

海峡两岸及香港、澳门地区创伤修复(愈合)与组织再生 创新成果及转化应用论坛



2015年11月13-14日 中国 深圳

香港中文大学深圳研究院

主办单位



解放军总医院



中国工程院



香港中文大学

摘要



会议地址：深圳市南山区虚拟大学园粤兴二道10号

香港中文大学深圳研究院

为进一步加强海峡两岸及香港、澳门地区在创伤医学领域，特别是组织修复与再生领域的合作，发现共同关注的研究热点，促进开展更深入的合作研究及技术推广。由中国工程院、解放军总医院、香港中文大学共同于2015年11月13-14日在香港中文大学深圳研究院举办“海峡两岸及香港、澳门地区创伤修复（愈合）与组织再生创新成果及转化应用论坛”。

特邀院士：



樊代明 院士

教授、主任医师、
中国工程院副院长
(第四军医大学)



沈祖尧 院士

教授、研究员
(香港中文大学)



付小兵 院士

教授、研究员
(解放军总医院生命科学院)



张兴栋 院士

教授、研究员
(四川大学国家生物医学
材料工程技术研究中心)



王正国 院士

教授、研究员
(第三军医大学野战
外科研究所)



苏国辉 院士

教授、研究员
(香港大学神经科学
研究中心)



夏照帆 院士

教授、研究员
(第二军医大学长海医院
烧伤外科)

会议日程

2015年11月12日(星期四) 会议代表报到 地点: 丽雅查尔顿酒店	
2015年11月13日(星期五) 香港中文大学深圳研究院报告厅	
08:30-10:00	第一节: 院士论坛: 转化医学在中国大陆 主持人: 付小兵院士, 郑振耀教授
08:30-09:00	中国再生医学的发展和未来 王正国院士(第三军医大学野战外科研究所)
09:00-09:45	医学与科学 樊代明院士(第四军医大学)
09:45-10:15	骨诱导性生物材料——从科学基础到临床转化 张兴栋院士(四川大学)
10:15-10:45	组织修复与再生新的挑战: 实现多种组织在损伤部位的原位修复与再生 付小兵院士(中国人民解放军总医院)
10:45-11:00	茶歇和展览
11:00-11:30	第二节: 开幕式 主持人: 陈启明教授, 李刚教授
	致欢迎辞 香港中文大学校长 沈祖尧院士 香港中文大学深圳研究院院长 郑汉淇教授 解放军总医院 付小兵院士 中国工程院领导 其他深圳市相关的支持单位领导 集体合影留念
11:30-12:30	第三节: 转化医学在香港, 台湾和澳门 主持人: 陈启明教授, 段崇智教授
11:30-11:50	前沿技术与中医药转化医学 刘良校长(澳门科技大学)
11:50-12:10	肌腱组织的损伤与再生研究的热点 陈启明教授(香港中文大学医学院 创伤与矫形外科)
12:10-12:30	毛发再生的新理念 陈志强教授(台北荣民总医院皮肤科)
12:30-13:00	讨论
13:00-14:00	午餐和展览
14:00-16:20	第四节: 干细胞, 骨骼组织修复与再生(I) 主持人: 周光前教授, 潘晓华教授
14:00-14:20	低氧下间充质干细胞的培养: 基础与临床应用 洪士杰教授(国立阳明大学医学院)
14:20-14:40	循环间充质干细胞的生物学机制与临床意义 李刚教授(香港中文大学医学院 创伤与矫形外科)
14:40-15:00	糖尿病足创面修复 姜玉峰教授(解放军总医院)

会议日程

15:00-15:20	软骨损伤的干细胞治疗 许海波教授（新加坡国立大学）
15:20-15:40	骨科医用镁金属材料的研发与临床转化 秦岭教授（香港中文大学医学院 创伤与矫形外科）
15:40-16:00	讨论
16:00-16:20	茶歇和展览
16:20-18:00	第五节:生物材料与组织再生 主持人: 秦岭教授, 吴成铁教授
16:20-16:40	可注射生物材料的研究及临床新发展 吕维加教授（香港大学医学院 创伤与矫形外科）
16:40-17:00	3D打印生物材料用于骨修复与治疗 吴成铁研究员（中国科学院上海硅酸盐 研究所）
17:00-17:20	新型高分子水凝胶生物材料的研发和应用 边黎明助理教授（香港中文大学 机械与自动化工程系）
17:20-17:40	讨论
17:40-18:40	第六节: 如何加强两岸四地的合作 主持人: 付小兵院士, 夏照帆院士, 洪士杰教授, 刘良教授, 秦岭教授 全体与会的嘉宾和代表
19:00-21:00	会议欢迎晚宴（全体嘉宾和注册的代表）
2015年11月14日（星期六）	
9:00-11:00	第七节: 软组织修复与再生 主持人: 李青峰教授, 郑铭豪教授
9:00-9:20	皮肤再生的临床思考与转化 李青峰教授（上海交通大学医学院第九人民医院 整形科）
9:20-9:40	Autologous tenocyte therapy and bioreactor for tendinopathy: from bench to bedside 郑铭豪 教授（西澳大利亚大学医学院）
9:40-10:00	骨骼肌干细胞对骨骼肌组织损伤再生修复的调控研究 朱大海教授（北京协和医学院 基础所）
10:00-10:20	组织特异性ECM在组织构建与再生中的作用与临床应用 金岩教授（第四军医大学组织工程研发中心）
10:20-10:40	讨论
10:40-11:00	茶歇与展览
11:00-12:30	第八节: 大师讲堂 主持人: 李刚教授, 欧阳宏伟教授,
11:00-11:30	造血细胞工程研究进展 裴雪涛教授（中国人民解放军军事医学科学院 血液所）
11:30-12:00	运动与脑内源性神经干细胞的前沿进展 苏国辉院士（暨南大学粤港澳中枢神经再生研究院, 香港大学眼科学系）

会议日程

12:00-12:30	下肢复杂畸形矫正功能重建临床进展与启示 秦泗河教授（中国国家康复中心医学 矫形外科）
12:30-14:00	午餐及展览
14:00-16:20	第九节：新技术与组织再生 主持人：蒋青教授，张晓玲教授
14:00-14:20	Promises and Challenges of Tissue Engineering and Regenerative Medicine: Repair, Restore, and Re-create 段崇智 教授（美国匹次堡大学）
14:20-14:40	生物3D打印技术在骨与软骨再生中的应用 蒋青教授（南京鼓楼医院 骨科）
14:40-15:00	骨科小干扰核酸药物靶向递送系统研究进展 张戈教授（香港浸会大学中医学院）
15:00-15:20	抗感染骨修复材料的3D打印和评价 汤亭亭教授（上海交通大学附属第九人民医院 骨科）
15:20-15:40	超级抗原在组织修复中的研究进展 郭巍/张锦芳教授（沈阳协合集团有限公司/香港中文大学医学院创伤与矫形外科）
15:40-16:00	脐带血源干细胞复合富含血小板血浆治疗难治性肌腱病的基础与临床研究 唐康来教授（第三军医大学西南医院 骨科）
16:00-16:20	茶歇及展览
16:20-18:30	第十节：研究生论坛 及自由投稿演讲 评奖委员：段崇智教授, 李郁伟教授, 张锦芳教授, 周光前教授, 陈琍教授
	研究生论坛演讲 主持人：段崇智教授, 陈琍教授
16:20-16:30	Stromal cell-derived factor-1 plays an important role in subchondral bone abnormal changes during osteoarthritis development（陈元峰 香港中文大学医学院）
16:30-16:40	Dexamethasone inhibits the differentiation of rat tendon stem cells into tenocytes by targeting the scleraxis gene（陈万 第三军医大学）
16:40-16:50	The Role of CFTR on Tenogenic Differentiation（刘洋 香港中文大学医学院）
16:50-17:00	The Alteration and Crosstalk of Articular Cartilage-Subchondral Bone Unit in Osteoarthritis（袁雪凌 中国人民解放军总医院）
17:00-17:10	MicroRNA-503 promotes bone formation in distraction osteogenesis through targeting smurf1（孙育欣 香港中文大学医学院）
17:10-17:20	Small molecular Kartogenin works as an endogenous mesenchymal stem cells activator（李晓琳 深圳大学医学院）
	自由投稿演讲 主持人：蔡冬青教授, 周光前教授
17:20-17:30	1代和2代自体软骨细胞移植（ACI）修复大面积软骨损伤的临床效果比较研究（朱伟民 深圳大学第一附属医院）

会议日程

17:30-17:40	Epigenetic memory gained by priming with osteogenic induction medium improves osteogenesis and other properties of mesenchymal stem cells (徐亮亮 香港中文大学医学院)
17:40-17:50	自体骨髓间充质干细胞复合PLGA/纳米级软骨细胞外基质 (ACECM) 组成和结构仿生支架修复兔膝关节软骨缺损 (王明杰 中国人民解放军总医院)
17:50-18:00	Smad7: a new molecular target for treatment of osteoarthritis (林思恩 香港中文大学医学院)
18:00-18:10	干扰NR2F1的表达能促进骨髓间充质干细胞向胰岛素分泌细胞分化 (庞希宁 中国医科大学)
18:10-18:20	The effects of Substance P on tendinopathy are dose-dependent: an in vitro and in vivo model study (周兵华 第三军医大学)
18:20-18:30	骨搬运治疗下肢慢性缺血性疾病的基础及临床研究 (王江宁 北京世纪坛医院)
18:30-18:50	论坛获奖题目颁奖, 会议小结。 蔡冬青教授, 李刚教授
18:50	会议结束 欢送晚宴(部分留守嘉宾)

2015年11月14日 (星期六) 深圳市宝安人民医院分会场

9:30-11:50	创伤修复与组织再生 主持人: 付小兵院士, 黄居科院长
9:30-10:30	严重创伤的修复与再生 (互联网与创面修复重建) 付小兵院士 (中国人民解放军总医院生命科学院 全军创伤修复与组织再生重点实验室)
10:30-11:00	可注射生物材料的临床应用及创新 吕维加教授 (香港大学医学院 创伤与矫形外科)
11:00-11:30	体表慢性难愈合创面发病新特征 姜玉峰教授 (解放军总医院生命科学院创面治疗中心)
11:30-11:50	讨论

欢迎辞

香港中文大学校长欢迎辞

欢迎大家参加2015年中国工程院院士论坛，暨海峡两岸及香港，澳门地区创伤修复与组织再生创新成果及转化应用论坛。



再生医学是在21世纪现代医学的重要进步。胚胎，成体干细胞，和生物材料的发现使受损组织有可能再生；再生疗法已被证实治愈许多过去难以治疗的疾病，如严重骨损伤，烧伤，失明，心脏病，帕金森氏病和多种退行性疾病。

在过去几年中，香港中文大学不断扩大其在再生医学领域的研究潜力和能力。我们投资建立了专门的研究团队和最先进的科研设施，以促进该领域研究的基础研究和临床应用之需要。自2011年起，我们已经成功举办了5届香港中文大学国际再生医学和干细胞生物学的研讨会，大力促进了再生医学在香港和区域内的发展。2013年，由吕志和基金会的慷慨捐赠成立了香港中文大学创新医学研究所，专门鼓励研究运动医学与再生技术；心血管健康和脑科学技术的研发。我们的计划已经取得初步的成果，已与瑞典卡罗林斯卡医学院，荷兰乌得勒支医学眼和美国的斯坦福大学签署合作备忘录并展开定期的人员交流。

今年研讨会的主要议题包括再生和转化医学，这两个目前热门的话题。我非常高兴地看到两岸四地的资深科学家，中国工程院的院士们能够在金秋的季节聚集在深圳，一起与年轻而充满活力的研究人员和临床医生分享他们的专业知识和经验，这是一个难得的交流和学习的平台，也是对珠江三角洲地区创伤修复与组织再生领域的一个促动和鼓舞！谢谢大家！

祝大家在深圳的时间愉快！祝研讨会圆满成功！

沈祖尧

香港中文大学校长
中国工程院院士

欢迎辞

大会组委会欢迎辞

为了进一步加强两岸三地在创伤医学领域，特别是组织修复与再生领域的合作，发现共同关注的研究热点，促进开展更深入的合作研究及技术推广。由中国工程院、解放军总医院、香港中文大学共同拟于2015年11月13日-14日在深圳举办“海峡两岸及香港，澳门地区创伤修复（愈合）与组织再生创新成果及转化应用论坛（暨中国工程院院士论坛）”，会议将在深圳香港中文大学深圳研究院举行。

本次会议将有中国工程院樊代明、王正国、张兴栋、付小兵等院士参会，同时邀请了30-40名台湾，香港，澳门和中国大陆的组织修复与再生领域的知名学者和专家来深圳参会。本次会议将是一次再生医学领域的学术盛会，是促进海峡两岸及香港，澳门地区创伤修复（愈合）与组织再生领域的合作和交流合作，结交新朋老友的一次难得的机会。您的参与和贡献是大会成功的重要保证。

热烈欢迎，并祝在深圳期间身体健康！



付小兵 研究员

中国工程院院士
解放军总医院生命科学院



李刚 教授

香港中文大学医学院骨科
香港中文大学深圳研究院



潘晓华 教授

南方医科大学附属深圳宝安医院
创伤外科及矫形骨科

欢迎辞

深圳市宝安区人民政府梁敏华副区长致辞

尊敬的各位领导、专家学者，各位嘉宾：

上午好！

金秋送爽，丹桂飘香。

在这美好的季节里，由中国工程院、解放军总医院、香港中文大学共同举办的“海峡两岸及香港、澳门地区创伤修复（愈合）与组织再生创新成果及转化应用论坛”在深圳隆重开幕。海峡两岸及香港、澳门地区医学界精英共襄盛会，同谱大中华医学学术交流的新篇章。在此，我谨代表中共深圳市宝安区委、区人民政府，向莅临这次论坛的各位领导、专家学者和嘉宾表示热烈的欢迎！

转化医学、再生医学是近年来蓬勃发展的新型医学发展模式，是当前医学领域最大的亮点。近年来深圳特区从城市未来发展的战略高度，围绕建设现代化、国际化先进城市的发展定位，提出加快打造国际化医疗中心的目标，启动实施了医疗卫生的“三名工程”，为推动高质量跨越式的发展，实现可持续的全面发展提供全面的支撑。在此，我特别呼吁：欢迎国内外的医学科学家、专家学者来深圳开展学术交流和技术合作，共同促进深圳地区社会经济和卫生事业的发展。

最后，祝本次学术盛会取得圆满成功！

谢谢！

梁敏华

深圳市宝安区人民政府

欢迎辞

深圳市宝安区卫生及人口计划局杨北兵局长致辞

尊敬的各位领导、各位专家，同志们，朋友们：

上午好！

今天，“海峡两岸及香港、澳门地区创伤修复（愈合）与组织再生创新成果及转化应用论坛”顺利召开了，这是我国医学界的一次盛会，在此我谨代表宝安区卫生和计划生育局对会议的召开表示热烈的祝贺，向与会的各位专家学者致以崇高的敬意！

21世纪是知识经济的时代，知识逐渐成为经济增长的源动力。21世纪也是生命科学的世纪，生命科学已经发展成为21世纪最活跃的学科之一，成了自然科学的前沿学科。转化医学、再生医学是当今时代生命科学重要的发展趋势，是当代医学科学王国一道最为靓丽的风景线。

本次会议是在本地区举办的一次较高规格的医学学术会议，登上论坛的每一位学者，都是活跃在科研、教育、医疗、转化医学领域第一线的学术带头人。大会主题明确，旨在发现共同关注的研究热点，促进开展更深入的合作研究及技术推广。这将是海峡两岸及香港、澳门大中华区域内创伤医学领域的一次学术大碰撞、大融合，必将促进学科间的相互渗透、融合和集成。

乘着改革开放的春风，深圳市宝安区医疗卫生工作取得了辉煌的成就，成为深圳城市发展奇迹的重要组成部分。当前，宝安面临着来自区域竞争、产业转型、资源环境等诸多方面压力和挑战。江河汇聚成川，山丘崛起为峰；当今时代是一个科学飞速发展的时代，为此，我代表宝安区卫生和计划生育局向与会专家发出诚挚的邀请：今天的宝安，将以更加开放的视野、更加包容的胸怀、更加优美的环境，迎接海内外医学领域的高端人才（项目）来宝安创新创业，将宝安打造成为医学领域的人才集聚高地！

最后，预祝大会取得圆满成功！祝各位领导、各位代表工作顺利，身体健康！

谢谢！

杨北兵

深圳市宝安区卫生及人口计划局

深圳市宝安区人民医院黄居科院长致辞

各位领导、各位嘉宾、各位朋友：

大家上午好！

今天我们在这里聚会，参加由中国工程院、解放军总医院、香港中文大学共同举办的“海峡两岸及香港、澳门地区创伤修复（愈合）与组织再生创新成果及转化应用论坛”，在此我谨代表深圳市宝安区人民医院向参加大会的领导、专家、朋友们表示热烈的欢迎和诚挚的感谢！

转化医学近年来发展迅猛，在以自主创新能力为焦点的新一轮全球科技竞争中，海峡两岸及香港、澳门地区的同仁们携手应对这一挑战，举办学术论坛，大力推动创伤医学领域的创新成果及转化应用，最终提高我国的综合实力，为全人类医学科学水平和生命健康做出贡献。深圳市宝安区人民医院作为承办单位之一，能参与本次学术论坛的具体筹办，如我们深感荣幸！我们将全力做好有关的会务工作！

深圳市宝安区人民医院（深圳市第八人民医院）名列全国首批百佳医院，是一所集医疗、科研、教学、预防、保健、康复于一体的大型综合性医院，承担了深圳西部医疗中心、深圳西部急危重症病人救治中心的职能，覆盖人口接近七百万。2011年通过广东省卫生厅综合医院等级评审，成功晋升为三级甲等医院。我们始终坚持“以科研促临床，以技术谋发展”；“以人性化的服务、专业化的诊疗、权威化的技术、科学化的管理”为办院方针；以高起点、高质量、高效益为我们追求的目标，现在正以暂新的姿态，昂扬的斗志，扬帆远航。

在此，我再一次的感谢各位领导、专家和朋友们的光临，深圳市宝安区人民医院的发展离不开你们的关心、支持和帮助！

最后祝本次会议取得圆满成功！

祝各位领导、专家、朋友们身体健康、万事如意！

谢谢大家！

黄居科

深圳市宝安区人民医院

香港中文大学

香港中文大学（The Chinese University of Hong Kong），简称港中大（CUHK），书院联邦制大学建制，为东亚AACSB认证成员、亚太高校书院联盟成员、世界大学联盟成员、亚太国际教育协会创始成员，是一所以“中国研究”、“生物医学科学”、“信息科学”、“经济与金融”、“地球信息与地球科学”为五大重点研究领域的研究型综合大学，被誉为亚洲最美的大学校园之一。



香港中文大学由三所中文专上学院——新亚书院（1949年成立）、崇基学院（1951年成立）及联合书院（1956年成立）——于1963年合并组成；1966年，成立香港首所研究院；1986年，全面检讨课程结构，改用学分制，并加强通识教育；2013年，中大金禧校庆。

香港中文大学的创立，打破了大英帝国殖民地近五百年来只允许一所高等学府存在的铁律，是20世纪亚洲地区“非殖民化”的表征之一。中大的出现掀起了香港七十年代的“中文运动”，终结了英文垄断官方语言地位的局面。

根据2015年4月学校官网显示，学校校园占地面积137.3公顷，建筑面积710302平方米；辖8个学院及研究院，开办各类本科课程265个；有在校本科生及研究生19263人。



中国工程院

中国工程院（Chinese Academy of Engineering, CAE），是中国工程科学技术界的最高荣誉性、咨询性学术机构，由院士组成，致力于促进工程科学技术事业的发展。中国工程院，成立于1994年。1994年6月2日，中国工程院产生首批院士；2013年新增院士后，中国工程院院士总数达到802人。

中国工程院是我国工程技术界的最高荣誉性、咨询性学术机构，由院士组成，对国家重要工程科学与技术问题开展战略研究，提供决策咨询，致力于促进工程科学技术事业的发展。它的主要任务是促进全国工程科学技术界的团结与合作，推动我国工程科学技术水平的不断提高，加强工程科学技术队伍和优秀人才的建设和培养，为国民经济的持续发展服务。主要在以下几个方面开展工作：

一、发挥院士群体多学科、跨部门、跨行业的综合优势，参与国家和地区经济发展和社会进步中重大决策、重大工程建设和高技术产业发展战略的研究、咨询和评估，为国家和地方政府提出优先发展领域和重点投资方向和建议；

二、组织对重大工程科学技术方向性、前沿性问题的研究，提高工程技术创新的能力和管理科学与工程的水平；

三、广泛开展不同层次、多种形式的国内国际学术交流与合作，为全国工程科技界、特别是在一线工作的优秀中青年专家的成长创造开放的学术环境；

四、大力开展科学普及和科技出版工作，为提高我国工程科学技术水平、各级干部与全社会的科学文化素质作贡献；

五、维护科学道德，弘扬科学精神，积极推进社会主义精神文明建设；

六、完成国务院交办的各项工作。



主办单位



解放军总医院

解放军总医院是全军规模最大的综合性医院，集医疗、保健、教学、科研于一体，是国家重要保健基地之一，负责中央、军委和总部的医疗保健工作，承担全军各军区、军兵种疑难病的诊治，医院同时也收治来自全国的地方病人。

全院共展开床位4400余张，其中院本部3400余张，三〇四临床部1000余张。共设临床、医技科室103余个，其中耳鼻咽喉-头颈外科、骨科、老年医学等6个国家级重点学科，8个全军重点实验室，13个全军医学专科中心，13个全军医学研究所，1个全军医学专病中心。

医院位于北京市复兴路28号院，占地面积118.8万平方米，建筑面积110.07万平方米。



承办单位

香港中文大学深圳研究院

香港中文大学深圳研究院成立于2007年5月，获深圳市政府的大力支持，由香港中文大学出资兴建。作为香港中文大学在中国内地的重要平台，研究院兼顾高校优势与深圳经济发展需求，旨在将香港中文大学优秀的研究人才及成果与深圳的高科技产业相结合，推动科研成果产业化，加快深港创新圈和区域创新体系的建设。

