了後二個月內 由理事會編造年度工作報告、收支決算表、現金出納表、資產負債表、財產目 錄及基金收支表,送監事會審核後,造具審核意見書送還理事會,提會員大會 通過,於三月底前報主管機關核備(會員大會未能如期召開者,先報主管機關。)

第三十三條 本會解散後,剩餘財產歸屬所在地之地方自治團體或主管機關指定 之機關團體所有。

第六章 附 則

第三十四條 本章程未規定事項,悉依有關法令規定辦理。

第三十五條 本章程經會員(會員代表)大會通過,報經主管機關核備後施行,變更時亦同。

第三十六條 本章程經本會93年2月7日第一屆第一次會員大會通過。

報經內政部93年5月14日台內社字第0930018951號函准予備查。

台灣再生醫學學會會員名單:

編號	姓 名						
001	劉華昌	029	林瑞模	061	鍾瑞嶂	091	李宣書
002	侯勝茂	030	徐郭堯	062	范揚峰	092	楊長彬
003	陳耀昌	032	吳輝傑	063	戴浩志	093	王貞棣
004	楊台鴻	033	蕭逸民	064	洪士杰	095	楊曙華
005	楊榮森	034	李建和	066	劉有漢	096	邱錦輝
006	楊俊佑	036	黄振勳	067	許致榮	097	郭兆瑩
007	林峰輝	037	施庭芳	068	黄國淵	098	陳學明
008	林文澧	038	侯連團	069	李裕滄	099	林柳池
009	王清貞	039	陳志華	070	陳沛裕	100	潘如瑜
010	黄義侑	040	李炫昇	072	林頌然	101	楊維宏
011	王兆麟	041	張瑞根	073	游敬倫	102	劉明偉
012	江清泉	044	李敏旭	075	陳吳坤	103	王文志
013	石朝康	045	江鴻生	076	鄧文炳	104	方旭偉
014	蔡清霖	046	陳昭宇	077	鄭耀山	105	陳敏慧
015	張恆雄	047	張宗訓	079	簡松雄	106	張明熙
017	蘇芳慶	048	釋高上	080	郭繼陽	107	陳興源
018	陳瑞明	050	張至宏	081	王世杰	108	蔡文龍
019	陳全木	051	蔡慶豐	082	蔡友士	109	郭宗甫
020	童瑞年	054	楊治雄	083	王至弘	110	王禎麒
021	殷金儉	055	蔡文基	084	張志豪	111	湯月碧
022	何始生	056	林高田	085	趙建銘	112	黄玲惠
023	孫瑞昇	057	古鳴洲	087	曾鵬文	113	王佩華
026	陳文哲	058	宋信文	088	徐明洸	114	郭源松
027	周正義	059	姚俊旭	089	詹益聖	115	翁文能
028	陳英和	060	呂紹睿	090	吳錫銘	116	徐善慧

編號	姓 名						
117	蘇正堯	144	黄維超	170	嚴孟祿	196	陳郁君
118	楊世偉	145	陳安泰	171	顏伶汝	197	黄惠君
119	林偉彭	146	謝清河	172	林泰元	198	洪堃哲
120	謝豐舟	147	彭慶安	173	陳尹愷	199	曾庭箴
121	方紀宇	148	劉滄梧	174	許元銘	200	黄鉉琴
122	蘇慶華	149	薛敬和	175	鄭有仁	201	許素菁
123	曾育弘	150	林毅成	176	侯添財	202	嚴勻謙
125	史中	151	顏君哲	177	賴文福	203	歐祖翔
126	鄭乃禎	152	陳江山	178	施子弼	204	馬惠康
127	謝式洲	153	侯君翰	179	黄鼎鈞	205	陳怡文
128	蘇鴻麟	154	吳俊昇	180	陳宣佑	206	陳右昇
129	曾清秀	155	廖振焜	181	邵宏仁	207	陳信水
130	劉百栓	156	傅再生	182	徐永康	208	林欣杰
131	唐逸文	157	蔡宗廷	183	賴瑞陽	209	許哲嘉
132	王清正	158	羅文政	184	薛元毓	210	王耀賢
133	王盈錦	159	王德原	185	施明光	211	宋貴華
134	吳信志	160	賴志毅	186	曾效參	212	長聖生技
135	簡雄飛	161	吳佳慶	187	趙崧筌	213	林惠娟
136	高國慶	162	沈延盛	188	黃柏誠	214	謝秉舟
137	徐新生	163	李一麟	189	彭凱彥	215	陳泓志
138	許文明	164	何美泠	190	李奎璋	216	李亦宸
139	黃鶴翔	165	楊宗霖	191	陳崇桓	217	李芳艷
140	陳偉勵	166	吳坤佶	192	朱恆毅	218	葉漢根
141	劉席瑋	167	趙本秀	193	傅尹志	219	李宜珍
142	李冠瑢	168	鄭明德	194	陳達慶		
143	胡育誠	169	李源芳	195	吳順成		

台灣再生醫學學會 個人會員入會申請書

姓名	性別	出生年月日	出生地	身分證 號 碼
學歷	民國 年 月畢業於			
户籍住址				
現任職務	醫院或單位:		: 堤楼	職稱:
服務單位 地 址				專科醫師證書字號: (無者免填)
電話	(交)	(宪)		傳真:
其他連絡 方 式	電子信箱(e-mail):			行動電話:
審查結果 (由學會填寫)		會員類別 (由學會填寫)		會員證號碼 (由學會填寫)
本人贊同貴	本人贊同貴會宗旨,擬加入為會員,嗣後	嗣後並願意遵守	並願意遵守會章,共圖發展	
此致	台灣再生醫學學會			申請人: (簽章)
掛	風	#	町	

會員資料異動申請書

本單填妥後請回傳至台灣再生醫學學會 Fax: 02-8921-3969

會員姓名:		
變 更 為:		
郵遞區號:		
通訊地址:		
服務單位:		
聯絡電話:		
傳 真:		
e-mail:		