根据国家科技发展规划结合深圳市科技发展需求，研究院重点推动生物科技、信息科技及环境与可持续发展等领域的建设。引入先进科研成果推动产学研合作，建立多个国家级重点实验室深圳研究基地及联合研发中心，发掘地方产业发展技术瓶颈，加大横向项目合作力度，推动技术成果高效转化；加强与内地业界的合作创新，从研究初期的项目合作开发的模式，逐步转变至以市场为导向的产品开发及高端人才输送的全方位合作模式；建设开放型科研平台，突出强调关键技术及科研设备优势资源互补，建立多领域的公共技术服务平台及开放性工程实验室；注重高层次人才培养，依托香港中文大学的优势师资资源和科研基础，开展高水平的教育培训课程，建设职业、专业的人才深造基地。

研究院主体大楼坐落于深圳虚拟大学园国家大学科技园内，建筑面积约25000平方米，为未来国家重点实验室、技术转移、教育及培训提供场地和设施。目前，已有300名中文大学教职员注册成为研究院成员，自2011年，承担国家、广东省及深圳市级科研课题近百项，科研经费超过一亿元人民币。

香港中文大学深圳研究院将继续在深圳及珠三角地区积极开展科研、教育培训及有关产业化工作，为深港科技融合提供高效的平台，为粤港地区乃至国家的科技创新、经济及文化发展作出贡献。



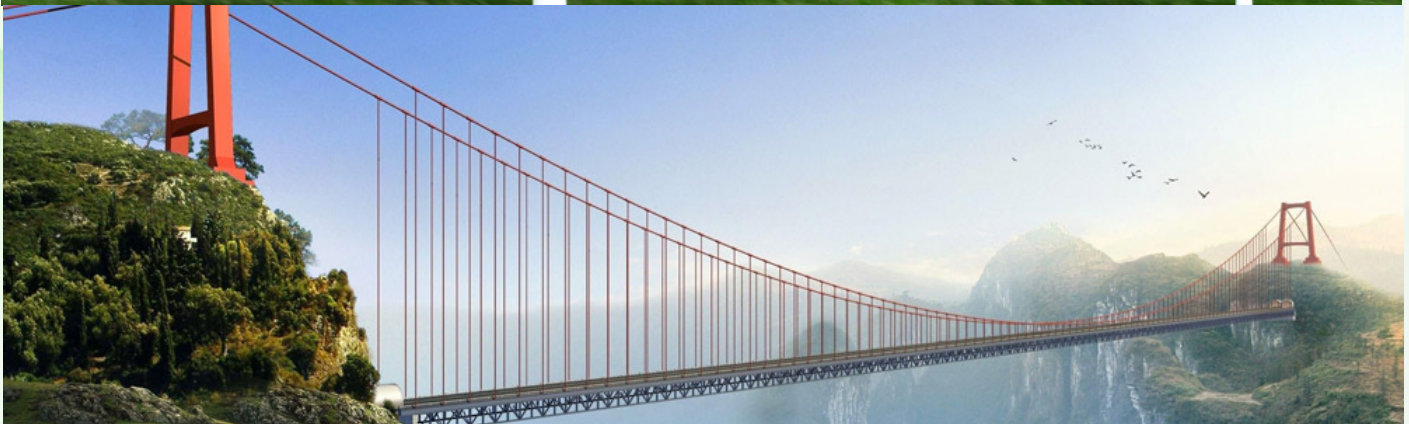
承办单位

深圳中国工程院院士活动基地

深圳中国工程院院士活动基地是中国工程院与地方政府联合创建的首家工程院院土地方性活动基地，是合作委员会领导下的经常性办事机构，主要工作是完成合作委员会确立的各项任务。

院士活动基地的主要任务有：

- 1、组织实施中国工程院与深圳市政府合作委员会确定的年度工作计划；
- 2、组织院士和专家，为深圳市及其大中型企业(集团)的高科技发展规划，企业技术创新和技术改造、投资方向及重大工程建设项目立项等提供咨询评估；
- 3、举办有院士参加的国内、国际学术会议，科技论坛和学术报告会，传播普及科技知识；
- 4、组织院士，专家研究解决由深圳企业和建设工程提出的技术难题和攻关项目；
- 5、牵线搭桥、联系、促进院士及院士所在单位的科研成果转移到深圳，实现产业化；
- 6、充分发挥中国工程院的优势，联系港、台及海外工程科技界，开展科技交流与合作；
- 7、通过组织各类院士报告会、技术讲座、科技攻关、产品演示等活动，为深圳市培养中、青年工程技术骨干人才；
- 8、为工程院院士、专家到深圳开展科技活动提供服务和帮助。



承办单位

宝安区人民医院

宝安医院始建于1984年，经过三十多年的发展，已建设成为集医疗、科研、教学、预防、保健、康复于一体的大型综合性医院，也是南方医科大学附属医院、中山大学博士后流动站科研基地、广东省高等医学院校教学医院、广东医学院硕士研究生联合培养基地、全省住院医师和全科医师规范化培训基地，承担了宝安区医疗中心、宝安区急危重症病人救治中心的职能。2011年通过广东省卫生厅综合医院等级评审，成功晋升为三级甲等医院。

医院占地面积6.3万平方米，建筑面积14.4万平方米，开放病床1050张。现有职工总数1837人，其中正式职工880人，聘用人员957人，聘用人员占全院职工52%；全院专业技术人员1586人，占全院86.34%；病床与工作人员之比为1.8，病床与护士之比为0.8。现有高级职称420人，博士、博士后42人，硕士学历168人，本科以上学历达60.42%。医院现有硕士导师20名，每年培养硕士研究生10名左右，接收各医学院校本科实习生约200名。

2014年，医院门、急诊量188.8万人次，出院病人37825人次，住院手术16810人次，业务收入81968.5万元。

医院设有临床、医技科室51个，社康中心10个。目前，我院临床护理、急诊医学科为省级重点学科，急诊医学科为广东省临床重点学科和深圳市医学重点学科；重症医学科、临床护理、急诊医学科、心血管内科、妇产科、普通外科等6个学科为宝安区医学重点专科，康复科、肿瘤科为宝安区医学重点专科建设单位。

医院先后获得全国“百佳医院”、“全国颅内血肿微创治疗协作医院”、“全国颅内血肿微创治疗先进单位”等荣誉。每年的医疗服务质量整体评估均保持A级，2010年评估总成绩和顾客满意度获全市区级医院第一名，护理满意度获全市综合医院第一名。2015年3月，在全省公立医院群众满意度测评中，我院满意度总分88.7分，位列第三名。



承办单位

深圳市人民医院

深圳市人民医院，始建于1946年，前身是宝安县医院，1979年伴随深圳经济特区成立更名为深圳市人民医院。1994年被评为深圳首家“三级甲等”医院。1996年经国务院侨办批准成为暨南大学医学院第二附属医院，2005年升格为暨南大学第二临床医学院。伴随着经济特区的成长，深圳市人民医院已发展成为一个功能齐全、设备先进、人才结构合理、技术力量雄厚，集医疗、教学、科研、保健为一体的深圳市最大的现代化综合性医院。医院占地面积13.82万平方米，建筑面积21.3万平方米，编制病床2100张，开放病床2400张。2013年出院病人8.04万人次，门诊量300多万人次。目前医院有两个门诊部（一、二门诊部）、一个住院部（又称留医部）及一个分院（深圳市人民医院龙华分院）。

医院现有呼吸内科、肾内科、消化内科、感染内科、内分泌科、胸外科、口腔科、麻醉科、妇科、产科、新生儿科、急诊科、病理科、检验科、临床护理及包含CT、放射、超声、介入、核医学在内的医学影像科16个省级重点学科，优势医学重点学科（群）7个、深圳市医学重点学科14个、深圳市医学重点实验室4个。2013年我院介入微创诊疗中心被评为亚洲冷冻治疗培训基地，承担起培训港澳台及中国南方地区专家的任务，凭着医院的整体医疗技术水平，吸引了香港、澳门以及深圳周边地区的大批患者，受到国内外媒体广泛关注。作为暨南大学第二临床医学院，拥有卫生部全科医生培训基地、暨南大学第二临床医学院博士后创新实践基地。医院现有内科学、外科学、妇产科学、儿科学等18个教研室。目前有博士生导师16名，硕士生导师107名。现已招收硕士生730余名、博士生40余名，本科生264余名。每年招收临床实习生近130余名，进修生120余名。2013年全院申报包括国家自然科学基金在内的各级课题326项。在SCI收录期刊及核心期刊发表论文581篇。

医院积极开展高层次、国际性的交流与合作，先后与德国纽伦堡大学医学院、不莱梅港中心医院、加拿大西安大略大学器官移植中心、美国休斯敦卫理公会医院、法国里尔大学医疗中心、韩国全南大学校病院、韩国大田宣医院建立起长期合作与交流的平台，缔结友好医院，与国际医学大舞台进一步交融。2013年4月基于深圳市超级计算中心云平台的深圳市人民医院网络医院正式运营，网络保健、远程监测、全程医疗等获得了社会的广泛好评，被列为深圳市健康产业重点扶持民生工程计划。深圳市人民医院以强烈的社会责任感积极承担着特区重大活动的医疗保障工作，用她的历史、文化、勇气、智慧，努力呵护着市民的健康，铸就深圳医疗的辉煌。



支持及赞助单位

再生医学教育部重点实验室 暨南大学-香港中文大学



暨南大学，始创办于1906年，是国内历史最悠久的高等学校之一，同时也是国家“211工程”重点建设大学。再生医学教育部重点实验室是在2007年4月17日由暨南大学和香港中文大学联合创办再生医学联合实验室的基础上，同年申报再生医学教育部重点实验室，于2007年12月获批建设。再生医学教育部重点实验室于2013年12月通过教育部的建设验收。再生医学教育部重点实验室是目前内地高校与香港高校联合共建的唯一一个教育部重点实验室，重点实验室使用与国际接轨的运行体系运行，推动再生医学领域高水平的科研、学科建设和人才创新培养。2008年，重点实验室获批广东省科技厅国际合作重点科研机构，2009年11月获批国家科技部“国际科技合作基地”。重点实验室总面积达3600平方米，拥有先进的仪器设备，价值近5000万。重点实验室团队的研究方向包括：（1）干细胞与衰老的相关机制；干细胞分化、转化与再生的分子机制及应用；（2）成体细胞去分化、再分化及转化机理与应用；（3）终末分化组织与器官损伤的修复与再生；（4）天然活性成份与功能因子在再生修复中的应用。重点实验室的核心研究成员都有在海外著名学府留学经历，其专业与研究背景包括：再生生物学、再生医学、发育生物学、细胞和分子生物学、组织工程学、生理学和免疫学等。





深圳大学医学部简介

深圳大学是深圳市唯一学科全面的综合性大学，深圳大学医学院是深圳市唯一的高等医学院校，成立于2008年12月。通过整合学科资源，优化学科布局，快速推动深圳大学医学学科的发展的理念，深圳大学医学院迅速成长，于2013年4月组建了深圳大学医学部。

深圳大学医学部坚持“高端、精英、超前、精湛”的办学理念，和以“小规模、研究型、精英化”的建设原则，建了4个本科专业（临床医学、药学、生物医学工程、医疗器械工程），2个硕士学位授权点（临床医学、生物医学工程），1个专业学位授权点（生物医学工程领域工程硕士），并有国家、省、市多个重点研究平台。学部还将护理、康复医学、公共卫生等专业纳入了未来发展蓝图，大力打造肿瘤、代谢疾病、肾脏疾病、免疫学疾病、心血管疾病，以及再生医学等集医、教、研和产业化为一体的深圳大学医学中心。同时，为积极探索适应21世纪医学科学发展和医疗卫生服务模式转变需要的创新人才培养模式，学部积极拓展外部办学空间，与国际医学教育模式接轨，已与爱尔兰都柏林大学等联合构建临床医学硕、博士培养体系，并与澳大利亚莫纳什大学、伦敦大学学院等国内外一流医学院校开展了深入的合作。

医学部已经聚集了一大批以美国“三院院士”、“双聘”院士、教育部长江学者、国家“千人计划”特聘专家、鹏城学者等优秀学者。他们带着理想和热情加入了深圳大学医学部的医学教育和科学研究事业中，通过加大领军人才和青年优秀学者引进力度、完善教学和科研管理和激励机制、建立一个成规模的高质量博士后队伍。

深圳大学医学部承担为国家，特别是深圳地区培养和输送高质量医疗人才的重任。目前新建的深圳大学学府医院不仅是从事高质量医疗人才的场所，也是培养各级优秀临床人才、实现疾病防治研究突破的基地。深圳大学直属附属学府医院与医学部同步建设，其目标是建成与国际接轨的集医疗、教学、科研、康复和预防保健为一体的、具有专科特色的综合型、高端三级甲等教学医院。

深圳大学医学部全体师生将秉承开拓进取、追求卓越的精神，为培养一流的医学人才、为推动医学科学发展、为服务一方医疗事业作出最大的贡献！



支持及赞助单位

深圳市科学技术协会

深圳市科学技术协会于1982年5月成立，1993年10月，市编委[1993]078号文批复“市科学技术协会与科学技术局合署办公”。2004年10月，根据深办发[2004]3号、深府办〔2004〕58号文，设置深圳市科技和信息局，深圳市科学技术协会与深圳市科技和信息局合署办公。2007年1月，按照深编[2006]135号文件精神，深圳市科学技术协会由与深圳市科技和信息局合署办公调整为单独设置。2009年9月，深圳市政府进行机构改革，根据深府办[2009]100号文，深圳市科学技术协会增加了“科技成果评审和科技创新奖评定的组织工作”的职能，并将深圳市科技专家委员会办公室（深圳市技术引进咨询评议委员会办公室）、市科技开发交流中心、市科学馆等三个事业单位划归市科协管理。

深圳市科学技术协会是中共深圳市委领导下的人民团体，其宗旨是团结组织科技工作者以经济建设为中心，促进科学技术的繁荣和发展，促进科学技术的普及和推广，促进科技人才的成长和提高，维护科技工作者的合法权益，为科技工作者和科技团体服务。深圳市科学技术协会的主要任务是开展决策咨询、调查研究、学术交流、深港与国际科技交流合作、科学普及和科普资源建设等活动，加强所属团体之间的联系，培养、引进、表彰、举荐科技人才，率先成为区域创新体系的重要参与者、创新型城市解决方案的提供者、创新文化的建设者、国内外科技合作的实践者和科学技术普及工作的推动者。

截止2009年底，深圳市科学技术协会有3个下属事业单位，管理71个市级学会，有会员十余万人，有6个区级科协，已建有市级以上科普教育基地43个。



支持及赞助单位



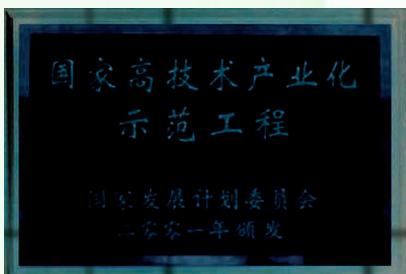
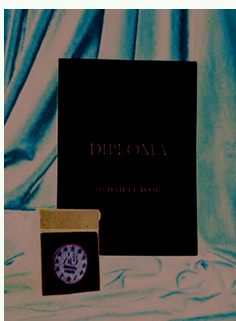
沈阳协合集团有限公司创建于1988年，专长于超级抗原抗癌、抗病毒等原创小分子生物制品的自主研发、生产、销售，是国际领先、高速成长的国家重点高新技术企业。（*超级抗原是1989年由瑞典科学家提出的现代免疫学新理论，是国际公认的最强大的细胞因子诱生剂）

27年风雨，“协合集团”取得了累累硕果，目前已拥有24项发明专利；先后承担国家“十一五”、“十二五”重大新药创制科技重大专项、“国家重点火炬计划”、“国家级蛋白质创新药物工程技术平台”等11项国家级重点科技项目；拥有国家级“院士科研工作站”、“博士后科研工作站”、“国家生命科学与技术人才培养基地”；进站院士13位，为企业研发的厚积薄发提供了强有力的技术支撑。2008-2014年，先后四次将多个超级抗原、中药标准品菌种成功搭载“神七”、“神八”、“神九”、“神十”，开展太空航天育种，实现了超抗原应用领域历史性突破，震惊海内外。

主导产品“高聚生”（国药准字S19990010）是应用自主专利技术研制、生产的国家一类生物新药、填补国内抗肿瘤生物新药的空白，更是世界上第一个应用于临床治疗恶性肿瘤的超抗原生物制剂；是世界超级抗原理论在抗癌应用上的一次重大突破；“高聚生”于1999年成功问世至今16年，临床应用证明：具有对人体自身免疫能力激发和主动调动的超强能力；显著增强机体免疫功能，对抗放、化疗毒副作用，升高白细胞，消除恶性胸、腹水，抑制肿瘤细胞生长；在癌症康复期治疗中，明显改善病人生活质量，延长病人生存期，有效抑制复发转移。“高聚生”作为生物免疫治疗的先锋药品以其高效低毒的功效为治疗肿瘤、防控病毒性疾病、提高免疫力等提供了有效和持久的防线。“高聚生”等超级抗原系列产品广泛应用于小汤山非典、禽流感、艾滋病、白血病、埃博拉、中东呼吸症等突发复杂的病毒感染性疾病的防控与治疗，效果显著；向海内外捐款捐药累计达到1.8亿元人民币，董事长陈巨余被世界圣约翰爵士团授予大司令级爵士、德国圣殿骑士团（S.I.T.O.）王室机构授予康斯坦丁公爵勋衔。

目前，“协合集团”按照欧盟标准升级改造车间项目刚刚通过国家食药监总局新版GMP认证；产业升级与资本运营工作的全面启动，必将助力协合集团展翅高飞，走向国际！

支持及赞助单位



支持及赞助单位



Micro Technology Hong Kong Ltd.

Micro Technology Hong Kong Ltd. 是从事高分辨分析仪器的专业公司。其主要产品有电子显微镜(SEM & TEM), 光学显微镜及高分辨小动物成像系统(CT, MRI, PET, SPECT 及光学成像系统)。其产品广泛应用于生物医学、材料科学等科研领域以及电子、食品、石化等工业企业。其在北京, 上海, 广州及香港办事处为客户提供及时周到的服务。

Skyscan1176 活体 Micro-CT



分辨率高至9微米的活体小动物全身3D空间分辨率

应用范围: 小鼠, 大鼠和兔子

25,000 小时稳定 X 射线源

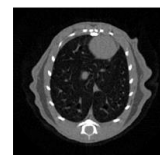
1100 万像素 X 射线相机

快速低剂量螺旋扫描

生理监控系统



小鼠头颅结构



小鼠胸腔断层截面



小鼠气体麻醉中

Skyscan2211 纳米 CT



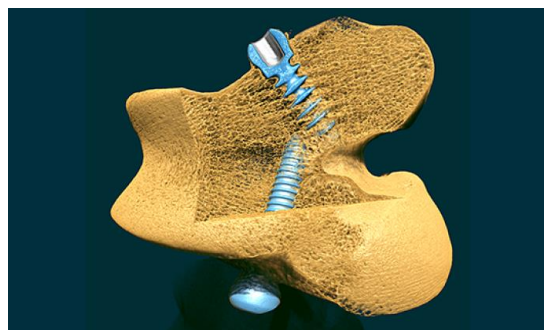
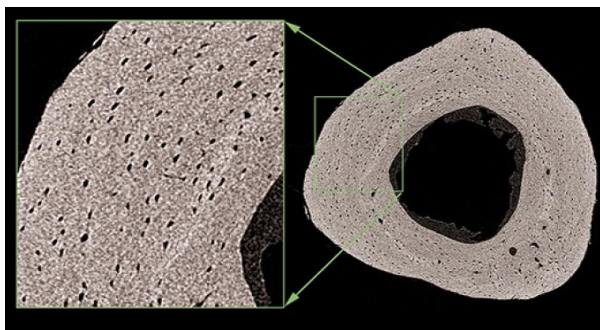
最高分辨率达到 100 纳米。

X 射线电压 20-190KV, 可穿透不锈钢植入物

最大样品尺寸: 200 毫米 x 200 毫米

最大样品重量: 25 公斤

GPU 加速重建算法, 比普通重建快 20 倍



Micro Technology Hong Kong Ltd.

北京海淀区大柳树富海中心 2 号楼 502-021 室 电话: 010-88579185 传真: 010-88579186

上海市四平路 775 弄 1 幢 914 室 电话: 021-65754775 传真: 021-65754787

广州市天河北路侨林街 39-49 号中旅商务大厦西塔楼 23 楼 D 室 电话: 020-38840491 传真: 020-38841078

香港永吉街 29-35 号恒丰大厦 17 楼 A 室 电话: 852-25769050 传真: 852-25769507

張家港市亞堤仕醫療諮詢管理有限公司

企業名稱（中文）：張家港市亞堤仕醫療諮詢管理有限公司

（英文）：ZHANGJIAGANG CITY ARTISE MEDICAL CONSULTATION CO.,LTD

公司類型：外商投資企業

股東(發起人)：Artise Medical Investment & Consultation Co., Ltd.

投資總額：50萬美元 註冊資本：50萬美元 經營年限：叁拾年

註冊地址：張家港市錦豐鎮錦繡路3號揚子江國際冶金工業園區

經營範圍：

- 從事先進醫療技術的引進、轉讓、諮詢及相關培訓和服務
- 從事投資諮詢、企業管理諮詢、商務資訊諮詢，行銷策劃、會議及展覽服務
- 從事電腦公共軟體發展、電腦維修服務，電腦及其輔助設備批發（不涉及國營貿易管理商品，涉及配額、授權管理的商品，按國家有關規定辦理申請）

LOGO設計理念：

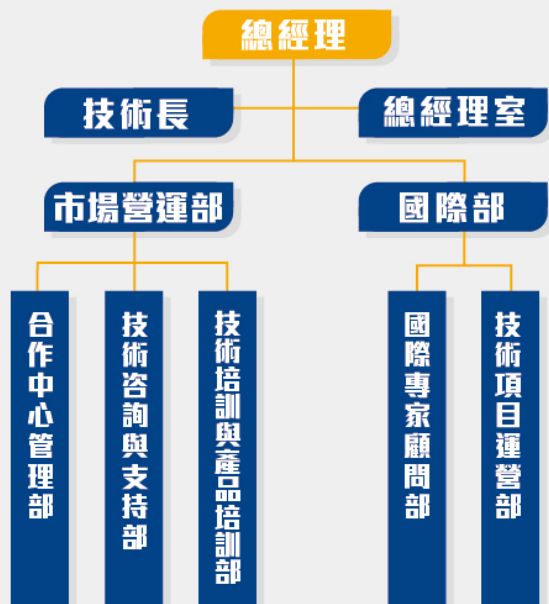
十字部分象徵醫療，藍色代表公司技術；綠色代表重生。

向上展開雙臂的人形，象徵健康、活力



以器械的外觀作為LOGO的外圍圖形，而圓形也象徵不斷運轉，不斷精進，永不止息的生根求知，精益求精的深耕精神。

公司組織機構



專案市場運營商業模式

商業模式	性質	合作要點
技術型合作	會診制	專家會診、技術推廣、產品應用
項目型合作	合作制	專家顧問、專案推廣、利益共享、風險共擔
承包型合作	承包制	遵章守紀、自負盈虧
租賃型合作	租賃制	遵章守紀、自負盈虧
股份制合作	股份制	共同出資、明確分工、資源共享、利益共享、風險共擔
併購型合作	併購制	醫院轉讓、所有權變更

中国再生医学的发展和未来

王正国院士

第三军医大学野战外科研究所



再生医学是一门研究如何促进受损组织器官结构重建和功能恢复的学科。它有望继药物治疗、手术治疗后成为第三种治疗途径，特别对先天性遗传缺陷疾病和后天获得性退行性疾病。1999年以来，干细胞与再生医学相关研究九次入选《科学》(science)杂志十大世界科技进展。专家认为，干细胞与再生医学正处于重大科学技术革命性突破的前夜。与20世纪抗生素的发明具有同等重要(甚至更重要)的意义。

我国有糖尿病患者5,800万人;重症肝病患者约3,150万人,每年等待肝移植患者约50万人,获得移植者仅5,000人;等待肾移植患者40万人,获得移植者3,000余人;此外皮肤烧、烫伤约500万人;心脑血管病致死者约260万人;癌症160万人;恶性血液病109万人。这些病人都希望得到再生医学的治疗。

未来再生医学的研究重点将集中在:胚胎干细胞、成体干细胞、重编程干细胞、干细胞保存和干细胞库、组织构建、生物材料、基因治疗、异种器官移植等领域。

转化医学的出现将基础和临床连接起来,为临床应用铺平了道路,并带动了相关学科为人类健康发挥积极作用。

个人简历

王正国,中国工程院院士。现任国际交通医学学会副主席(候任主席),《Traffic Injury Prevention》杂志副主编;《中华创伤杂志》主编;中华医学会常务理事,解放军科学技术委员会常务委员。

王正国院士是我国冲击伤、创伤弹道学、交通医学研究的主要创始人之一,国家重点学科“野战外科学”学术带头人。他致力于战创伤基础理论和应用基础研究五十余年,取得了一批国际先进以至领先的重大科研成果,为我国战创伤医学的发展做出了卓越贡献。先后获国家科技进步一等奖1项、二等奖4项,其他省部级奖项20余项。1997年获香港何梁何利基金医学科学技术奖;1998年获美国联合保健勤务大学Michael DeBakey(迪贝克)国际军医奖;2000年获陈嘉庚医学科学奖和国际交通医学重大成就奖;2002年获第四届光华工程科技奖。

医学与科学

樊代明院士

第四军医大学西京消化病医院



医学是什么?从40年前学医我就开始思考这个问题,但一直未得满意答案。不过还是有些进步,但有时豁然明了,可又迅即转入糊涂。至今,我不能明确地说出医学是什么,但我可以说它不是什么了。依我看,医学不是纯粹的科学,也不是单纯的哲学,医学充满了科学和哲学,但还涵盖有社会学、人学、艺术、心理学等等。因而,我们不可以笼统地用科学的范律来解释医学,也不可以简单地用科学的标准来要求医生。

医学既研究病也研究人

医学要比科学起源早。科学一词的出现也才1000多年,而医学已有数千年甚至更早的历史。因此,应该是医学的积累、进步以及需求催生了科学。而医学研究的对象是人,尽管有人物的说法,但不等同于物。医学研究的是“知人扶生”,知人当然需要格物,科学上只要格物就可致知,但医学上只有格物难以知人,更难以扶生。因此,将医学视为科学的一个分枝或隶属于科学、服从于科学,甚至把医学视为医学科学的简称,看来是不恰当的。

医学研究的不仅是疾病的本身(或其本质),而且要研究疾病这种现象的载体、即有着不同生活经历和生理体验的活生生的人,要研究人体各种机能的本质和进化规律。因此,医学不仅重视事物高度的普遍性,而且重视人体结构、功能及疾病的异质性或称独特性。医学是通过长期大量不间断的理论探索和实践检验,最终形成最大可能适合人体保健、康复和各种疾病诊疗的知识体系。

因此,医学要远比科学复杂。据经典医学书籍记载,现有病种已达40000种之多,加之不同疾病有不同的分期和分型,而且又发生在不同人群或不同个体身上,这就更为复杂。因此,我们认识医学就不能千篇一律,对待病人更应因人而异,因时而易,因地制宜。

医生不仅治病还要救命

医学关乎生命。医学研究的对象恰恰是有着高级生命形式的人类及其组成形式,而科学研究的对象则并非是如此高级的生命形式、甚至是无生命的普通物质。科学研究再复杂,最终的定律是“物质不灭”,而医学除了物质不灭外,更要回答为何“生死有期”。

科学可以按照已奠定的精确的理论基础去分析甚至推测某一物质的结构和功能变化,但医学目前由于对生命本质的无知,故多数的理论和实践还是盲人摸象,雾里看花。显然,在生命起源奥秘没被揭示之前,所有关于生命现象本质的解读和认识都是狭义、片面和主观的,充满了随意性。对生命的思考和解读,中医和西医充满分歧,甚至南辕北辙,其实这并不奇怪,实际上是观察角度不同所致。西医的整个体系是建立在科学基础之上的,所以常有医学科学的提法。中医的整个体系是建立在实践经验的归纳分析和总结之上的,所以不常有中医科学的提法。双方对科学和经验的重要性都无异议,可对经验之科学或科学之经验,则认识迥异,这恰恰说明了医学和科学的区别。

医学,特别是临床医学,说到底做两件事,一是治病;一为救命。二者相互关联,但也有些差别。治病是“治”物质,是以物质换物质,或以物质改变物质;而救命不是“救”物质,救命是在调节物质表现的特殊形式,以确保这种形式的正常存在。这就是我们中医所说的整体中的平衡,或西医所说的内环境的

摘要

稳定。

人总是希望越来越好的结果，但生命却是一个越来越差的过程，医学不是万能的，医生是人不是神。所以，人类对医学和科学的要求应该是不一样的。

“医学就是科学”是误区

说医学就是科学，我坚决反对。科学的巨大进步，把科学推上了至高无上的地位，导致了科学主义的出现，于是乎什么学科都把自己往科学上靠，似乎一戴上科学的帽子，就会更接近真理，就会名正言顺。但医学自从戴上科学的帽子后，其实好多问题不仅解决不了，反而导致医学与人的疏离，甚至越来越远。

“医学就是科学”，尽管它已成为当下大众的普识，也是近百年来一次又一次，一步又一步，逐渐形成并锁定的习惯性概念。正是这种普识与概念，导致时下医学实践出现了难堪的现状：我们不仅在用科学的理论解释医学，用科学的方法研究医学、用科学的标准要求医学、也是在用科学的规律传承医学。最终的结果，医学的本质将被科学修改；医学的特性将被科学转变，复杂的医学将被单纯的科学取代，医务工作者将成为科研工作者；医学院将成为科学院；病人不再是医生关怀呵护的人群而将成为科学家实验研究的对象。这既不是医学发源的初衷，更不是医学发展的目的。

医学的本质是人学，若抽去了人的本性，医学就失去了灵魂；若抽去了人的特性，只剩下其中的科学，那就成了科学主义。它所带来的严重后果将不堪设想。

曾经，科学脱胎于自然哲学，其后获得了巨大发展；现在，医学出现科学化，导致出现不少难解的问题；将来，医学如果能从科学回归本源，必将引起医学发展史上的一场革命。

个人简历

樊代明，院士、教授、主任医师、中国工程院副院长、第四军医大学西京消化病医院院长、美国医学科学院外籍院士、世界消化学会常务理事兼科计委员会主席、亚太消化学会副主席、中国抗癌协会副理事长、倡导整合医学的理念与实践，先后获国家科技进步一、二、三等奖各1项，法国医学科学院塞维亚奖、何梁何利科技进步奖。

骨诱导性生物材料——从科学基础到临床转化

张兴栋院士

四川大学国家生物医学材料工程技术研究中心



骨诱导性生物材料是被通过材料自身优化设计，而不是外加生长因子或活体细胞，植入体内后可刺激机体发生特定反应，激活细胞内成骨基因级联表达，调控细胞沿成骨细胞系分化，最终形成或再生有生命的骨组织的骨修复或替换材料。

传统观念认为，只有活性生物物质才可能诱导有生命的人体组织形成或再生，无生命的生物材料不可能。骨诱导性生物材料成功研发和推广临床应用是对传统观念的突破，“划时代地宣告用于再生医学的骨诱导性生物材料的到来”，并进一步引发对于非骨组织诱导性材料研究。组织诱导性生物材料（Tissue Inducing Biomaterials），即可通过材料自身优化设计诱导组织或器官再生的生物材料，已成为当代生物材料科学与产业发展的方向和前沿。

本报告将简要介绍1) 基于当代医学进展和临床需求对骨诱导性生物材料的提出与最基本的科学依据，2) 骨诱导性材料的发现、试验确证及初步的机理解释，即科学基础的建立，3) 临床转化的条件和要求及临床应用情况；并从中概括新型生物材料的设计及向临床转化的基本要求。

个人简历

张兴栋，四川大学教授、中国生物材料学会理事长、全国医疗器械生物学评价和全国口腔材料和器械设备技术标准化委员会主任委员。上世纪80年代，于国内率先开展磷酸钙基生物活性陶瓷及植入器械研究，研发出羟基磷灰石人工骨、牙种植体、人工关节等生物材料产品，获得国家食品药品监督管理总局生产注册证，并广泛应用于临床。上世纪90年代，率先发现并确证无生命的生物材料可诱导有生命的机体组织或器官再生或形成，提出组织诱导性生物材料新概念，于国际首创新一代人工骨——骨诱导人工骨及其工程化技术。2007年当选中国工程院院士，2014年当选美国国家工程院外籍院士，2015年当选美国医学与生物工程院Fellow，以及国际生物材料科学与工程学会联合会下任（2016-2020）主席。

摘要

组织修复与再生新的挑战：实现多种组织在损伤部位的原位修复与再生



付小兵院士

解放军总医院生命科学院院

经过广大创烧伤、危重病与急救医学界同仁的共同努力，总体来讲，我国严重创伤救治的成功率明显提高，死亡率显著下降。据不完全统计，我国烧伤救治成功率从2000年报告的98%左右上升至2012年的99.5%左右，严重创伤死亡率从2000年的35%下降至2013年的12%左右。创新理论和关键技术的应用使急性创面的愈合时间较传统的治疗方法缩短2-4天，而慢性难愈合创面的愈合率则由83%上升至94%左右。这些成绩的取得，得益于国家加强对创伤、烧伤和组织修复与再生医学基础研究的投入和大量创新技术的快速转化应用。但值得注意的是，尽管救治成功率提高了，死亡率下降了，但许多救活病人的功能并没有完全恢复，既影响生活，也妨碍工作，难以回归社会。因此，社会上对完美的组织修复与再生的呼声越来越高，是组织修复与再生医学面临的新问题与新挑战。

什么是完美的组织修复与再生？简单来讲，就是使受损伤的组织 and 器官通过某种自身或人为的干预，恢复到损伤以前的解剖和功能状态。目前，严重创烧伤后的组织修复之所以还没有达到人类所希望的“完美”再生的目标，据报告一方面是损伤组织快速的瘢痕形成是高等动物的一种自我保护机制，另一方面则是损伤部位涉及的组织种类多，而不同种类的组织由于遗传与发育等因素的影响，在修复与再生的启动过程、信号网络、调节机制与影响因素等许多方面并不完全相同，因而存在修复与再生的不协调性和不一致性。而寻找这种“协调和一致”的修复机制，创造适宜这种“协调和一致”修复的条件，启动“协调和一致”修复的过程，可能是实现同步协调“完美修复与再生”的有效途径之一。特别是近年来有关细胞去分化、诱导性多能干细胞（iPS）和再生胚芽（Blastema）等机制的阐明，有可能是再生医学的突破口。

个人简历

付小兵，中国工程院院士。现任解放军总医院生命科学院院长、教授、创伤外科研究员、博士生导师。担任国务院学位委员会学科评议组成员，国家技术发明奖、国家科技进步奖评委，中华医学学会组织修复与再生分会主任委员、中华医学学会创伤学分会前任主任委员、国家973“创伤和组织修复与再生项目”首席科学家，国家自然科学基金创新群体负责人，1995年国家杰出青年基金获得者。主编出版《中华创伤医学》、《再生医学：基础与临床》等学术专著17部，参编30余部，在Lancet等国内外杂志发表学术论文400余篇，以第一完成人获国家科技进步二等奖3项。获“何梁何利基金科学与技术进步奖”、“求实”杰出青年奖、中国人民解放军杰出专业技术人才奖、中华医学学会创伤学分会“中华创伤医学终身成就奖”、中华医学学会烧伤外科分会“终身成就奖”和“国际创伤修复研究终身成就奖”等多项荣誉。荣立一等功。

前沿技术与中医药转化医学

刘良教授



澳门科技大学中药质量研究国家重点实验室

中医学是基于长期临床医疗实践的传统医学,可资研究发掘和转化应用者众多。中医学又是一门复杂科学,只有集成多学科的先进技术开展整合和创新研究,才能阐释其科学内涵,并获得转化应用成果。为此,澳门科技大学中药质量研究国家重点实验室(SKL)采取以前沿技术为引擎,驱动新方法和新标准的建立,及研发新产品的发展策略。SKL目前拥有的主要前沿技术平台包括:创新基于生物活性的药材DNA图谱分析与鉴定技术,建立辨别贵重中药材的药材真伪与优劣鉴别的新技术与新方法;采用LC-NMR液质联用-核磁共振联用技术,对微量中药化学成份进行高速分离并对活性化学成分进行快速在线结构鉴定;集成多元色谱-质谱联用药材及其制成品质量控制技术,建立中药材及中成药质量稳定性评价的“色谱-质谱-核磁共振光谱指纹图谱-药效指纹图谱”综合分析方法和标准;优化蛋白质组学、鞘脂代谢组学和糖组学技术;研究中医药治疗多成分、多途径、多靶点作用的体内过程,发现药物作用新机制并创制新药物;采用多功能活细胞显微成像可视化技术,以实时影像方式观察中药活性成分对细胞和分子整合调节机制的影响,阐明中医药治疗的科学原理;高速流式细胞分选技术,分离和纯化中药活性成分作用的靶细胞群,并分离单细胞对药物作用进行最精细化的细胞和分子水平研究;纳米中药制剂新技术,改善中药活性成分的生物利用度和药理作用强度等。近年来,SKL着力引进多学科的前沿技术人才,实验室研究团队已达170多人,发表SCI论文数百篇,获得国际专利近百项,2014年通过了中期评估,已成为中医药研究领域的国家级平台。

个人简历

刘良, 讲座教授, 医学博士, 博士生导师, 现任澳门科技大学校长、中药质量研究国家重点实验室(澳门科技大学)主任, 世界卫生组织传统医学项目顾问、国际标准组织(ISO)传统中医药ISO/TC249技术委员会委员及第一工作组召集人、国家中医药管理局深化医疗改革专家委员会委员、国家自然科学基金中医药学科组评审专家、世界中医药学会联合会中医药免疫专业委员会会长及教育专业委员会和诊断专业委员会副会长、中国免疫学会中医药分会副会长、中国高等教育学会常务理事、香港卫生署荣誉顾问、香港中药研究及发展委员会委员、澳门特区政府人才发展委员会委员、科技委员会委员和医务委员会委员等学术和社会职务。刘教授长期从事中医风湿免疫临床医疗及转化医学研究, 先后获得国家科技进步奖二等奖2项、国家教育部自然科学奖一等奖等部省级一等奖2项和二等奖3项。在国际SCI期刊发表论文逾百篇, 总IF逾400点, 包括一批国际知名学术期刊, 如Nature (Supl), Science(Supl), Nature Medicine, Oncotarget, Analytical Chemistry, Organic Letters, Cell Death & Diseases, Scientific Reports, Briefings in Bioinformatics, Chromatography A等。获得发明专利项目32个, 包括PCT专利1项、美国专利4项、中国专利2项、澳大利亚专利25项。10项专利已获实施, 4个中药产品已投放市场。

肌腱组织的损伤与再生研究的热点

陈启明教授

香港中文大学医学院矫形外科及创伤学系



肌腱病好发于人体各个部位，表征为受累肌腱的疼痛和断裂。目前主要以对症治疗为主，尚没有任何治疗方式可推迟或逆转该病。

我们旨在针对发病机制治疗。研究表明，肌腱病表现为肌腱愈合障碍，即早期愈合障碍，并伴细胞、血管增生，细胞分化异常导致肌腱软骨化或钙化。

目前的研究重点：寻找肌腱愈合过激的可能原因；探索干扰肌腱分化的控制点；建立更好的肌腱病动物模型，能够紧密联系危险因素和病理改变。

过劳是引起肌腱病的主要因素之一，其加重了肌腱愈合中机械负载和氧化应激。通过在动物模型中结合机械负载和氧化应激是一个更有效引发肌腱病的方法，从而可用作测试新疗法。

对肌腱分化控制点的研究可促进针对细胞异常分化的治疗方式的探索。研究表明，microRNA在正常和异常肌腱分化中具有潜在作用，这将促进以microRNA为基础的药物开发。

微生物是潜在病因，其引起的慢性炎症可致愈合障碍。我们正针对肌腱病的遗传物质进行研究；以及在体外通过微生物诱发肌腱病。

个人简历

陈启明，教授，国际知名的骨科运动医学专家，香港中文大学医学院骨科教授及博士生导师。前任香港骨科学会会长，香港骨科医学院主席，香港医学会副会长。2002-2006年就任国际运动医学联合会FIMS主席，成为该会自1928年成立以来首位亚洲裔主席。在骨科及运动医学国际期刊上发表300多篇研究论文，编着了60多本有关书籍。并在约800多个国际会议上发表演讲。并为《骨科临床与研究》杂志JOSR及《亚太运动医学、关节镜、康复治疗及科技》杂志AP-SMART担任主编。

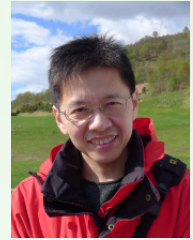
1997年获得国际关节镜膝外科及运动医学会议的John Joyce奖，2008年获得国际运动医学联合会金奖，2009年获得美国史丹福大学Alpha Omega Alpha荣誉医学学会荣誉会员，2010年成为骨与骨关节十年BJD大使，2012年中华医学会骨科分会授予仁心奖，并于2014年获得亚太膝关节镜及运动医学学会高木及渡边奖。

摘要

毛发再生的新理念

陈志强教授

台北荣民总医院皮肤科



头发在人类社交生活中扮演一个很重要的角色,因为秃发会使人缺乏自信并显得苍老。毛囊是我们器官中少数能终其一生不断的进行退化与再生的组织,因此毛囊是研究干细胞生理学及再生医学的最好目标。以前的研究发现毛囊干细胞的活化是伴随着周期性的Wnt/ β -catenin的表达所导致,然而我们近几年的研究则显示除了毛囊内的微环境(也就是所谓的niche)之外,毛发的生长与退化也受到毛囊外巨环境所调控。我们发现毛囊外的脂肪组织会释放出各种不同的刺激(如follistatin)及抑制因子(如BMP-2, DKK-1, SFRP-4)来调节毛囊干细胞的活化与再生,而老化所导致的毛发再生循环异常则是肇因于环境中抑制因子的过度表达或刺激因子的表现减少。除此之外,越来越多的研究也显示毛囊干细胞不仅受到其周边的脂肪组织影响,许多毛囊外因子包括荷尔蒙、免疫系统、神经系统甚至昼夜节律(circadian rhythm)都可调节毛囊干细胞的再生循环。因此,针对毛囊外环境而非干细胞本身做调控将对治疗落发与促进毛发再生的领域带来新的契机。

个人简历

学历:

- 1991.9-1998.7 国立阳明大学医学士
- 2005.9-2014.5 国立阳明大学临床医学研究所博士

经历与现职

- 2014-迄今 社团法人台湾检验及品保协会监事
- 2014-迄今 国立阳明大学皮肤学科助理教授
- 2006-迄今 台北荣民总医院皮肤科主治医师
- 2008-2010 美国南加州大学组织工程实验室访问学者
- 2004-2006 桃园荣民医院主治医师
- 2000-2004 台北荣民总医院皮肤科住院医师

摘要

低氧下间充质干细胞的培养：基础与临床应用

洪士杰教授

国立阳明大学医学院



我们利用低氧(1-7%)的环境来培养人类骨髓间充质干细胞。利用低氧环境增殖的骨髓间充质干细胞,可以表现胚胎干细胞基因,如Oct4及Nanog,这些基因可以透过促进Dnmt1之表现来维持干细胞的分裂及未分化状态 (Molecular Cell, 47: 169-182, 2012);低氧也可以透过HIF-1转录因子,来促进Twist表现,进而调降E2A-p21以抑制细胞因细胞分裂所造成老化现象(Blood 117:459-69, 2011);同时间充质干细胞于低氧状况下也会表现较多的趋附因子受体,因而增加移植后移动及着床的能力。且分泌更多和血管新生或组织再生的因子,因而可以促进损伤组织的修复。除此之外,低氧气浓度下培养增殖骨髓间充质干细胞相关研究,实验结果发现低氧培养可以增进间充质干细胞的很多效能。相关研究成果也申请多国专利。我们目前已经完成多种疾病的临床前试验,包括骨折、肌腱愈合、关节软骨修复、动脉粥样硬化及肝炎之治疗。目前正在利用低氧下增殖的异体间充质干细胞进行临床试验,治疗下肢缺血疾患。未来将扩展于退化性关节炎(OA)及移植物抗宿主疾病(GvHD)的治疗。这些研究成果说明低氧培养可以提升以间充质干细胞做为新式治疗之成功发展。

个人简历

Current position

Director, Integrative Stem Cell Center, Chinese Medical University Hospital
Professor, Institute of Clinical Medicine, National Yang-Ming University,
Joint Appointment Research Fellow, Institute of Biomedical Sciences, Academia Sinic

Education & Training:

M.D. National Yang-Ming University (1983-1990), Ph.D. The University of Tokyo (1993-1997)

Senior Research Scientist: Center for Gene Therapy, Tulane University Health Science Center: Prof. Prockop-DJ (2004/8-2005/8)

Postdoctoral Fellowship: Department of Biochemistry, The University of Tokyo (1996-1997)

Research Fellowship: Department of Orthopaedics, Faculty of Medicine, The University of Tokyo (1993-1997)

Award:

2012: The 1st place, best scientific paper award, Taipei Veterans General Hospital

2012: Award, 1st place, Cumulative SCI IF, Taiwan Orthopaedic Research Society

2012: Distinguished Research Award, National Science Council, Taiwan

2011: Award, 1st place, Cumulative SCI IF, Taiwan Orthopaedic Research Society

2010: The 2nd Award for Medical Technology Innovation, Taipei Veterans General Hospital

2007~2010: Outstanding award, National Yang-Ming University

2002: The best scientific paper award, Taipei Veterans General Hospital

2001: The best research award, Taiwan Orthopedic Association

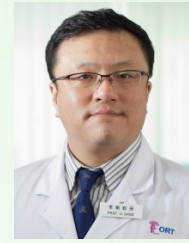
1996: Award, Japanese Medical Association

1993~1997: National Scholarship for oversea PhD education

循环间充质干细胞的生物学机制与临床意义

李刚教授

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Mesenchymal stem cells (MSCs) have been found in cord blood and peripheral blood (PB) of mammalian species including human, guinea pig, mice, rat, dog, horse and rabbit. The number of MSCs in PB (PB-MSCs) is rare and their biological role was not fully defined. We have found increased numbers of circulating MSCs in peripheral blood in patients with long bone fracture, non-union and in patients with cancers. The number of PB-MSCs was approximately 9 times higher in the cancer patients, suggesting there is systemic recruitment of MSCs during cancer development. We have compared the difference between the circulating MSCs and bone marrow derived MSCs and found that they share similar phenotype in vitro, but the gene expression profile between the two cell populations was significantly different. We have demonstrated that systemically administrated MSCs could home to tumor sites and participated tumor growth. We are now working on using MSCs as a systemic gene delivery vehicle for management of wound healing and cancer therapy, and the ways of enhancing the homing and recruitment of MSCs toward specific sites after their systemic delivery. In conclusion, PB-MSCs are new cell source of cells that may play very important roles in development, repair and disease progression. PB-MSCs may be used for disease monitoring, diagnosis, cell and gene therapy applications.

个人简历

李刚, 1991年中国西安第四军医大学医学学士; 1997年英国牛津大学医学哲学博士; 2000年英国贝尔法斯特女王大学高等教育学硕士。1991-1994任北京解放军总医院急诊外科住院医师。1994-1997在英国牛津大学医学院骨科攻读博士学位, 于1997年12月获得英国牛津大学医学哲学博士; 1998-1999英国牛津大学骨科博士后。1999-2004年历任英国贝尔法斯特女王大学医学院骨科学系讲师和高级讲师。2004年-2009在英国贝尔法斯特女王大学任癌症和细胞生物学研究中心教授, 独立研究员, 在英国有多项独立研究基金资助。2009.04-至今受聘香港中文大学医学院任矫形外科及创伤学系教授; 香港中文大学生命科学院干细胞与再生医学研究组主任及香港中文大学深圳研究院研究员, 航天医学基础与应用国家重点实验室-香港中文大学深圳研究院骨关节健康维护基地助理主任。研究方向: 干细胞的生物学, 骨折愈合的基本原理及肢体延长技术的生物学原理、组织工程学(生物材料)和干细胞的临床应用。发表SCI论文100余篇, 专著15篇, 主编3本书。论文共被引用超过3500次。曾任英国骨科学会执行委员; 美国骨科学会学术委员会委员。现任国际华人骨研学会秘书长, 中华骨科学会基础组委员, 中国生物医学学会组织工程与再生医学分会理事, 中国医师学会骨科医师分会肢体延长与重建委员会秘书长; 基础医学会委员; 数字与再生医学会委员; 中国中西医结合学会骨科分会副主任委员。Journal of Orthopaedic Research 副主编; Calcified Tissue International, 中华骨科杂志, 中国矫形外科杂志等多个杂志的编委会委员和国际杂志的审稿人和国际学会的会员。李刚教授还在以下的中国大学和科研机构兼任客座教授和访问教授, 研究员: 北京纳通国际骨科研究中心; 四川大学华西医学院; 上海交通大学; 中国医科大学; 山西医科大学; 东南大学; 第四军医大学; 广东医学院; 北京骨外固定技术研究所等。

糖尿病足创面修复

姜玉峰教授

解放军总医院生命科学院



糖尿病足创面修复的根本目标是使足部形态的完整性得到恢复, 足的行走和站立功能得到保留。修复过程多采用保守或者外科技术。修复原则旨在采用最简单、侵入性最小的方法, 达到迅速、持久及功能性闭合伤口。

在修复以前, 进行有效合理的清创对创面愈合至关重要。付小兵院士在《现代创伤修复学》一书中, 对创伤修复的一般过程及原则进行了科学的阐述: 清创是伤口愈合的基础, 彻底清创是防止创面感染的重要措施, 及时闭合伤口又是防止组织进一步发生坏死的重要手段。当完成对创面的预判工作后, 适当的创基处理、合适的敷料覆盖以及闭合方法在加速愈合中有重要作用。其中, 我们可以看到, 彻底的清创对良好的创面愈合所具有的重要性。

因此, 在糖尿病足创面修复治疗中, 外科彻底清创及修复技术是根本的治疗手段。还有一些辅助治疗, 如负压创面治疗、高压氧治疗、血小板凝胶等技术, 如果能够合理地联合使用, 对于修复成功可起到事半功倍的效果。另外, 在创面修复后, 如果能再进行一些矫形方面的治疗, 如切除骨性突起或矫正踇外翻等, 或者采用矫形支具对修复后创面起到良好的保护作用, 这些措施的实施对于预防溃疡复发及发生至关重要。

个人简历

姜玉峰, 解放军总医院生命科学院创面治疗中心; 解放军306医院全军糖尿病诊治中心, 足病组组长。基础医学博士后, 创伤与烧伤外科学博士, 中西医结合临床医学硕士。

师从我国创伤修复研究领域首席科学家中国工程院付小兵院士, 主要研究方向为创伤修复与组织再生, 在慢性创面尤其是糖尿病足创面外科修复及中西医结合诊治方面进行了大量深入的研究并治愈了大量病人, 具有丰富的临床经验。

中国医师协会 创伤外科医师分会第一届委员会委员兼副总干事; 中国医师协会创伤外科医师分会创面治疗医师专业委员会副主任委员; 中华医学会创伤学分会创面修复专科联盟学术委员会, 委员兼秘书长; 中华医学会创伤学分会组织修复与再生学会委员; 中华医学会糖尿病学分会糖尿病周围血管病变与足病学组秘书; 中国中西医结合学会青年工作委员会委员; 中国中西医结合学会灾害医学专业委员会青年委员; 中国康复医学会修复重建外科专业委员会北京分会委员; 中国微循环学会周围血管疾病专业委员会糖尿病足学组委员; 北京中西医结合学会周围血管病专业委员会委员; 《感染、炎症、修复》第二届编辑委员会通讯编委; 《中华创伤杂志·英文版》英文稿件特约审稿; 《中华糖尿病杂志》特约审稿; 《中华卫生应急电子杂志》第一届编辑委员会编委; 普通高等教育“十二五”规划教材-中国科学院教材建设专家委员会规划教材《外科学基础(英文版)》编委。

获北京市科学技术一等奖 1项; 全军医疗成果二等奖1项; 解放军总医院科学技术进步奖一等奖1项; 中华医学会创伤分会组织修复与再生学会创新奖; 中国中西医结合学会科学技术奖三等1项; 中华医学会糖尿病学分会糖尿病足与下肢血管病变学组学术年会优秀论文一等奖(2014), 二等奖(2013); 近3年发表SCI文章7篇, 第一作者5篇; 参编、参译专著5部; 负责国家级课题1项, 执行负责工程院院士咨询项目2项, 学会课题2项。

软骨损伤的干细胞治疗

许海波教授

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关节炎作为发病率最高的关节疾病往往造成关节疼痛, 关节功能丧失, 甚至残疾。关节炎正在影响着越来越多的病人, 特别是老年人和肥胖人群。然而常规的治疗方法(物理治疗或者药物治疗)只能暂时性的缓解临床症状, 无法恢复正常的关节功能。间质干细胞作为内生的多能性细胞具有分裂为骨骼肌肉和软骨细胞的能力, 同时还具有免疫调节功能, 可以通过旁分泌途径来调节炎症反应。间质干细胞治疗对于关节炎的治疗在临床中具有显著的有效性, 可行性和安全性。对比传统的软骨细胞自体移植治疗法, 间质干细胞治疗的优势在于无需软骨活体切片采集, 因此不会造成关节表面的二次伤害。然而基于干细胞治疗关节炎临床试验结果显示临床应用剂量, 介入时间, 干细胞来源和介入途径还存在很多的争议。我们对间质干细胞用于软骨再生进行了非常全面的研究。我们对于不同来源的间质干细胞(骨髓, 脂肪和外周血)进行了软骨生成细胞的分化试验, 骨髓干细胞由于良好的增殖和分化能力而被用于临床应用。我们验证了有效的干细胞培养方法和临床介入途径。通过多年的临床研究, 数以百计的关节炎病人受益于干细胞治疗方法。然后目前干细胞治疗的临床应用没有相关性的指导文件以供参考。为了能够提供更好的细胞疗法和组织工程学治疗, 更多深入的间质干细胞研究显然非常有必要。

个人简历

Prof James Hui received his MBBS degree from National University of Singapore in 1990. He received his FRCS (Royal College of Surgeons, (Edinburgh UK)) in 1994, FAMS(Academy of Medicine, Singapore) in 1999 and Doctor of Medicine National University of Singapore) in 2008. Dr Hui is currently an Associate Professor at the Department of Orthopaedic Surgery, National University of Singapore. He is heading Division of Paediatric Orthopaedics and is Director of Clinical Services for Department of Orthopaedic Surgery, National University Hospital. He is also appointed as Director for Tissue Engineering and Cell Therapy(GMP) Laboratory, National University Health System, Singapore and is a Group Leader for Cartilage Division of National University of Singapore, Tissue Engineering Programme(NUSTEP). His main research interests are on musculoskeletal tissue engineering and reconstructive surgery in paediatric orthopaedics.

骨科医用镁金属材料的研发与临床转化

秦岭教授

香港中文大学医学院矫形外科及创伤学系



纯镁或镁合金其材料力学特征接近骨组织，在体内可降解，有研发成为骨科内植物的潜能。在体内降解这一特征可避免第二次取出手术，可降低病人医疗费用。我国在可降解镁合金材料研发方面国际先进。2011年我们参与成立了广东“生物可降解镁合金及相关植入器件创新研发团队”。通过创新团队四年来的集体努力在骨科生物可降解镁合金的临床前和临床研发方面取得一定突破和阶段性成果，部分产品已被列为CFDA创新医疗器械，并进入产品注册多中心临床测试阶段；与国际团队合作，启动建立可降解医用金属的ISO和ASTM国际标准，相关研究成果填补国际ISO标准中无针对可降解医用金属检测标准的空白，推动可降解金属临床转化研究的进程。但以下3方面是我们迫切要推进的：1) 建立有效的临床应用适应症；2) 建立禁忌症；3) “官(管)-产-学-研-用”紧密结合，早日实现创新产品的临床转化，服务患者。

个人简历

秦岭，香港中文大学医学院骨科教授和实验室主任。二十多年来，秦岭教授建立多学科跨领域合作团队，常见和多发的骨质疏松和骨坏死以及腱骨等骨科疾患的病因、病生理、诊断与防治方向从事基础和临床医学应用研究，包括有自主知识产权的多学科活性3D支架生物材料和生物活性骨科金属材料的研发和临床转化。

目前秦岭教授获6项专利，30多项国际/地区性科研和贡献奖项；发表9本专著和90多章节，学术期刊发表了380篇学术论文(英、德、中三种杂志期刊)，其中230篇SCI论文，被引5000多次，H-Index 41。秦岭教授是国际华人骨研学会前主席(2009-2011) (www.icmrs.net)、美国医学与生物工程院Fellow (<http://www.aimbe.org>)、5个国际专业杂志的编委和Journal of Orthopaedic Translation(主编) (<http://ees.elsevier.com/jot>)。

可注射生物材料的研究及临床新发展

吕维加教授

香港大学医学院矫形外科及创伤学系



No matter what the source, injectable biomaterials must meet several criteria to perform successfully in clinical applications. They must be biocompatible, or able to function in vivo without eliciting an intolerable response in the body either locally or systemically. Adequate mechanical properties are also an important criterion for biomaterials, especially those used in devices intended to replace or reinforce load-bearing skeletal structures. The aim of this study was to compare the properties of the strontium containing bioactive bone cement with those of polymethylmethacrylate (PMMA) clinically.

Strontium-containing hydroxyapatite (Sr-HA) bioactive bone cement consists of a filler blend of strontium-containing hydroxyapatite and a resin blend of bisphenol A diglycidylether methacrylate, triethylene glycol dimethacrylate, poly(ethylene glycol) methacrylate, and N, N-dimethyl-p-toluidine. Its properties, including setting temperature, mechanical strength, biocompatibility as well as osteoinduction, were compared with other cements in vitro and in vivo, followed with a pilot study of clinical trial. This study suggest that strontium delivered locally has the same effect; thus, the combination of strontium with HA in an injectable biomaterial or cement with a low setting temperature, adequate stiffness, and low viscosity makes this a good bioactive cement for vertebroplasty. The injectable biomaterials and their future development as well as clinical applications such as hip fractures, plastic surgery and dentistry will be discussed.

个人简历

Professor Lu, Ng Chun-Man Professor in Orthopaedic Bioengineering, obtained his PhD degree and the “Distinguished Graduate Award” from the University of Waterloo, Canada, in 1994. He joined the Department of Orthopaedics & Traumatology, The University of Hong Kong (HKU) in 1995 as an Assistant Professor (non-clinical) and was promoted to Associate Professor in 2001, and full Professor in 2009. He was established Orthopaedic Research Centre in 1995 and has served as director since then. Professor Lu has specific experience in the areas of Orthopaedic Biomechanics, Biomaterials, bionano-technology as well as Clinical Bioengineering teaching and research. He has achieved substantial international recognition in the area of bioengineering and is widely acknowledged as top 1% scholars (2009-2015) according to ISI’s Essential Science Indicators. Professor Lu has consistently secured a significant proportion of the research funding of HK\$44 millions from Hong Kong and RMB20 millions from PR China in his areas of activity from a number of major funding bodies, which demonstrates his aptitude for creative application of knowledge. He held a number of patents for his innovations and has published more than 220 papers in international Peer Reviewed Journals, with more than 5200 citations and H-index 41.

3D打印生物材料用于骨修复与治疗

吴成铁研究员

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For therapy and regeneration of bone defects resulting from malignant bone disease, it is of great importance to develop multifunctional biomaterials for bone therapy and regeneration. Conventional biomaterials always lack multifunctional properties, limiting their application for treating and repairing bone disease (e.g. bone tumors)-initiated defects. How to design and prepare bioscaffolds with favorable microenvironments for disease therapy and tissue regeneration is one of interesting topics in the fields of biomaterials and tissue engineering. We developed several strategies, including harnessing nutrient elements, biomimetic structure and functional interface as well as thermo-therapy to construct multifunctional scaffolds for therapy and regeneration of bone tissues. It is interesting to find that both nutrient elements and biomimetic structure of bioceramic scaffolds have important effect on the stimulation of osteogenesis and angiogenesis of stem cells, and thermotherapy plays an important role to treating bone tumors. Therefore, we put forward new concept that multifunctional scaffolds combined bone therapy and regeneration could be a new direction of bone tissue engineering via 3D printing strategy.

个人简历

吴成铁，中国科学院上海硅酸盐研究所生物材料研究中心副主任、博士生导师、中央组织部青年千人计划、中科院百人计划、德国洪堡学者、上海市优秀学术带头人、上海市浦江人才计划及科技部863重点项目负责人。学术期刊“Biomedical Glasses”副主编，“Progress in Natural Science: Materials International”“Journal of Stem Cells Research, Reviews and Reports”等期刊编委。主编CRC英文专著一部，并参与撰写5本英文专著的章节。在生物材料相关领域发表SCI 期刊论文120多篇，主要包括Adv Funct Mater, Adv Mater Interface, Biomaterials (16篇), J Control Release, Small, Carbon, J Mater Chem (共16篇), Acta Biomater (共24篇)等。论文共被SCI引用3000余次，h指数33。共申请专利12项，获3项中国专利及2项国际专利(PCT)授权，其中2项中国专利和2项国际专利技术已经转让公司。

新型高分子水凝胶生物材料的研发和应用

边黎明教授

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近年来,越来越多的天然高分子材料,例如透明质酸、胶原蛋白和明胶,由于具有优良的生物相容性和生物活性被广泛应用到了组织工程上。现有的大部分天然高分子材料为依托的水凝胶都是共价化学交联的,因此十分稳定;但同时由于化学交联的不可逆性,也缺少良好的延展性和自修复性。而近年来发展起来的非共价物理交联的超分子水凝胶,其交联的可逆性使其具有了一些特别的物理性质,包括良好的拉伸压缩性质,以及可自身修复的性质。我们以明胶为基质,通过主客体的物理结合,制备得到了一种新型的超分子水凝胶。该种水凝胶不仅拉伸压缩性能优异,而且具有自修复性、生物粘性以及可载药性,另外还具有突出的生物相容性,是一种极具潜力的药物/细胞组织工程支架载体,在再生医学领域有着广泛的应用前景。

个人简历

边黎明, 助理教授。分别与2002年及2004年在新加坡国立大学获得本科学士及生物工程硕士学位。2004年赴美哥伦比亚大学生物医学工程学系继续攻读博士学位。2009年获博士学位后,在宾夕法尼亚大学生物工程学系进行博士后研究。2012年夏开始就职于香港中文大学。其研究的主要方向是生物支架材料的设计及在干细胞组织工程方面的应用。具体的研究方向有仿生生物材料的设计开发,细胞微环境信息对干细胞行为的影响,干细胞软骨组织工程等。

皮肤再生的临床思考与转化

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促进创面愈合和人工生物皮肤的构建，是创面治疗的研究热点。而临床缺损区皮肤软组织的功能性重建，尚需具有完整皮肤组织层次、成份和功能的重建。这一基于临床的要求，表明皮肤的原位再生及其诱导技术和方法，将是这一领域的另一核心研究。

指端封闭治疗，中医湿性疗法等在个别病例上曾实现过原位再生，提示其相关病理生理和生物学规律有待进一步了解和掌握。本文从另一传统的临床治疗技术，皮肤软组织扩张生长现象入手，试图了解皮肤在牵引力引导下再生的规律，探索皮肤可能的原位再生技术。

临床病例提示，皮肤在牵张力引导下，经历生长、平衡和衰竭三个阶段。通过大量临床病例现象的观察，组学数据的采集和高通量数据的分析，体外及体内模型的验证，我们发现了启动皮肤再生的关键通路，和甲基化修饰引发的皮肤再生衰竭。这二个机制的明确，为临床获得大面积的结构完整的再生皮肤，提供了一重要基础。

个人简历

李青峰，上海交通大学医学院附属第九人民医院副院长、整复外科主任，为国家教育部“长江学者”奖励计划特聘教授和国家“杰出青年”科学基金获得者。

长期以来致力于整复外科临床和基础研究。相关研究获得国家中长期科技支撑计划，国家自然科学基金重点项目等30余个项目的资助。发表论文200余篇，在皮肤再生、组织预构重建和脂肪移植等领域，取得多项原创性成果。多篇文章、通讯刊登在国际著名的“Lancet”、“Ann.Surg.”、“StemCell”、“PRS”等学术期刊。相关成果获得中华医学科技进步奖、上海市科技进步奖等系列奖励。是中国医师协会整形外科分会，中整协整形与重建外科分会等的会长，是美国移植重建学会发起会员（Founding Member, ASPT）和国内唯一的美国整形外科协会（AAPS）会员。

Autologous tenocyte therapy and bioreactor for tendinopathy: from bench to bedside

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Background: Tendinopathies and tendon injuries are the most common soft tissue disorders seen in primary care, sports medicine and orthopaedic and rheumatology practice. Despite their relatively high prevalence and morbidity, most treatments have been proven to provide no, or only modest short-term benefits. Traditional first-line treatments might include rest and activity modification, exercises such as eccentric strengthening and bracing. Topical or oral non-steroidal anti-inflammatory drugs (NSAIDs) and local glucocorticoid injections may provide modest short-term benefits for pain. More recently, novel treatments including extracorporeal shock wave therapy, and injectable autologous blood products and botulinum have been studied but have either been proven to be ineffective or remain unproven. We and others have observed that elevated rates of apoptosis and autophagy of tenocytes leading to depletion of the functional tenocyte pool in the region of the tear may account for fatigue of the normal healing response. This results in loss of cohesive tendon structure and eventually tendon tear. On the basis of the pathology studies, we proposed that restoration of the population of functional cells capable of synthesising ECM and repairing the damaged tissue within the tendon might be an effective therapeutic strategy for tendon repair in patients with tendinopathy.

Materials and methods: Based on previous pre-clinical cell tracking and animal studies, we have developed protocol for the autologous tenocyte injection technique (ATI). Patients with chronic, refractory tendinopathy were recruited for study. Patients with lateral epicondylitis, gluteal tendinopathy, rotator cuff tendon tear, Achilles tendinopathy who have failed for previous injection therapies were recruited into the case cohort. A tiny needle tendon biopsy (most often the patellar tendon) was used as the source material for autologous tendon cells. The cells are isolated from the tendon tissue by enzymatic digestion and expanded in vitro in a GMP-certified laboratory. Cell characterisation were conducted to examine the purity, potency, identify and viability. Cells are reconstituted in an assembly medium containing autologous serum and implanted in the site of tendinopathy by ultrasound-guided injection. Maximum follow up of these patients with functional score and MRI were 5 years.

Results: Characterisation of phenotype on human autologous tendon-derived cells showed that majority of these cells display the characteristics of expressing tendon transcriptional factors, type I collagen, tenomodulin and tendon related growth factors including FGF, TGF beta and PDGF bb. Ability of neo-tendon tissue formation by human tenocytes was tested in a bioreactor system. The result showed tenocytes

摘要

in high density with 6% cyclic mechanical stimulation forms neo-tendon tissues evidenced by histology, and tendon molecular profiling. Clinical case series on ATI showed that all of participants had an average symptom of more than 18 months. Clinical outcomes were assessed from baseline up to 5 years post-treatment. Significant improvements were observed for all of site specific functional scores including QuickDASH, UEFS, Oxford hip score VAS maximum pain score and grip strength starting from one month post-treatment. These improvements were maintained for up to 5 years post-treatment. MRI scores were significantly improved up to 12 months post-treatment, and demonstrated tendon in-fill and reduction in the extent of tendinopathic lesions in LE, rotator cuff and Achilles but less in gluteal tendinopathy. Conclusion: Autologous Human tendon-derived cells offer a strong advantage for use in tendon tissue regeneration, as they are not immunogenic, have the capacity for collagen and matrix synthesis and are able to generate tendon-like tissue in an ex vivo bioreactor. ATI, the first homologous cell therapy technique developed for the treatment of tendinopathy, has the potential to address this unmet clinical need by replenishing the pool of functional tenocytes in the site of tendinopathy, facilitating structural repair as well as improving pain and function.

个人简历

郑铭豪1992年获得西澳大学医学院理学博士学位，毕业后任美国波士顿原基因研究所高级助理科学家，1993年在西澳大学创立澳大利亚第一个骨科细胞工程研究室，任研究室主任、西澳大学医学院讲师。1998年再获西澳大学医学院医学博士学位。1996年起历任高级讲师、副教授，2003年起成为西澳大学医学院终身教授。2002年成为英国皇家病理学院院士；2006年起为澳大利亚皇家病理学院科学院士。2008年成为浙江大学外科学（骨移植）长江学者讲座教授。先后发表文章150篇，H index 43分。获得美国和澳大利亚等多个国家的专利8项。参编专著8部。现任西澳大学医学院副院长，骨科研究室主任，澳大利亚Orthocell上市公司创始人及首席科学家，曾任澳大利亚佩利珍细胞移植中心执行总裁，澳大利亚国家医学自然科学基金评委；澳大利亚卫生和医学基金会评委；香港政府研究基金会评委，西澳大利亚珀斯和组织库科学委员会执行委员；浙江大学中澳生物治疗及再生医学研究合作中心常务副主任。

摘要

骨骼肌干细胞对骨骼肌组织损伤再生修复的调控研究

朱大海教授

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骨骼肌组织创伤后的修复是生物进化过程中机体所获得的一种自我保护机制，是一个涉及发育、遗传、细胞生物学、分子生物学、生物材料学和临床医学等多学科的综合性研究领域。朱大海教授实验室利用基因敲除和过表达小鼠作为研究材料，系统性开展骨骼肌发育与疾病关系的遗传学和细胞信号传导的分子机制与转化医学的研究，特别是非编码RNA和小分子代谢产物在发育与疾病发生发展中的调控功能。比较有趣的是，研究发现小分子代谢产物和非编码RNA均参与了组织创伤修复的过程。

采取蛋白组学和转录组学相结合的系统生物学方法，发现和鉴定了一个内源性代谢小分子在骨骼肌再生中的重要功能，进一步的分子机理研究表明，该内源性代谢小分子通过激活Erk信号转导通路，促进骨骼肌干细胞的增殖从而提高了骨骼肌再生的能力。

除小分子代谢产物外，miRNA也参与了组织损伤修复的过程，研究发现，miR-431转基因小鼠中骨骼肌组织损伤修复进程明显比野生型（WT）小鼠快，更重要的是我们发现miR-431具有重要的临床意义：miR-431转基因小鼠与肌营养不良疾病小鼠杂交能够显著缓解疾病表型。此研究结果表明miR-431可能作为人类肌营养不良疾病治疗的潜在药物。

此外，采用生物信息学方法筛选鉴定了一个受MyoD调控的骨骼肌组织特异表达的长非编码RNA（Linc-RNA Activator of Myogenesis, Linc-RAM）。功能研究发现Linc-RAM显著促进骨骼肌细胞分化，同时Linc-RAM能将成纤维细胞转分化为肌细胞，Linc-RAM 基因敲除小鼠骨骼肌纤维数量显著减少、敲除小鼠骨骼肌损伤再生能力减弱。因此，率先阐明了长非编码RNA对骨骼肌发育和再生的在体（in vivo）调控功能。

个人简历

朱大海，教授，1994年获美国北卡州立大学分子遗传学专业博士，先后在美国杜克大学医学院HHMI和NIH从事博士后研究。1998-1999为美国NCSU助研究教授。2003年任协和医学院/中国医学科学院特聘教授，医学分子生物学国家重点实验室副主任。2000年国家杰出青年基金获得者、1997获美国NIH Merit Award和Fellow Award For Research Excellence奖。国家有突出贡献的中青年专家。朱大海教授领导的课题组利用基因敲除和过表达小鼠以及人类样品作为研究材料，系统性开展发育与疾病关系的遗传学和细胞信号传导的分子机制与转化医学的研究。特别是非编码RNA和小分子代谢产物在发育与疾病发生发展中的调控功能，这些目前国际研究的前沿领域是朱大海教授实验室正在开展的最具特色的研究方向。

组织特异性ECM在组织构建与再生中的作用与临床应用

金岩教授

第四军医大学组织工程研发中心



Although tissue engineering and regenerative medicine (TERM) is related to many subjects, the key factors in cellular products of TERM are cell-cell and cell-scaffold interactions, including induced differentiation of stem cells. In early development stages, these cellular activities present as cell-cell and cell-extracellular matrix (ECM) interactions, which control the morphogenesis and growth of organs. In addition, the cell-cell and cell-ECM interactions not only exist in morphogenesis processes, but also play an important role in morphology maintenance, wound healing and regeneration of organs in a whole life. Thus, the research of cell-cell interactions and induced differentiation of cells in development and regeneration become one of the key problems in TERM.

Through imitating skin morphogenesis we successful construct a bilayered structure tissue engineered skin depending on epithelia cell and fibroblast coculture. Furthermore, our research demonstrated that the interaction of various stem cells and ECM proteins is capable of improving the morphology of sophisticated anatomical structure, such as bilayered structure, capillary network, sensory innervations and subcutaneous adipose tissue. In addition of skin, we prepare a corneal stromal ECM that can specifically interact with corneal epithelia and stromal cells. Experimental and clinical trial also confirm that this stromal ECM was able to morphogenesis of normal corneal structure after transplantation. Specific ECM benefits tissue regeneration. The structural and functional molecules of the ECM are in a state of dynamic equilibrium, and also provide the means by which cells communicate with each other and the external environment. The bioinductive properties of ECM is allowing the constructive remodeling of tissue after in vivo implantation of ECM.

Based on these results, we developed a cells aggregate (CA) technique that self-assembled by in vitro cultured cell to enhancing cell-cell and cell-matrix interaction. Self-produced ECM is the consequence of cell behaviors during morphogenetic processes. Depending on the technique, our prepared chondrocyte and periodontal ligament stem cells (PDLSCs) CAs successful and effectively regenerate defect articular cartilage and periodontal tissue. Therefore, the sociality of cells, interdependence and mutual restriction between cell and cell, cell and microenvironment play important role in tissue engineering construction, which can also be used as method for sophisticated tissue and organ morphogenesis in vitro.

个人简历

金岩,为教育部“长江学者”特聘教授(2007年)、国家杰出青年基金获得者(2007年)、国家重大科学研究计划(973计划)项目首席科学家(2011年)、教育部“创新团队”牵头人(2013年)、入选国家百千万

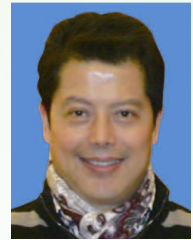
摘要

人才工程领军人才(2013年)。创建第四军医大学组织工程研发中心并担任主任。为中国组织工程与再生医学分会主任委员,中华口腔医学会口腔生物医学侯任主任委员。

长期从事组织工程与再生医学的研究。研制成功我国第一个组织工程产品——组织工程皮肤、国际上第一个生物角膜产品;发现了炎症、衰老等因素对干细胞影响的新机制,在牙、骨再生等方面的基础与应用研究方面有所贡献。在Cell Metabolism、Cell Death Diff、Stem Cells、Biomaterials、JBMR、CDDis、J Control Release、Scientific Report、Mol Therapy等发表SCI收录文章150余篇。获国家科技进步一等奖1项、军队和省级科技进步一等奖4项。

造血细胞工程研究进展

裴雪涛教授



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干细胞领域的快速发展及技术突破使得体外获得和正常血细胞完全一样的血细胞替代品成为可能。人多能干细胞具有分化成机体所有类型组织细胞的潜能,将人多能干细胞在体外大规模诱导分化为血液细胞可作为新的血液替代来源。基于干细胞技术的“造血细胞工程”是指利用多能干细胞的高度增殖能力和多向分化潜能,通过细胞工程技术,在体外模拟或部分模拟体内的造血过程,对干细胞进行体外扩增、定向诱导分化、功能激活与调控等,在短时间内大量获得早期造血干/祖细胞及各阶段的造血前体细胞,以及定向诱导扩增大量的红细胞、巨核细胞/血小板、淋巴细胞等功能性血细胞和免疫活性细胞,并可对部分细胞的功能进行激活和调控,诱导分化的细胞将最终用于血细胞输注和造血干/祖细胞移植。

个人简历

裴雪涛,医学博士,教授,博士生导师。军事医学科学院全军干细胞与再生医学重点实验室及军事医学科学院华南干细胞与再生医学研究中心主任。主要从事干细胞与再生医学的基础和应用研究。国家863计划“干细胞与组织工程”重大项目总体专家组组长,国家干细胞研究指导协调委员会委员,国家卫计委“干细胞临床研究与应用管理委员会”委员,中国输血协会副理事长、国家干细胞与再生医学产学研创新技术联盟常务副理事长、中国细胞生物学会干细胞专业委员会副主任委员等学术职务。获国家科技进步二等奖等7项成果奖励,在Hepatology、Blood等学术杂志发表论著330余篇,主编及合作主编专著9部,3项干细胞产品获CFDA临床试验批文,获国家专利授权51项,PCT专利1项。

运动与脑内源性神经干细胞的前沿进展

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随着社会前进的步伐的加速,老龄化的到来、国民生活水平的提高及生活方式的改变,因久坐和缺乏运动造成的慢性非传染性疾病的发病率正在剧增。在脑健康方面,生活方式的改变和节奏的加快使人承受前所未有的精神压力。由此引起的包括神经精神性疾病,不容忽视。以抑郁症为例,目前统计显示中国发病率接近4%。多变的临床症状以及精神专科医生的缺乏,实际病患的规模很可能比统计的数量大得多。仅2002年,抑郁症在中国就造成了520亿人民币的损失。此外,现今人口高流动性和特定性工作、休闲活动的增多,加大了中枢神经系统受损的几率。

近年国际科学研究证实运动是行之有效的非药物治疗手段。在保护中枢神经方面,运动在肌肉、肝脏、脂肪等外周组织释放“运动因子(Exerkines)”来调控脑功能,运动能增加脑内源性神经干细胞增生(神经发生)。运动亦被证实能促进认知、改善焦虑和抑郁等负性情绪,甚至有助于神经损伤的修复。

个人简历

苏国辉,广州暨南大学粤港澳中枢神经再生研究院院长,香港大学眼科学系及脑与认知国家实验室解剖学讲座教授,何冯月燕基金明德教授(神经科学),中科院院士,中国教育部“2011计划”专家咨询委员会委员,中国科技部973计划专家顾问组成员,中国脊髓损伤研究协作组董事会联席主席,香港脊髓损伤基金主席,中国Neural Regeneration Research杂志总编辑。1977年于美国麻省理工大学获得博士学位。致力研究视神经系统轴突再生。于1985年首先证实了使用外周神经的移植方法可以使成年哺乳动物的视网膜节细胞长距离再生。研究方向是使用多渠道的方法,来促进视神经及脊髓轴突再生,致力研究探索神经保护和再生的因素,包括纳米医学,营养因子,运动,中草药提取物,其他一些小分子,免疫反应,康复训练等。1995年荣获国家自然科学奖(中国国家自然科学基金),1999年获选为中科院院士。共发表360多篇文章;拥有专利23项。

摘要

下肢复杂畸形矫正功能重建临床进展与启示

秦泗河教授

中国国家康复中心医学矫形外科



中国遗留了大量严重复杂的下肢残缺畸形，各大医院几乎没有设立“下肢矫形外科”与研究生导师。作者手术治疗3万多例下肢畸形、瘫痪，引进Ilizarov技术，融入欧美国家矫形外科技术，根据国情与肢残病人的特点、医疗需求，用“顺势而为、医法自然、时空一体”的中国哲学观融会贯通，提出并践行“骨科自然重建理念”。在30多年的临床实践、总结中，形成了不同于西方、具有秦泗河医学思想、手术风格、医疗模式的一——下肢矫形外科技术体系。能用简单、微创的手术方法治愈严重、复杂的下肢残缺畸形，挽救了50多例濒临截肢的下肢残缺病人。这个报告将展现秦泗河的进化医学思维、医疗模式、别具风格的肢体重建外科技术体系。

个人简历

秦泗河，现任国家康复辅具研究中心附属医院名誉院长、矫形外科主任，国际肢体延长与重建协会（ILLRS）中国部主席。中国骨科医师协会外固定与肢体重建工作委员会（CEFS）主委。截止2014年12月，主持四肢矫形手术32414例（完成中国最大下肢畸形手术病例数据库），其中脊髓灰质炎后遗症手术22330例。第一位赴俄罗斯学习Ilizarov技术，主持完成了Ilizarov技术中国本土转化与发展，创立了具有秦泗河医学思想、手术风格、医疗模式的下肢矫形外科技术体系，治愈了数千例严重复杂的下肢残缺畸形，挽救了一批经典手术难以治疗濒临截肢的下肢残缺畸形，使500多例术前只能爬行-蹲移患者术后获得直立行走。临床推崇与践行“医法自然、医患同位、顺势而为”中国哲学观。认为控制了“应力”和医者智慧、患者潜能的双调动，就掌握了肢体畸形矫正与功能重建的金钥匙。

摘要

Promises and Challenges of Tissue Engineering and Regenerative Medicine: Repair, Restore, and Re-create



段崇智教授

美国匹次堡大学

The tremendous advancements in life sciences, engineering and information technology that have taken place in the last several decades have combined to make biomedicine a uniquely promising research discipline. Recent advances in biomedicine, in areas such as stem cells and molecular biology, and in bioengineering and biomaterials, have led to the emergence of the field of tissue engineering and regenerative medicine (TE/RM). The field has captured the attention and imagination of young and established scientists, as well as of the general public and medical and biotech industries, and is one of the most rapidly developing fields in biomedicine.

One prominent area of active TE/RM research concerns musculoskeletal disorders, which pose a well recognized heavy disease burden on the quality of life, as they represent the primary cause of physical disability. In particular, the social and economic burden of musculoskeletal diseases, such as osteoarthritis and low back pain, are considerable, in view of the global aging demographic. This lecture will outline some of the accomplishments of TE/RM in musculoskeletal medicine, including the development of cell-based therapies, biomimetic biomaterial scaffolds, and the application of bioactive factors to promote cell differentiation and neo-tissue formation. Challenges to TE/RM-based therapies and treatments will also be discussed, such as cell sourcing, functional integration of engineered tissues, and regulatory hurdles. Strategic pathways towards accomplishing the main goals of TE/RM – Repair, Restore, and Re-create - will be discussed, particularly the importance of multidisciplinary global collaborations and consortial partnerships.

个人简历

Dr. Tuan received his Ph.D. from the Rockefeller University and completed his postdoctoral research at Harvard Medical School. After serving professorships at the University of Pennsylvania and Thomas Jefferson University, Dr. Tuan was recruited to the NIH (NIAMS) as Chief of the newly created Cartilage Biology and Orthopedics Branch in 2001, and in 2009, he accepted the position of the Founding Director, Center for Cellular and Molecular Engineering, and Arthur J. Rooney, Sr. Chair and Professor and Executive Vice Chair, Department of Orthopaedic Surgery, University of Pittsburgh School of Medicine. He is also a Professor in the Department of Bioengineering, University of Pittsburgh Swanson School of Engineering. Currently Dr. Tuan is the editor of the developmental biology journal *BDRC: Embryo Today*, founding editor-in-chief of *Stem Cell Research and Therapy*, and serves on multiple editorial boards. Since 2010, Dr.



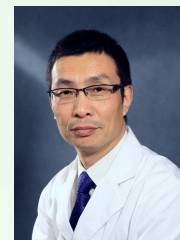
摘要

Tuan has served as Co-Director of the U.S. Armed Forces Institute of Regenerative Medicine, a Department of Defense funded, multi-institutional consortium focused on developing regenerative therapies for battlefield injuries. In 2012, he became the Founding Director of the Center for Military Medicine Research and Associate Director of the McGowan Institute for Regenerative Medicine. In addition, Dr. Tuan was appointed a Distinguished Professor in 2014 and received the Chancellor's Distinguished Research Award in 2015. Dr. Tuan directs a multidisciplinary program focusing on the development, growth, function, and health of the musculoskeletal system, the biology of adult stem cells, and the utilization of this knowledge to develop stem cell-based technologies that regenerate and/or restore function to diseased and damaged musculoskeletal tissues. Dr. Tuan has authored more than 450 research publications and has lectured widely. Ongoing research projects are directed towards multiple aspects of skeletal and related biology, including skeletal development, stem cells, growth factor signaling, bone-biomaterial interaction, extracellular matrix and cell-matrix interaction, nanotechnology, biomaterials, 3D printing, tissue-on-a-chip, mechanobiology, regenerative medicine, and tissue engineering, utilizing an integrated experimental approach combining contemporary technologies of biochemistry, cell and molecular biology, embryology and development, cellular imaging, and engineering.

生物3D打印技术在骨与软骨再生中的应用

蒋青教授

南京鼓楼医院骨科



随着生物3D打印技术在近年来受到的关注越来越多,其在组织工程方面的应用研究也不断深入。目前应用该技术已经可以打印出心肌组织、血管、心脏瓣膜、气管等结构,并已将其植入患者体内。而由于骨与软骨的结构与功能相对简单,更加适合与生物3D打印技术结合,国内外学者对于这方面的研究与探索也很多。

1. 生物3D打印在骨再生中的应用

生物3D打印技术在骨科领域使用最广泛的是术前手术方案的设计,根据患者术前的影像学资料,将手术部位的三维模型打印出来,用于设计手术入路、复杂手术的手术方案等。已有多篇关于将3D打印应用于复杂骨盆骨折、脊柱疾病、关节骨折的术前手术方案设计的报道,证实采用该技术可以提高手术效率、减少医源性并发症及术中透视次数,具有重要的临床应用价值。

其次是个性化金属内植物的设计,国内外均有相关报道,骨盆、髋关节、膝关节、颅骨的个性化定制3D打印金属内植物均被证明在复杂缺损形状的应用中有较好地疗效。

应用于组织工程的支架结构是生物3D打印技术研究的另一项热点,多篇研究报道使用三维印刷技术打印的羟基磷灰石与磷酸钙支架经高温烧结后具有较好的生物力学强度与微结构,且后期加入TGF- β 、BMP、种子细胞或在支架表面覆盖胶原等生物活性物质后均能表现出良好的细胞相容性及骨传导、骨诱导作用。

2. 生物3D打印技术在软骨再生中的应用

与骨再生研究不同,软骨再生领域中对生物3D打印技术主要应用于支架结构的建立与后处理。目前主要采用三维印刷或熔融沉积技术,使用聚乳酸、聚己内酯等高分子材料或海藻酸盐、壳聚糖等生物材料制作支架,由于打印过程较温和,可以同时添加胶原、转化生长因子等其他生物活性成分,均被证实对软骨损伤的修复具有显著的促进作用。

另一方向则是对损伤处进行直接打印修复,由于软骨支架对力学强度要求不高,因此为直接在体修复提供了可操作性,目前对这一方式的研究还处在起步阶段,有待进一步探索。

3. 总结

总而言之,现阶段国内外对于生物3D打印技术在骨与软骨损伤修复的研究虽然很多,但是并没有确立真正公认的打印方式与修复材料,因此相关方面的应用值得进一步研究。

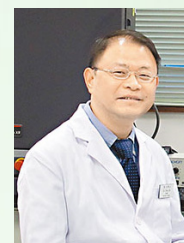
个人简历

蒋青,南京大学医学院副院长、南京大学医学院附属鼓楼医院运动医学和成人重建外科主任,教授、博导、杰青。主要从事骨关节炎基础和临床研究以及骨和关节软骨损伤修复。

骨科小干扰核酸药物靶向递送系统研究进展

张戈教授

香港浸会大学



骨科疾病相关的异常高表达的分子作为药物设计的靶点近年来被大量发现。核酸干扰作为可以静默几乎任何分子的技术可以应用于抑制上述异常高表达的分子。如何准确地投送干扰核酸到成骨细胞、破骨细胞等骨科相关疾病细胞是临床开发小核酸药物的关键技术，也是目前骨科小核酸药物临床转化的瓶颈。

成骨细胞靶向递送系统的研发分别经历了第一代基于特异性识别骨形成表面的寡肽来修饰的脂质体和第二代基于特异性识别成骨系细胞表面的核酸适配子来修饰的纳米脂质颗粒。第一代递送系统成功地验证了中国学者在中国实验室自己发现的调控成骨细胞活性的泛素相关基因的功能以及骨质疏松疾病转化性成骨治疗的潜能。第二代递送系统助力中国学者成功地发现了世界上第一个从临床标本中获得鉴定的调控成骨细胞的非编码的小核酸基因的功能。

第一代破骨细胞靶向递送系统的设计是基于特异性识别骨吸收表面的寡肽来修饰的脂质体，这个类型的递送系统已经成功地应用于破骨细胞通过释放非编码核酸调控成骨细胞功能的机制研究。

个人简历

张戈(骨伤科临床医学博士)，于2004年开始在香港中文大学医学院矫形外科系及创伤学系从事博士后研究，2007年开始受聘研究助理教授；2012年开始，正式加入香港浸会大学受聘副教授，组建香港浸会大学骨与关节疾病转化医学研究所(<http://tmbj.hkbu.edu.hk/>)。现任香港浸会大学骨与关节疾病转化医学研究所副所长。

张戈博士的主要研究领域覆盖肌肉骨骼系统疾病。目前，张戈博士获得政府资助的竞争性研究项目分别包括：“酪蛋白激酶2相互作用蛋白1在骨组织中调控成骨细胞参与骨形成的分子机制与骨质疏松成骨治疗研究”、“老年妇女骨形成下降的分子机制研究：CKIP-1的功能性作用”、“抑制成骨细胞内的miR-214来促进老年绝经后妇女骨形成”、“靶向CKIP-1的核酸干扰静默策略逆转严重的绝经后骨质疏松”，“理解CKIP-1在类风关骨破坏病灶成骨能力下降的分子机制”和“适配子功能化的成骨细胞靶向递送系统实现成骨细胞特异性成骨核酸治疗”。上述研究项目的潜在发现能够推动深入理解临床具有挑战性的肌肉骨骼系统疾病的分子机制，对于转化核酸干扰策略以及开发天然产物来源的小分子药物，更有效性地治疗骨质疏松、类风关骨修复、骨坏死骨破坏病灶修复失败以及老年骨折修复能力下降。

摘要

抗感染骨修复材料的3D打印和评价

汤亭亭教授

上海交通大学附属第九人民医院骨科



骨替代材料或组织工程支架的3D打印,可满足不同骨缺损修复的个性化需求;如何赋予打印材料更好的生物学性能,是目前亟待发展的主要研究方向。考虑到大段骨缺损常常合并开放性损伤,有较大的细菌感染的风险;骨替代材料或组织工程支架本身,也是细菌粘附的良好载体。因此本课题组拟通过添加抗菌成分的方法,利用3D打印技术制备兼具良好骨生物活性和抗感染能力的新型骨修复材料。在前期研究中,我们和秦岭教授课题组合作,对采用低温快速成型技术制备的PLGA/TCP/Mg支架的体外生物学效应进行了研究,发现其在体外可以抑制金黄色葡萄球菌的黏附、增殖和生物膜形成(Scientific reports, 2015)。随后我们又通过接枝的方法,将前期研制的抗菌材料-壳聚糖季铵盐(HACC)复合到3D打印PLGA/HA多孔支架,体外研究证实其对骨科常见的多种致病菌(包括耐药菌)有较强的抑制能力,同时可以促进干细胞的黏附和成骨分化。初步的动物实验研究也证实其具有较好的抗感染性能。

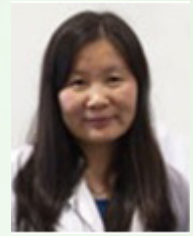
个人简历

汤亭亭,教授。目前担任上海市骨科内植物重点实验室主任,上海交通大学医学院附属第九人民医院骨科副主任;是国际华人骨研学会的候任主席,并兼任中国生物材料学会理事、全国生物力学专业委员会委员、中国医师学会骨科分会基础工作委员会副主席等职;担任Journal of Orthopaedic Translation、Bone Research、Journal of Bone and Mineral Research(2016-2018)、中华创伤骨科杂志等16本国际、国内杂志的副主编和编委等职。先后入选上海市优秀学术带头人、教育部新世纪优秀人才、新世纪百千万人才等人才培养计划。近年来致力于骨修复再生、骨科植入物抗感染、干细胞与肿瘤微环境等方面的研究,成果已在Biomaterials、Journal of Pathology、Cancer letter、Scientific Reports等国际权威杂志上发表论文130余篇,以第一完成人获上海市科技进步二等奖3项。

超级抗原在组织修复中的研究进展

张锦芳教授

香港中文大学医学院矫形外科及创伤学系



金黄色葡萄球菌肠毒素 (SE) 是由金黄色葡萄球菌在金黄色葡萄球菌肠毒素, 这种一直被认为具有强烈毒性能导致人体中毒的物质在被发现具有超级抗原的神奇特性后, 摇身一变成为科学家寄予无限希望治疗人类疾病的福音。我们的研究中发现的C2型金葡菌肠毒素能明显促进人的骨髓来源的间充质干细胞向成骨细胞的分化, 并且促进大鼠模型中骨折的愈合。作为一种正在临床上使用的药物, 此类超级抗原极有可能会成为一种用于多种骨科疾病治疗的潜在药物。

个人简历

张锦芳, 香港中文大学研究助理教授, 目前从事的研究工作包括non-coding RNA在干细胞分化方面的研究。已获得及申报中国专利5个, 主持国家自然科学基金2项及香港卫生署基金2项。在国际杂志发表研究论文 (SCI) 40余篇, 其中第一或通讯作者达20篇, 总影响因子超过100, 总引用次数达600余次。现担任核心期刊《现代生物医学进展》的编委, SCI杂志的Human Gene Therapy, RNA Biology, Plus One, Ontotarget, Beneficial Microbes, experimental cell ressearch 等杂志的特邀审稿人, 并为香港生物化学与分子生物学协会会员。

摘要

脐带血源干细胞复合富含血小板血浆治疗难治性肌腱病的基础与临床研究

唐康来教授

第三军医大学西南医院骨科



本研究拟探讨脐带血源干细胞复合富含血小板血浆治疗难治性肌腱病的疗效,开展了相关基础与临床研究,总共分三部分:(1)对比分析了脐带血源干细胞、富含血小板血浆及二者复合治疗大鼠跟腱病的疗效,影像学及组织学研究证实,脐带血源干细胞、富含血小板血浆及二者复合治疗大鼠跟腱病有效率100%,其中,脐带血源干细胞复合富含血小板血浆比单独使用脐带血源干细胞、富含血小板血浆治疗大鼠跟腱病疗效更为明显;(2)动物实验表明,脐带血源干细胞复合富含血小板血浆治疗难治性肌腱病具有良好的有效性和可靠的安全性;(3)人脐带血源干细胞复合富含血小板血浆治疗顽固性“网球肘”、“跳跃膝”、肩袖腱病和跟腱病均取得良好的初步临床疗效。

个人简历

唐康来,医学博士,第三军医大学西南医院骨科(国家重点学科)副主任,肩肘及足踝外科病区主任,重庆市运动创伤研究所负责人,教授、主任医师,博士生导师。目前担任:Journal of Foot and Ankle Surgery AP主编,亚太足踝外科协会秘书长,亚洲肩关节协会执行委员,中国医师协会骨科医师分会常务委员兼足踝外科工作委员会主任委员,中华医学会骨科学分会足踝外科学组副组长,中华医学会运动医疗分会委员兼上肢学组副组长等;SMART、Arthroscopy和中华医学杂志等18个杂志编委或审稿人。先后在德国、美国等多个国际著名的运动医学中心学习近3年,一直以肩肘及足踝外科为临床特色,以运动创伤为研究重点。个人手术超过1200台次/年,门诊超过10000人次/年,连续多年获得西南医院手术总量冠军。主持国家自然科学基金重点项目、国家支撑计划等课题20余项;发表学术论文160余篇,SCI收录48篇;2014年以第一完成人获得重庆市科技进步奖一等奖;主编国内第一部《足踝外科手术学》等专著5部,副主编专著6部,参编专著12部。获得国家授权专利28项。

The Effect of Ca^{2+} on the Mechanics of Collagen fibrils

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Abstract:

Osteoarthritis (OA) is the leading cause for the disability of elderly people worldwide and should mainly due to the failure of collagen fibril meshwork in articular cartilage (AC). Previous studies found that, with the progression of OA, elastic modulus of collagen fibrils harvested from OA AC increase significantly together with abnormal Ca^{2+} ion distribution, which indicates that Ca^{2+} concentration should play an important role in the pathology of OA. However, the direct relationship between the Ca^{2+} ions and elastic modulus of collagen fibrils are still ambiguous. In this study, systematically experiments were performed to investigate the effect of Ca^{2+} on the mechanical behavior of AC tissue and collagen fibrils. The elastic modulus of AC tissue and collagen fibrils under different concentrations of Ca^{2+} were measured using indentation-type atomic force microscopy (IT-AFM). It was found that the stiffness of AC and collagen fibrils show an increasing trend with the increase of Ca^{2+} , from 0.88 GPa at 0 M to 1.39 GPa at 20 mM, and from 1.55 GPa at 0 M to 2.45 GPa at 20 mM, respectively. The results obtained in presented work indicated that the increase of Ca^{2+} concentration during the OA might be a possible reason for the collagen fibrils failure and consequently OA progression.

Bioreactor cultivation and stimulation for bioregeneration of cartilage

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Abstract:

Objection Cartilage tissue engineering have been widely used in regeneration of cartilage in vitro, and repairmen of damaged cartilage. The studies of bioreactors that mimic the environment of cartilage development in vivo, aimed to increase the bionic of tissue engineering cartilage scaffold and effectiveness of cartilage repairmen.

Methods Knee joint chondrocytes were isolated from New Zealand white rabbits and expanded in vitro. The chondrocytes at passage 2 were seeded onto a scaffold of articular cartilage extracellular matrix (ACECM) in the concentration of $1 \times 10^6/\text{mL}$ to prepare cell-scaffold composite. Cell-scaffold composites were cultivated in the chamber of bioreactor with mechanical compression (experimental group) (parameters of mechanics: 1Hz, 3hours/day, and 0.5Mpa), and control group was cultivated without mechanical compression. The experimental group comprised 4 times, including 7days, 14 days, 21 days, and 28 days. Additionally, after different time points, cell-scaffold composites were assessed through real-time quantitative PCR, histological staining, mechanical tests and immunohistochemistry staining. **Results** Morphological observations demonstrated that the thickness and elastic modulus in experimental group were significantly higher than those in control group, and positively related to time. Mechanical tests indicated that the experimental group is more stable to bearing compressive loads. Histological staining showed more proliferation of chondrocytes, formation of cartilage lacuna, synthesis of GAG, and positive results for collagen type II in experimental group than those in control

group, by HE staining, Safranin-O staining, and immunohistochemistry staining, with the highest results in the group of 21 days. Real-time quantitative PCR revealed that mRNA expression of collagen type I, collagen type II were significantly higher in experimental group than that in control group. And the group of 21 days showed the highest expression of mRNA expression of collagen type II. **Conclusion** With the mechanical stimulation of bioreactor, the cartilage composite can produce more extracellular matrix, such as collagen and GAG, and strengthen the mechanical properties, which coincident with the environment of cartilage development in vivo. With the progress of tissue engineering, the bioregeneration of damaged cartilage in clinical will be achieved.

Human umbilical cord mesenchymal stem cells-derived extracellular matrix promote peripheral nerve regeneration

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Abstract: Extracellular matrix (ECM) including collagen, laminin, or fibronectin play an important role in peripheral nerve regeneration. Recently, Schwann cell-derived ECM with classical biomaterial was used to mimic a neural niche, however, it is not practical to extensively use SCs in clinic due to limited origin, sacrifice of an autologous nerve, and long culture time in vitro. Here we aimed to human umbilical cord-derived mesenchymal stem cells (hUCMSCs) which is more easily accessible and have higher proliferative and secretory ability than SCs. A protocol was adopted to prepare and characterize the hUCMSCs-derived ECM. Compared with tissue culture dish culture coating with Poly-L-Lysine, hUCMSCs-derived ECM enhanced Schwann cell viability and proliferation, increased nerve growth factor and brain-derived neurotrophic factor expression in Schwann cells, and enhanced neurite growth from dorsal root ganglion explants. These findings suggest that hUCMSCs-derived ECM promote peripheral nerve repair and will therefore prepare the ground for a more rational design of engineered neural niche.

Small molecular Kartogenin works as an endogenous mesenchymal stem cells activator.

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Abstract:

Degeneration of the endogenous mesenchymal stem cells (MSC) in cartilage tissue results in disorders of regeneration and repair. Kartogenin (KGN) has been reported having the effect of chondrogenesis in MSCs by activating traditional TGF- β signaling pathway through up-regulate the Smad2/3 phosphorylation.

Recently, we found KGN was able to stimulate the proliferation of primary cartilage derived progenitor cells

which we isolated from rat knee joint cartilage. Our data shows that 10uM KGN treatment for a week, the percentage of G2 - M phase cells in mitosis reached 9.6%, almost twice of the control group, and the total cell number was doubled in following. Cells confirm the marker of 96% CD34-, 93% CD90+ and 98% CD105+. As a control, no significant changes of that in mature human T lymphocyte with the treatment of KGN. Apart from that, MSCs can be induced into cartilage after 21 days by only KGN treatment without TGF- β . Rat CPC RNA-Seq analysis discovery about 20 cell cycle related genes change significantly after KGN 72 hours treatment. IL-6 and its receptor Gp130 were the most significant genes which was increased 6 folds more than that of control. We confirmed IL-6's level significantly increased in both cytoplasm and supernatant media. Furthermore, we found that the phosphorylation of Stat-3 up-regulated at the same time. *In vivo* experiment evidences of the increased thickness in articular cartilage with KGN treatment has also been confirmed in knee joint injury animal model. IHC staining of KGN treatment group shows up-regulate of Stat-3 phosphorylation. Based all above, we believe KGN could work as an endogenous mesenchymal stem cells activator for the cartilage tissue regeneration and repairing by not only inducing cartilage differentiation but also endogenous mesenchymal stem cells self-renew.

Building a decellularized meniscus extracellular matrix (DMECM)/ demineralized bone matrix (DBM) diphasic scaffold for meniscus tissue engineering

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Abstract:

Introduction Tissue engineering meniscus regeneration is a hopeful treatment strategy for meniscus lesion, however the meniscal scaffold material is a huge challenge. The key is to find one kind of scaffold material that can not only meet the requirements for biomechanics properties of meniscus, also has good biocompatibility. The aim of this study is to construct a diphasic meniscus scaffold for tissue engineering meniscus regeneration. **Methods** We utilize decellularized meniscus extracellular matrix (DMECM) nanomaterial and demineralized bone matrix (DBM) to construct three different kinds of three-dimensional porous meniscus scaffolds (DMECM scaffold, DBM scaffold and DMECM/ DBM diphasic scaffold), and then define the physicochemical characteristics of the three different scaffolds. We incubate meniscus cells in the scaffolds leads to formation of neotissues that resemble meniscus-like tissue. The scanning electron microscopy (SEM), confocal microscopy, and real-time PCR were used to monitor the viability, morphology and gene expression profiles of meniscus cells, respectively. Morphology and mechanical properties of the three scaffolds (with and without cells) were investigated via SEM. Seeded scaffolds were used to produce meniscus-like constructs and were examined via histology. We also detect the total production of GAG and collagen in the scaffolds and medium in the different time point after seeding cells in the scaffolds, 3th day, 7th day, 14th day. We define the immunogenicity of the three different scaffolds by rats subcutaneous implantation experiment.

Results The DBM scaffold and DMECM/DBM diphasic scaffold have the better biomechanical properties compare to the DMECM scaffold. Both the DMECM scaffold and DMECM/DBM diphasic scaffold supported

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meniscus tissue formation with increased collagen and GAG compare to the DMECM scaffold, yet no difference in gene expression between the two. The DBM, DMECM scaffold and DMECM/DBM diphasic scaffold do not have immunological rejection after they have been implanted subcutaneously in the rats.

Conclusions DMECM/DBM diphasic scaffold, which possess mechanical strength of meniscus and can support neotissue formation, show potential for use in cell-based meniscus regeneration strategies.

Acknowledgement: This study is supported by the National High Technology Research and Development Program of China (2012AA020502).

The Alteration and Crosstalk of Articular Cartilage-Subchondral Bone Unit in Osteoarthritis

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Abstract:

Background: To investigate the pathology, angiogenesis, mechanical properties, molecular genetic level, permeability and interaction of the bone-cartilage unit in the different stage of human primary knee OA .

Methods: The 40 human tibial plateaus were obtained from patients undergoing TKA from October 2012 to March 2013. After gross observation, the cartilage-bone complex samples were divided into A, B, C, D four parts. A group was evaluated by Micro-CT and histological staining. B group was conducted biomechanical testing. C group was processed qPCR and Westernblot detection. D group was used contrast-enhanced computed tomography (CECT) to detect the permeability of cartilage.

Results: μ CT results showed that BMD, BV/TV, Tb.N and Tb.Th in later stage were significantly higher while Tb.Sp and SMI were lower. Mechanical test results showed that the elastic modulus of OA cartilage was the lowest in stage III and the bone elastic modulus and hardness of the OA cartilage was the maximum in stage IV. The PCR showed that the expression of osteogenesis-related genes contains Runx2, OCN, OPN were the highest in stage III. The expression of Osteoclast-related genes contains Cathepsin K, RANKL were the highest in stage II. Aggrecan, Sox9, COLII were downward trend and MMP9 was upward trend. Westernblot showed that the expression of Runx2, BMP2, BMP7 and OPG were the highest in stage III. The expression of RANK and RANKL were the highest in stage II. Permeability results showed that the permeability of cartilage was associated with cartilage degeneration, and the penetration rate was the fastest in stage III.

Conclusions: The interactions of bone and cartilage form a functional and crucial unit in which the individual components interact cooperatively and synergistically in OA progression. The subchondral bone remodeling is closely related with cartilage degeneration. The contrast-enhanced scanning method based on CT can detect the permeability of cartilage and reflecting the cartilage degeneration.

Staphylococcal Enterotoxin C2 Expedites Bone Consolidation During Distraction Osteogenesis

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Abstract:

Background Distraction osteogenesis (DO) successfully induces large-size bone defect regeneration, but it involves undesirably long duration of treatment. Developing innovative approaches to augment bone consolidation is in burning need. Staphylococcal Enterotoxin C2 (SEC2) has been developed and found to promote osteogenesis and suppress osteoclastogenesis of human mesenchymal stem cell in vitro. In this study, we investigated whether SEC2 could accelerate bone consolidation in a DO rat model.

Methods Two groups of rats aged 12 weeks (n = 20) underwent surgical procedure of middle tibial osteotomy and subsequent distraction at 0.25 mm/12 hours for 10 days. The experimental and control group received injections of SEC2 (10ng/ml, 100ul) and sterile saline (100ul) into the distraction gap every three days till termination, respectively. Animals were euthanized on postoperative day 43; bilateral tibias were harvested and subject to micro-computed tomography (MicroCT), mechanical testing, histology and immunohistochemistry examinations.

Results Compared to control group, SEC2 group had significantly higher bone volume and bone mineral density in the regenerates. Greater force was required on four-point testing to break SEC2-treated tibias. Bone morphogenetic protein-2 expression was up-regulated in SEC2 treated group. Interestingly, the contralateral tibias in SEC2 group were also significantly stronger than those of control group.

Conclusion This study demonstrated that local application of SEC2 into the distraction regenerate could promote bone consolidation during DO. The findings support use of SEC2 as a potential novel strategy to enhance bone consolidation in patients undergo DO treatment.

Human Fetal Mesenchymal Stem Cell Secretome Alleviates Replicative Senescence of Human Adult Mesenchymal Stem Cell

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Abstract:

“Cellular senescence” refers to a complex cellular processes in response to a variety of internal and external stimulations mainly to halt the cell division which could be detrimental to cellular activities and potential

malignant transformation. In *in vitro* culture, senescence of MSC including the decline of proliferation and multipotent differentiation, is also a significant phenomenon affecting the therapeutic potential of MSCs in tissue engineering. Recent evidences suggest that the regenerative and anti-inflammatory activities of MSCs are significantly attributed to the secretory bioactive substances, collectively named as secretome. Literature research shown that the superior stem cell properties of fetal MSCs (hfMSCs) over their adult counterparts might be attributed to their secretome with unique profile of fetal specific bioactive components. However, the beneficial effects of hfMSCs secretome is not well elucidated. Our result comparing with hfMSC(HAS), haMSC(HFS) significantly enhanced the proliferation and osteogenic differentiation activities, and reduced β -galactosidase activity of haMSC. HFS also promoted ectopic bone formation with no tumorigenicity in immunocompromised mice. Cellular studies showed that HFS treatment induced activation of *Sirt1* and *FOXO3A* in haMSC, which were associated with increased expression of *p21* and decreased expression of *BAX* and *p53*. This study provides insight into the novel biological function of HFS in regulating replicative senescence and stem cell properties *in vitro*. On-going study is investigating the effect of HFS on chondrogenesis of haMSC and on rat chondrocyte. Furthermore, we have identified a number of candidates through RNA sequencing and iTRAQ method. Further investigate on OVX and OA model is required to validate the threptic potential of candidates.

Stromal cell-derived factor-1 plays an important role in subchondral bone abnormal changes during osteoarthritis development

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Abstract:

Objective: Clinical samples, rat OA model and cell model were used to determine whether stromal cell-derived factor-1 plays an important role in subchondral bone abnormal changes during osteoarthritis development. Methods: At first, Clinical samples including severe OA part (OA+) or relative normal part (OA-) were analyzed by histology staining, micro-CT, enzyme-linked immunosorbent assay (ELISA) and western blotting, to compare SDF-1 concentrations in subchondral bone. Secondly, OA was induced in the right knee joint with ACLT + MMx in the SD rats. Then they received continuous infusion of the AMD3100 osmotic mini-pump implanted subcutaneously. 6 weeks after treatment, the rat was sacrificed. Cartilage damage was assessed via histology; subchondral bone aberrant changes were analyzed by micro-CT and immunohistochemistry. Finally, in cultured mesenchymal stem cells (MSCs), the effects of SDF-1 on MSCs osteogenic differentiation was evaluated by immunofluorescent, ALP Staining and western blotting. Results: SDF-1 concentration is high and pErk cell pathway is active in subchondral bone from humans with osteoarthritis. Safranin-O/fast green staining revealed less cartilage damage in the AMD3100-treated animals; subchondral bone abnormal change was also reduced, that evidences showing by down-regulate the BMD and BV/TV and the number of Nestin or Osterix positive. The ALP and western bolting results showed that SDF-1 by activating the pErk cell

signal pathway play an importance role in MSCs osteogenic differentiation. Conclusions: High concentration of active SDF-1 seems to initiate the subchondral bone abnormal changes of osteoarthritis and inhibition of this process could be a potential therapeutic approach to treating this disease.

Pathologic changes of patellar tendon in streptozotocin-induced diabetic rats

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Abstract:

Purpose: To demonstrate the histopathological alterations, especially the non-tenogenic characteristic changes of the patellar tendon in streptozotocin-induced diabetic rats.

Methods: All animal experiments were approved by the Animal Experimentation Ethics Committee, the Medical School of Southeast University. 36 SD rats (female, 200-250 g, 8 weeks) randomly divided into 2 groups, diabetic group (DG) and control group (CG). In DG (n=18), diabetes was induced via intraperitoneal injection of streptozotocin (STZ, 65 mg/kg) in SD rats, which were confirmed with blood glucose levels and pre- and post-STZ injection intraperitoneal glucose tolerance tests (IPGTT). All animals were sacrificed at 1, 2 and 4 weeks post-induction, and the patellar tendons were isolated for hematoxylin-eosin (H&E) staining and immunohistochemical (IHC) staining. Semiquantitative image analyses of target protein expression in IHC staining were performed using the Image-pro plus 6 Software (version 6; Media Cybernetics Inc). Data was presented as mean±SD and shown in histogram. Comparison of more than two groups was done using Kruskal–Wallis test followed by post hoc comparison with control group using Mann–Whitney U-test. All the data analysis was done using SPSS (version 16.0; SPSS Inc). $p < 0.050$ was regarded as statistically significant.

Results: A significant impaired glycemic control in the DG was detected in both of blood glucose levels and IPGTT when compared with those of CG ($p < 0.050$). Alternations of collagen fibers arrangement, micro-tears of collagen fibers (arrow), the rounded tendon cells (diamond), the chondrocyte-like cells (star), even some red blood cells and blood vessels (rectangle) were observed in diabetic tendons in H&E staining (Figure 1). Both of the tenogenic markers, including type I collagen (Col I) and Tenomodulin (Tnmd) were positively stained in patellar tendons in both CG group and DG group. The expression of Col I and Tnmd in diabetic tendons were decreased at 1 week when compared with matched normal tendons post induction ($p = 0.128$, $p = 0.087$, respectively), and the significance difference was detected in diabetic tendons at 2 weeks when compared with matched normal tendons post induction ($p = 0.004$, $p = 0.004$, respectively). There was no difference among the CG groups ($p > 0.050$) (Figure 2 and 3). The expression of osteo-chondrogenic markers, including osteopontin (OPN), Osteocalcin (OCN), SOX9 and type II collagen (Col II), were positively detected in the diabetic tendon while the CG group showed the negative stained. OPN and OCN were mainly expressed in the cytoplasm of diabetic tendon cells, especially surrounding these rounded tendon cells, and Sox9 was found positively stained in both the nucleus and the cytoplasm of these cells while Col II mainly expressed in the extracellular

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matrix (ECM). Both of OPN and SOX9 were showed the ascending expression in DG tendons accomplished with the process of DM. The expression of OPN and SOX9 in the DG subjects were significantly increased at 4 weeks when compared with those at 1 week ($p=0.003$ and $p=0.003$, respectively) and 2 weeks ($p=0.003$ and $p=0.004$, respectively) post induction (Figure 4).

Discussion: The patellar tendons in STZ induced diabetic rats demonstrated the altered structure of the collagen fibers and the appearance of rounded tendon cells in H&E staining. Decreased tenogenic markers expression and increased osteo-chondrogenic markers expression were detected in patellar tendon at the early stage of diabetes mellitus induced by STZ. Further study should be performed to discover the underlying pathogenesis of tendon disorder in diabetes mellitus.

Significance: Our findings suggested that streptozotocin-induced diabetic rats showed alterations of the patellar tendon with structural and non-tenogenic componential changes, which might provide some new cues for the pathogenesis of tendon disorder in diabetes mellitus

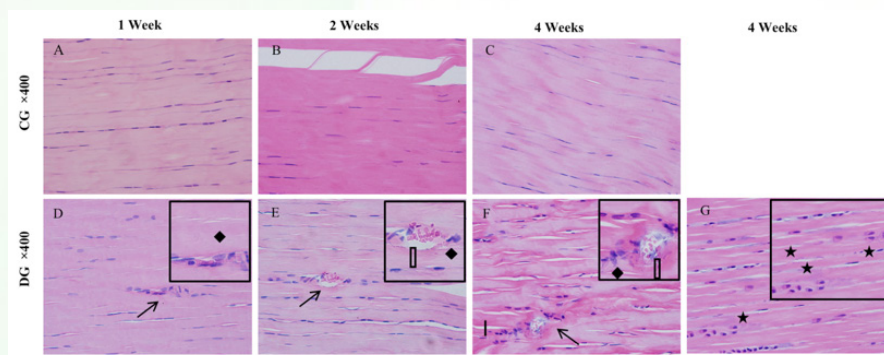


Figure 1. (Week 1,A,D; Week 2,B,E; Week 4,C,F,G)(A-G $\times 400$) Representative images of H&E staining of patellar tendon at different times after STZ injection. (A-C) All of the healthy controls at different time points showed the tight, parallel arrangement of collagen fibers distributed at the same orientation with slight waves. The bundles of collagen fiber were about the same size as well as the tendon cells. (D-G) Alterations of collagen fibers arrangement, micro-tears of collagen fibers (arrow), the rounded tendon cells (diamond), the chondrocyte-like cells (star), even some red blood cells and blood vessels (rectangle) were observed in diabetic tendons.

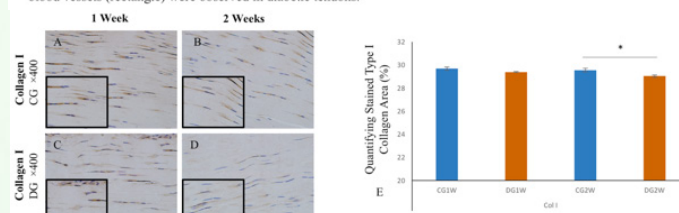


Figure 2. (A-D $\times 400$) Decreased of the density of type I Collagen in the patellar tendon in the DG at 2 weeks post induction ($*p=0.004$). The expression of Col I in diabetic tendons also decreased at 2 weeks when compared with 1 week post induction ($p=0.090$).

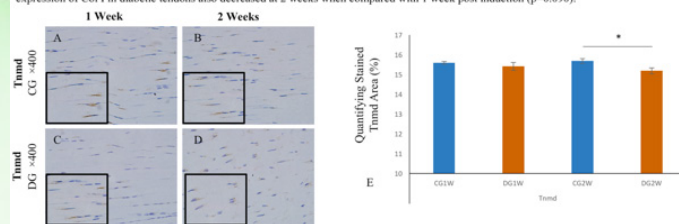


Figure 3. (A-D $\times 400$) Decreased of the density of Tnmd in the patellar tendon in the DG at 2 weeks post induction ($*p=0.004$). The expression of Tnmd in diabetic tendons also decreased at 2 weeks when compared with 1 week post induction ($p=0.078$).

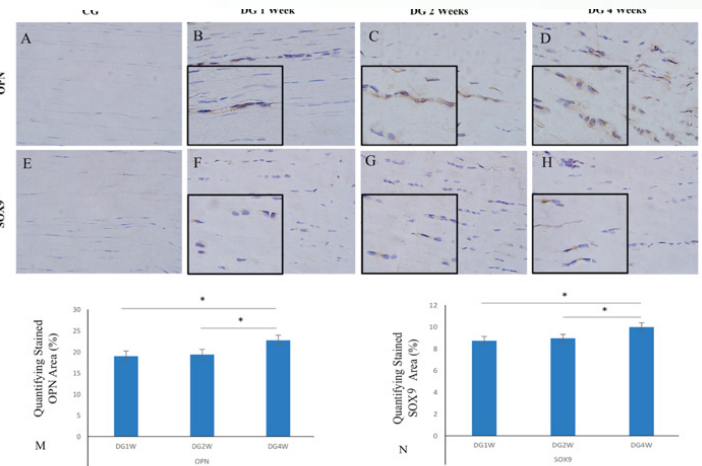


Figure 4. (A-H $\times 400$) The expression of osteo-chondrogenic markers, including osteopontin (OPN) and SOX9 were positively expressed in the diabetic tendon while the CG group showed the negative stained. The expression of both OPN and SOX9 were increased in the DG at 4 weeks when compared with 1 week ($*p=0.003$ and $*p=0.003$, respectively) and 2 weeks ($*p=0.003$ and $*p=0.004$, respectively) post induction.

Targeting CKIP-1 within osteoblast: A potential anabolic strategy for bone formation reduction during aging?

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Abstract:

Casein kinase-2 interacting protein-1 (CKIP-1) is an important ubiquitination-related molecule negatively regulates BMP signaling. Previously, we found that aberrantly increased CKIP-1 within osteoblasts was closely associated with suppressed BMP signaling and reduced bone formation during aging. Thus, we hypothesize that CKIP-1 within osteoblasts may participate in the pathological regulation on the bone formation reduction during aging. By genetic approach, we established osteoblast-specific *Ckip-1* conditional knockout (CKO) mouse model. The aged CKO mice showed higher bone mass, improved trabecular micro-architecture, increased bone formation and higher activity of BMP signaling compared with the littermate controls. By pharmacological approach, we found that the level of CKIP-1 mRNA within osteoblast (ALP+ cells) was remarkably downregulated in the OVX rats received eight consecutive intravenous injection of CKIP-1 siRNA encapsulated within our established osteoblast-targeted-aptamer-functionalized lipid nanoparticles (siRNA group) (**Fig 2b**). Consequently, the intraosseous CKIP-1 protein levels were decreased while the pSmad1/5 levels were elevated in these rats (**Fig 2c**). In addition, the rats in siRNA group showed higher bone mass and improved trabecular micro-architecture as well as increased bone formation rate at lumbar vertebra when compared to the rats in the other groups (**Fig 2d&e**). This study suggests that CKIP-1 within osteoblast plays an important role in the pathological regulation on the aging-induced bone formation reduction. Targeting CKIP-1 within osteoblast may be a potential anabolic strategy for the bone formation reduction during aging.

The Role of CFTR on Tenogenic Differentiation

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Abstract:

Introduction

Tendons are responsible for transmitting forces derived from muscle to bone and as a result, are subjected to dynamic mechanical stretching. However, how cells sense mechanical stretching and convert them into biochemical signals is not well understood. The current evidence has found that the stretching-activated ion channel may also play a role¹. Recently, it has been demonstrated that Cystic Fibrosis Transmembrane conductance Regulator (CFTR) can be robustly activated by membrane stretch induced by negative pressures². Given that CFTR can also have an unexpected function in mechanosensing, in addition to its roles as a ligand-gated anion channel and a regulator of other membrane transporters. In the current study, we first compare the tendons differences by using the most common CFTR mutation animal model ($\Delta F508$) and its wild type

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mice, to examine the tendon differences at microstructure, mRNA and histology level respectively. Moreover, we also build the CFTR-knockdown (CFTR-KD) cells line with C3H10T1/2 to further study the underline mechanisms.

Methods

Achilles tendons (AT) and patellar tendons (PT) were collected from 20-24 weeks old male CFTR mutant and wild type mice for examination. Immunofluorescence was performed on paraffin embedded patellar tendons to confirm the expression of CFTR on tendon. Transmission Electron Microscope (TEM) was performed to compare the microstructure of AT. RNA from AT was isolated for comparing the expressions of tendon related markers by qRT-PCR at mRNA level. PT was embedded for paraffin sectioning. The immunohistochemistry was also performed to compare the expressions of tenogenic markers (Tenomodulin) between CFTR mutant and wild type mice at histology level. The expression levels of tenogenic makers in CFTR-KD cells were also compared.

Results

Immunofluorescence showed that CFTR expressed on patellar tendon, especially on the cells in tendon tissue. At microstructure level, TEM indicated that tendon fibrils were loosely organized in mutant mice comparing to wild type mice, and sizes of fibrils were also unevenly distributed in mutant mice. The results of qRT-PCR showed that expressions of Tenomodulin, Scleraxis and Decorin are all lower in mutant mice comparing with wild type mice ($p<0.05$). Furthermore, the immunohistochemistry also showed lower expression of Tenomodulin in CFTR mutant mouse than that in wild type mouse. For *in vitro* studies, CFTR-KD cells were also showed significantly decrease of Tenomodulin, Scleraxis, Decorin, Col1A1 and Col3A1 ($p<0.05$).

Discussion

In the current study, we confirm the expression of CFTR on tendon tissues at microstructure, mRNA and histology level. We found that the CFTR mutant mouse showed lower expression of tenogenic markers (Tenomodulin, Decorin and Scleraxis) and loosely organized tendon fibrils by *in vivo* studies. Moreover, the results of *in vitro* were coincidence with the *in vivo* parts, which means that CFTR helped to promote tenogenic differentiation during tendon development.

Co-cultured Mesenchymal Stem Cells and Tendon-derived Stem Cells for Tendon Repair – A Strategy for Enhancing Tendon Regeneration

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Abstract:

The injury of tendon tissues presents a significant clinical challenge to orthopaedic surgeons. Cell-based tendon grafts have become an alternative for tendon rupture reparation. However, the ideal cell source for tendon repair remains controversial. The purpose of this study was to investigate whether bone marrow mesenchymal stem cells (BMSCs) exhibit enhanced tenogenic phenotype after co-cultured with tendon-derived stem cells

(TDSCs), representing desired cell resource for tendon healing. After harvested from rats, BMSCs and TDSCs were cultured alone or co-cultured in 1:20, 1:10, 1:5 and 1:1 ratio in vitro. Cells were characterized by MTT, qRT-PCR, sirius red staining and immunofluorescent staining. We produced cell sheets by BMSCs, TDSCs or co-cultured cells, then detected by H&E and immunohistochemistry staining. Finally, the formed cell sheets were implanted into a rat patellar tendon window injury model. Histology and biomechanical testing data indicated co-cultured cell sheets can promote tendon healing. In conclusion, cells mixture containing TDSCs possess much more similar character of tendon with that of pure TDSCs which is more suitable for tendon tissue engineering. BMSCs co-cultured with TDSCs represent a better cell source than BMSCs alone for tendon tissue engineering.

Dexamethasone inhibits the differentiation of rat tendon stem cells into tenocytes by targeting the scleraxis gene

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Abstract:

Glucocorticoid-induced tendon rupture is very common in clinical practice, and the overall outcome of surgical suture repair is rather poor. The mechanism remains unclear, and effective treatments are still lacking. In the present study, we investigated the effect of dexamethasone on the differentiation of rat tendon stem cells (TSCs) to tenocytes and the underlying molecular mechanisms and found that dexamethasone inhibits the differentiation of TSCs to tenocytes by analyzing the development of long, spindle-shaped cells and detecting the expression of tenocyte markers type I collagen and tenomodulin (TNMD) at both the mRNA and protein levels. We also discovered that after treatment with dexamethasone the scleraxis expression level is downregulated in vitro and in human specimen. Chromatin immunoprecipitation (ChIP)-PCR showed that dexamethasone promotes glucocorticoid receptor interacted with the TGGAAGCC sequence located between -734 and -726 base pairs (bp) upstream of the start codon of the scleraxis gene. Furthermore, TSCs were transfected with scleraxis knockdown or overexpression plasmids, and the results indicated that scleraxis plays a pivotal role in the differentiation of TSCs to tenocytes. In conclusion, dexamethasone inhibits the differentiation of TSCs to tenocytes by inhibiting the scleraxis gene.

MicroRNA-503 Promotes Bone Formation in Distraction Osteogenesis through Targeting Smurf1

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Abstract :

Distraction osteogenesis (DO) is a unique technique to promote bone formation in clinical. However the underlying mechanism of DO is still unrevealed. Recently, microRNAs have been reported to play important roles in regulating osteogenesis. In this study, we aimed to confirm the hypothesis that some special microRNAs could regulate the bone formation during the process of DO. After successfully established the DO model of rats, a microRNA microarray was performed to compare the microRNAs expression levels between the bone samples derived from distraction area and contralateral side. Total 100 different microRNAs were found changed, with 74 microRNAs up-regulated and 26 down-regulated. Through screening, as one of the most highly expressed microRNAs, miR-503 was also found gradually up regulated during osteogenic induction in mesenchymal stem cells of rats (rBMSCs). Besides, overexpression of miR-503 in rBMSCs could promote osteogenesis by up regulation Runx2 and BMP2. Furthermore, luciferase report assay confirmed that Smurf1 was the direct target gene of miR-503. Finally, rBMSCs overexpression miR-503 was successfully constructed and locally injected into the distraction gap in DO animal. The results indicated that miR-503 overexpression therapy could promote mineralization in DO process in vivo. In conclusion, microRNA-503 was found to regulate osteogenesis during the process of DO and overexpressing of miR-503 resulted in acceleration of mineralization of DO, which not only give clues to the underlying mechanism of DO but also provide potential therapeutic targets in clinical.

Fabrication of Chondroitin sulfate Strontium and its application on osteoarthritis

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Abstract:

Chondroitin sulfate and strontium both exert beneficial effects on the metabolism of cells related to osteoarthritis (OA), including chondrocytes, synoviocytes, etc. Chondroitin sulfate is a natural compound that will help to increase the synthesis of type II collagen and proteoglycans in human articular cartilage. Strontium could reduce osteoclast activity and bone resorption in vitro. Meanwhile, the chondroitin sulfate and strontium can help in maintaining the anabolic/catabolic balance of the extracellular cartilage matrix (ECM). In this study, chondroitin sulfate strontium (CSSr), a new compound that might be help in OA therapy was successfully synthesized. Meanwhile, the molecular composition and structure was characterized by FTIR, NMR, SEM, etc. XRD patterns and SEM/EDX results confirmed CS is successfully modified with Sr while the ¹H NMR spectra and FTIR spectral data indicated that SrCS we obtained is a *polysaccharide-metal* ion complex and the carboxyl groups of strontium-binding CS took a carboxylated ion form. Based on the cell studies, it is believed that the prepared compound should be beneficial to joint tissues during OA..

Fabrication of different morphology AB-type Carbonated Hydroxyapatite from Sea Shells.

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Abstract:

Hydroxyapatite (HA) is a commonly used biomaterial for bone grafting, while it's composition and morphology affected its bioactivity. The lack of carbonate ions in normal HA limits its ability to osseointegration. Alternatively, carbonate-substituted hydroxyapatite (CHA) was reported to be a better bone substitution because it has almost same chemical composition and structure as natural bone minerals. Meanwhile, different microstructure and morphology of the CHA also affect it's bioactivity. In this study, a novel method was proposed to directly synthesize CHA via one-step hydrothermal exchange from sea shells. Moreover, the morphology and the amount of carbonate-substitution of the CHA fabricated with the proposed method can be well controlled by adjusting the PH values during the reaction: as adjusted the PH value, the morphology of the final product changed from long sheet-like to petal-like and there was a concomitant increase in amount of CO₃²⁻ substitution. The cytocompatibility of the two typological CHA was evaluated by CKK-8 assay, the results reveal that both sheet-like and petal-like CHA present a good cell viability, and the former has a better cytocompatibility compared to the latter.

The effects of Substance P on tendinopathy are dose-dependent: an in vitro and in vivo model study

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Abstract:

OBJECTIVES:

Substance(SP) is known to be involved in neuropathic pain, chronic inflammation, and tendinopathy. The present study evaluated the effects of different doses of SP on tendon-derived stem cells (TDSCs) in vitro and tendons in vivo.

METHODS:

For the in vitro study, TDSCs cultured in growth medium with different concentrations of SP (negative control, 0.1 nM, and 1.0 nM). The effects of SP on TDSCs were examined with respect to their ability to proliferate and differentiate. For the in vivo study, we injected different doses of SP (saline control, 0.5 nmol, and 5.0 nmol) into rat patella tendons to investigate the effects of SP on tendons.

RESULTS:

Low and high doses SP significantly enhanced the proliferation ability of TDSCs. Low-dose of SP induced the expression of tenocyte-related genes; however, high-dose of SP induced the expression of non-tenocyte genes, which was evident by the high expression of PPAR γ and collagen type II. In the in vivo study, only high-doses of SP (5.0 nmol) induced the tendinosis-like changes in the patella tendon injection model. Low doses of SP (0.5 nmol) enhanced the tenogenesis compared with saline injection and the high-dose SP group.

Conclusions: SP enhances the proliferation of TDSCs in vitro and the effects of SP on tendinopathy are dose-dependent in vivo.

自体骨髓间充质干细胞复合PLGA/纳米级软骨细胞外基质 (ACECM) 组成和结构仿生支架修复兔膝关节软骨缺损

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摘要: 正常软骨没有血供、神经支配及淋巴回流, 其损伤后难以自我修复。相对于软骨下骨钻孔、微骨折等传统的软骨损伤治疗办法而言, 组织工程技术显得更加有希望和优势。对于关节软骨组织而言, 其胶原纤维网络排列有着自己独特的区域变化, 深层关节软骨的胶原纤维垂直于软骨下骨取向排列, 从而使得软骨组织的抗压能力较强。组织工程支架的形态结构能够引导种子细胞在支架上的生长和排列方式, 因而影响着再生组织的排列结构和生物学功能。因此, 理想的软骨组织工程支架材料需要力学和生物相容性的仿生, 也需要形态结构的仿生。人工合成的聚合物支架材料具有良好的力学强度、满意的生物相容性、可控制的降解率和完全降解性。然而, 合成聚合物的表面是疏水性的, 缺乏内在生物活性。所以, 特异的信号很难被细胞表面受体所识别; 天然材料保留了或者仿生了天然组织的主要生化成份, 具有更好的生物活性和功能性。结合天然材料和人工合成材料的优缺点, 本实验应用软骨细胞外基质 (ACECM) 提供的仿生的生物环境和PLGA提供的力学强度以及取向性的形态学结构制备出了新型的PLGA/纳米级ACECM组成和结构仿生的取向支架材料。该支

自由投稿摘要

架具有良好的亲水性和细胞亲和性，同时具有较高的孔隙率和平均 $107 \pm 30 \mu\text{m}$ 孔径大小。复合支架较ACECM支架有更高的力学强度，尤其在含水状态下（压缩模量分别 $1.03 \pm 0.1 \text{ MPa}$ 和 $3.53 \pm 0.25 \text{ MPa}$ ）；相对于PLGA支架，复合支架具有更好的亲水性和细胞亲和性。取向的复合支架引导细胞垂直取向排列；取向性结构仿生深层关节软骨的排列结构；取向性的PLGA/ACECM复合支架能够引导取向性的关节软骨再生；同时，ACECM成份在体内能够诱导MSCs分化成软骨细胞。应用该支架材料复合兔的自体骨髓间充质干细胞修复膝关节软骨缺损的实验中，通过组织修复评分以及组织学染色证明：1、PLGA/ACECM复合支架实现了兔膝关节透明软骨修复；2. 取向性PLGA/ACECM复合支架能够引导关节软骨取向性再生；3. 软骨ECM体内可以有效诱导MSCs成软骨分化。

Sea Shell based Carbonated Hydroxyapatite Fabricated by Ultrasonic Reaction

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Abstract:

Hydroxyapatite (HA) is known as biomaterials for bone tissue engineering. Unfortunately, pure HA's osseointegration ability is unsatisfied. Recently studies reported that the natural bone mineral actually are carbonate hydroxyapatite (CHA), and so it is believed that CHA should be a better bone replacement materials than HA. While the current preparation ways including hydrothermal reaction, sol-gel method, coprecipitation way and so on show many defects (i.e expensive raw materials, high energy consumption, strict reaction condition). In this study, we purposed a novel method to fabricate CHA using ultrasonic reaction from sea shells, which is generally to be considered as marine industrial waste. The XRD, SEM, FTIR analysis were performed to investigate the structure and chemical composition of CHA fabricated through the purposed method under various conditions, and it was found that under $\text{PH}=10.45$ and ultrasonic frequency 45kHz , the sea shell can be converted to CHA in 4 hours with conversion rate nearly 100%. It is believed that the purposed method should be the most economic and efficient way to fabricate CHA.

The Preparation of Decellularized Meniscal Extracellular Matrix and the Effects on Meniscal Fibrochondrocytes

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Abstract:

Objective: Functional restoration of injured meniscus remains a substantial challenge, the aim of this study was to produce a novel decellularized meniscal extracellular matrix (MECM), and further investigate the effect of coated MECM surface on passaged meniscal fibrochondrocytes in vitro.

Method: The porcine meniscus was performed decellularization process to prepare MECM. CCK-8 was used

to evaluate the effect of MECM on cell proliferation capacity. The various biomimetic surfaces were coated, including chondroitin sulfate (CS) surface, MECM surface, and MECM/CS surface (ratio of 5:1). Passaged meniscal fibrochondrocytes were cultured on these coated surfaces in vitro for 7, 14 days and assayed the cell adherence, cellularity, matrix production in comparison with the control group (TCP).

Results: MECM can enhance the proliferation capacity of passaged meniscal cells. MECM surface positively and significantly affected meniscal fibrochondrocytes adherence, cellularity, increased the proteoglycans and collagen production. The passaged meniscal fibrochondrocytes on MECM coated surface could redifferentiate as convinced by safranin O and toluidine blue staining.

Conclusion: MECM can enhance both the proliferation and redifferentiation capacity of passaged meniscal cells, making it a potential candidate biomaterial for future meniscal tissue engineering applications.

基于3D打印的生物骨植入支架成型技术

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摘要: 当前用于骨组织修复的生物材料和技术种类缺乏且不完善, 选用合适的方法和材料进行骨损伤的修复显得尤为重要。羟基磷灰石 (Hydroxyapatite, HAP) 是人体骨骼组织主要成分, 具有优良的生物相容性和生物活性, 可诱导骨再生。聚乳酸 (Polylactide, PLA) 是一种具有良好生物相容性的物质, 植入到人体后在一段时间内分解, 对人体无毒副作用, 是一种合适的支架材料。用3D打印制造骨组织工程支架有显著优点。每个病人都有特异性的损伤部位3D打印制造任意形状产品, 对治疗骨损伤有重要意义。另外, 控制内部结构可以影响孔隙率, 机械强度和生物相容性, 生成优化的骨植入物。

生物钟蛋白ARNTL在软骨干细胞中的功能及作用机制研究

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摘要: 生物钟蛋白参与调控软骨生长、代谢及疾病过程, 其成员ARNTL在OA软骨细胞中异常高表达。有趣的是, ARNTL也能与低氧诱导因子HIF- α 形成二聚体, 参与HIF信号通路的调控。HIF-1 α 促进软骨细胞分化及胞外基质合成, HIF-2 α 则主要促进基质降解而被认为是最重要的OA疾病因子之一, 二者对下游基因差别调控的机理尚不清楚。ARNTL在OA软骨细胞优先与HIF-2 α 形成二聚体, 但其对软骨相关基因的调控作用亟待阐明。鉴于此, 我们首先分离得到了软骨组织来源干细胞, 发现HIF-1 α , HIF-2 α 及ARNTL均存在一定水平的表达。然后, 我们构建了HIF-1 α , HIF-2 α 及ARNTL高表达的慢病毒, 拟分别或组合修饰ARNTL、HIF-1 α 和HIF-2 α 表达水平, 以分析它们对软骨干细胞增殖、软骨分化、胞外基质合成和代谢的作用; 此外, 拟进一步采用Chip-Seq技术, 探寻这些HIF亚基在全基因组水平分别对软骨相关基因的调控作用及其规律, 最终为开发靶向HIF通路的治疗技术提供依据。

Aberrant overexpression of CKIP-1 contributes to failure of osteoblast-mediated repair for articular bone erosion in rheumatoid arthritis

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Abstract:

Bone erosion is a central feature of rheumatoid arthritis (RA), which results from excessive osteoclast-mediated bone resorption and inadequate osteoblast-mediated bone formation. Evidences have demonstrated that the capacity of osteoblasts to repair articular bone erosions is impaired in RA. However, the molecular mechanisms still remain largely unknown. Casein kinase-2 interacting protein-1 (CKIP-1) is an intracellular negative regulator of bone formation. We found that aberrant overexpression of CKIP-1 within osteoblasts negatively correlated with bone formation in bone specimens from patients with RA. Moreover, initial increase in CKIP-1 happened before decrease in bone formation in rodents with inflammatory arthritis. In our prepared the osteoblast-specific CKIP-1 conditional knockout (*Ckip-1_{osx}*^{-/-}) mice based on the Cre-loxP strategy, we found that both the reduction of bone formation and the increase of bone erosion were attenuated after induction with type II chicken collagen. Consistently, by systemically application of CKIP-1 siRNA carried by our established osteoblast-targeted delivery system, we found that bone formation-mediated reparative process at erosive lesion was promoted in collagen-induced arthritis mice. Furthermore, we observed that articular bone erosion in adult tumor necrosis factor transgenic (TNF-Tg) mice was less found in offspring of TNF-Tg / *Ckip-1_{osx}*^{-/-} mice. Our results demonstrated that CKIP-1 was a pivotal negative regulator of osteoblast-mediated repair for articular bone erosion in RA and inhibition of CKIP-1 in osteoblasts might be a novel therapeutic strategy.

Epigenetic memory gained by priming with osteogenic induction medium improves osteogenesis and other properties of mesenchymal stem cells

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Abstract:

Mesenchymal stem cells (MSCs) are highly plastic cells that are able to transdifferentiate or dedifferentiate under appropriate conditions. In the present study, we reported here that after *in vitro* induction of osteogenic differentiation, MSCs could be reverted to a primitive stem cell population (dedifferentiated osteogenic MSCs, De-Os-MSCs) with improved cell survival, colony formation, osteogenic potential, migratory capacity and increased expression of Nanog, Oct4 and Sox2. Most importantly, our results showed great superiority of the De-Os-MSCs over untreated MSCs in ectopic bone formation *in vivo*. Furthermore, Nanog-knockdown in MSCs could reverse these enhanced properties in De-Os-MSCs *in vitro*, indicating a central role of Nanog

in the transcriptional network. In addition, epigenetic regulations including DNA methylation and histone modifications may play important roles in regulating the de-osteogenic differentiation process. And we found decreased methylation and promoter accrual of activating histone marks, such as H3K4me3 and H4ac on both Nanog and Oct4 gene promoters. Taken together, our study demonstrated that epigenetic memory in De-Os-MSCs gained by priming with osteogenic induction medium favored their differentiation along osteoblastic lineage with improved cell survival and migratory abilities, which may have application potential in enhancing their regenerative capacity in mammals.

Smad7: a new molecular target for treatment of osteoarthritis

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Abstract:

Objective It is reported that TGF- β signaling was highly upregulated in OA patients. We then raise the hypothesis that OA could be modulated by activating of Smad7. This study is to investigate the role of smad7 in the progress of OA.

Methods The genetically engineered Smad7^{AE1} (KO) and wild type (WT) mice (n = 15) was terminated at 6, 12, or 24 months, histology was performed to examine the pathological changes of articular cartilage. 32 KO (n=16) or WT (n=16) mice were subjected to anterior cruciate ligament transection (n=8) or sham operation (n=8), respectively. Histology, immunohistochemistry, and Micro-Computed Tomography (CT) analysis were performed to assess the pathological changes of articular cartilage and subchondral bone after 6 or 8 weeks.

Results Histological staining showed there was no significant difference in the morphology of tibial cartilage between KO and WT mice at 6, 12 or 24 months old. However, cartilage destruction was observed both in the KO and WT mice after 6 and 8 weeks of ACLT. Furthermore, results of Micro-CT showed total bone volume and bone density of subchondral bone was significantly increased in KO mice after ACLT, indicating a sclerosis status happened in subchondral bone area.

Conclusion After ACLT surgery, Smad7 KO mice showed a classical pathological changes of OA. Smad7 may be a new molecular target in the progress of OA. Future studies are needed to investigate whether the activators of smad7 could attenuate the progress of OA.

Antler collagen/chitosan scaffolds improve critical calvarial defect healing in rats

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Abstract:

Objective This study was to develop chitosan scaffolds combined with collagen derived from deer antler and

test its in vivo bone regeneration capacity in the calvarial defect model.

Methods Chitosan was crosslinked with or without collagen extracted from deer antler by chemical reaction. Proliferation rate of rat bone marrow-derived mesenchymal stem cells was measured at 3 or 5 day after seeded on the porous scaffold in vitro. Sprague-Dawley rats were subjected to calvarial defects surgery. Then the defects were left empty or implanted with chitosan scaffolds, or antler collagen/chitosan (A-collagen/chitosan) scaffolds. Samples were collected for micro-CT then decalcified for histology analysis after 8 weeks.

Results Cell proliferation was significantly increased when they seeded onto the A-collagen/chitosan scaffolds compared with chitosan only scaffolds. The volume of mineralized tissue was also markedly increased in the calvarial defect region when transplanted with A-collagen/chitosan compared with chitosan only scaffolds. Histological results also showed more new bone forming beneath the A-collagen/chitosan scaffolds, which was consistent with that of micro CT analysis.

Conclusion A-collagen/chitosan scaffolds showed promising reparative effect in rat critical-sized calvarial defect models

干扰NRF2的表达能促进骨髓间充质干细胞向胰岛素分泌细胞分化

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摘要：骨髓间充质干细胞（bmMSCs）来源于骨髓组织，由于其低免疫原性以及多向分化潜能，近年来受到广泛的关注。有研究显示，bmMSCs过表达胰岛β细胞相关转录因子能够实现其向胰岛素分泌细胞分化。为了发掘新的参与胰岛素分泌的转录调控因子，本研究中我们使用DNA亲和沉淀结合液相色谱-质谱技术（LC-MS）鉴定了转录因子：NRF2，其可以特异性结合到胰岛素启动子区，负调控启动子的活性。通过干扰bmMSCs中NRF2表达，能够重新编程bmMSCs为胰岛素分泌细胞。分化的细胞表达胰岛的内分泌细胞特异性标志物，如INS1，INS2，Pdx1，ISL-1，GLUT2和Pax6。诱导的细胞能够响应葡萄糖刺激释放C-肽和胰岛素，双硫腺染色阳性。动物实验显示，能提升糖尿病鼠体内胰岛水平，降低血糖。因此通过干扰bmMSCs中NRF2的表达，同时过表达MafA，能促进其向胰岛素分泌细胞分化，用于对I型糖尿病（T1D）的干细胞治疗。

外周血来源EPC与MSC的共培养及其复合掺锶聚磷酸钙构建血管化工程骨

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摘要：血管化骨再生的细胞共培养研究策略为组织工程骨再生的基础研究和临床应用提供了非常多的机遇和挑战。本研究旨在结合微创及能实现自体移植的目标在动员、分离外周血间充质干细胞(mesenchymal stem cells, MSC)和内皮祖细胞(endothelial progenitor cells, EPC)的基础上，构建外周血来源EPC与MSC二维共培养体系，并复合掺锶聚磷酸钙(strontium-doped calcium polyphosphate, SCPP)构建三维血管化工程骨为骨再生的进一步的临床应用提供参考。通过建立外

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周血EPC与MSC的单层二维共培养体系研究两种类型细胞的相互关系。不同配比的混合细胞在常规平面二维共培养1周,检测其成骨及成血管标志。通过CMTMR红色荧光探针和CFSE绿色荧光探针分别标记两种细胞,以不同的比例通过二次沉淀接种法将其种植于SCPP和CPP支架材料上构建血管化工程骨,体外培养7d,通过激光共聚焦显微镜观察细胞在支架材料上的生长,分别通过ELISA和ALP活性检测VEGF和ALP的表达。外周血EPC与MSC的单层二维共培养体系中,随着MSC细胞数量的增多和EPC的减少,长梭形细长的成纤维细胞样逐渐增多而圆形较且扁平的内皮细胞样细胞逐渐减少,且MSC的生长速度较EPC快。随着EPC比例的增加,CD31阳性表达、管形成的数量及管的长度逐渐增加。75:25 EPC/MSC组早期成骨标志ALP表达最强。且75/25 EPC/MSC组成骨特异基因Runx2, Col-I 和 OCN显著增加,随着EPC比例的下降成骨表达逐渐减弱,单纯EPC组成骨表达最弱。对于成血管基因的表达,随着EPC的增加,成管相关基因如CD31、VE-cadherin和VEGFR2的表达逐渐增强。外周血EPC与MSC复合支架材料构建血管化工程骨的研究中,共聚焦显微镜结果显示,培养3d后细胞粘附于支架材料上,大部分细胞尚呈圆形,按比例生长。随着细胞-支架复合物体外培养时间的延长至培养7d时,可见支架材料上细胞数量增多且长入支架材料内部,细胞形状沿支架材料生长伸展,SCPP支架组的细胞较CPP组贴附的更好。ELISA和ALP活性检测结果显示,随着培养时间的延长,SCPP组和CPP组成骨早期标志ALP和血管化标志VEGF的分泌都逐渐增多,且在3d、7d不同时间点SCPP支架组ALP和VEGF的含量均显著高于CPP支架。外周血EPC与MSC二维共培养体系中,细胞接种比例为75:25时可获得最佳的成骨和成血管效果。外周血EPC与MSC复合SCPP三维支架材料能促进组织工程骨血管化的构建。外周血来源的EPC与MSC因其取材微创及有利于实现自体移植的目标等优点具有非常广阔的临床应用前景。

Long non-coding RNA H19 mediates tenogenic differentiation by acting as a miRNA sponge

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Abstract:

A tendon is a tough band that connects muscle to bone to control bone moving. Tendons are subject to many types of injuries, such as acute tendon rupture and tendinopathy due to overuse. The process of tendon development and pathogenesis of tendinopathy remains largely unknown, which has limited the development of clinical therapy for tendon injuries. Studies on tendon differentiation at molecular level may help to understand tendon development and tendinopathy and to develop novel therapeutic strategies. Non-coding RNAs have attracted multiplying attention in the past decade as crucial regulators of diverse biological processes. In this study, we identified a long non-coding RNA (lncRNA) H19 as a novel modulator of tenogenic differentiation of tendon-

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derived stem cells (TDSCs). H19 was up-regulated by TGF β treatment in TDSCs and its overexpression enhanced the process of TGF β -induced tenogenic differentiation of TDSCs. The H19-overexpressing TDSCs promoted healing process in a mouse tendon injury model. We further investigated the underlying mechanisms in that H19 acted as a miRNA sponge inhibiting the expression of miR-29, a downstream target of TGF β signaling pathway as well as a regulator of type I collagen expression. H19 has a predicted binding site for miR-29 and modulated expression of endogenous miR-29. Collectively, our study demonstrated that H19 promotes tenogenic differentiation both in vitro and in vivo via acting as a miRNA sponge that represses miR-29 expression and the TGF β /H19/miR-29 regulatory network may be an essential pathway in controlling tenogenesis of TDSCs or MSCs.

1代和2代自体软骨细胞移植（ACI）修复大面积软骨损伤的临床效果比较研究

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摘要：【目的】探讨1代和2代自体软骨细胞移植（ACI）修复关节软骨缺损的疗效比较。【方法】选择 34 例临床确诊为膝关节大面积软骨损伤患者，随机分配于1代ACI组和2代ACI组，首次术中关节镜下取200ug软骨组织，在体外细胞增殖后于二次手术植入局部缺损区域，1代ACI组患者取自体胫骨前方取骨膜覆盖缝合于软骨缺损部位并注入软骨细胞；2代ACI组患者取I型胶原膜覆盖缝合于软骨缺损部位并注入软骨细胞。【结果】术后临床病例全部获得随访，平均随访9.4月（6月~17月），所有患者症状消失，恢复日常生活和运动，核磁共振或关节镜复查见软骨缺损已修复。1代ACI组患者的Lysholm评分从术前 48.9 \pm 5.7增加到 91.2 \pm 4.8, IKDC评分从术前52.1 \pm 6.3增加到90.3 \pm 3.9, 术后评分与术前比较均有显著性差异（ $P < 0.001$ ）；2代ACI组患者的Lysholm评分从术前 47.3 \pm 5.7增加到 90.1 \pm 4.6, IKDC评分从术前50.2 \pm 5.8增加到93.6 \pm 4.4, 术后评分与术前比较均有显著性差异（ $P < 0.001$ ），两组相关评分对比分析，差异无统计学意义（ $P > 0.01$ ）。【结论】1代和2代ACI自体软骨细胞移植均可修复关节软骨缺损，临床效果无差异，有良好的应用前景。

深度压疮手术后复发的医源性因素与修复方法

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摘要：目的探讨深度压疮手术后复发的医源性因素和修复方法。方法总结42例深度压疮手术后复发病例的临床资料，分析深度压疮手术后复发的医源性因素、治疗方法及注意事项。结果深度压疮手术后复发可以分为近期复发（半年内）和远期复发（半年后）。其中近期复发以医源性因素为主，包括手术扩创不彻底、骨性突起处理不到位、皮瓣血液循环不良、皮瓣或创口存在张力、创腔内存留异物或血肿、创腔引流不充分等众多因素。远期复发以其他因素为主，但也应该引起医生的足够重视，例如病人的自身因素（全身状况差、合并症情况等）、看护因素（再次压迫、感染等）。结论深度压疮手术后复发是临床上常见的难题，其中近期复发者以医源性因素为主，认真分析复发原

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因并指导进行再次手术是预防再次复发、保障治疗效果的主要途径。

The effect of BuShenHuoXueTang on MSCs migration ability and expression of CXCR4 during the fracture repairment

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Abstract:

The purpose of this study is to explore the effect of BuShenHuoXueTang on MSCs migration ability and expression of CXCR4 during the fracture repairment. The rat femur fracture model was conducted and treated with BuShenHuoXueTang. Then the MSCs of the fracture site was isolated and cultured at 7thday, 14thday and 21st day, respectively. Transwell assay was applied to examine the migration of 3rd passage MSCs. Chemokine receptors CXCR4 were tested by Western Blot and QPCR in protein and mRNA expression. The results of Transwell assay revealed that BuShenHuoXueTang could promote migration of MSCs significantly at 7th, 14th day, compared with the model group and control group. After the 21st day, the migration of MSCs in the fracture site become weak gradually, compared with the model group were insignificantly different, but have no statistical significance, compared with the model group. The results of Western Blot and QPCR revealed that the expression of protein and mRNA of CXCR4 in fracture site are significantly up leveled at 7th, 14th day, compared with the model group and control group were significantly different, with statistical significance. BuShenHuoXueTang could promote the migration of MSCs, and its mechanism could be related to the chemokine receptor CXCR4 up-regulation during the fracture repairment.

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补肾活血汤联合骨髓间充质干细胞静脉移植对骨折模型大鼠成骨分化的影响

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摘要: 目的 探讨补肾活血汤（简称BS）联合骨髓间充质干细胞（bone Mesenchymal Stem Cells, BMSCs）静脉移植对骨折模型大鼠不同时相成骨分化的影响。方法 ELISA法观察骨折模型大鼠运用补肾活血汤联合BMSCs静脉移植治疗后第3、7、14天血清碱性磷酸酶（alkaline phosphatase,ALP）活性，蛋白免疫印迹法（Western Blot）检测骨折断端Runx2相关转录因子2(Runt-related transcription factor 2, Runx2)蛋白表达。结果 所有骨折模型大鼠血清ALP含量在治疗后第3天、7天、14天均低于空白组；治疗第14天，BMSCs移植联合高、中剂量BS组血清ALP虽然升高，与模型组相比有统计学意义（ $P < 0.05$ ），但仍低于空白组；治疗后第3天、7天、14天，不同剂量BS联合BMSCs移植均能促进骨折断端Runx2蛋白的表达，与模型组及空白组比较，具有统计学意义

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($P < 0.05$)；模型组与空白组比较，也具有统计学意义 ($P < 0.05$)。结论 补肾活血汤联合BMSCs静脉移植能促进骨折模型大鼠愈合过程中不同时相成骨分化，其机制可能与其提高ALP活性，促进骨折端Runx2蛋白表达有关。

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干扰NRF2的表达能促进骨髓间充质干细胞向胰岛素分泌细胞分化

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摘要: 骨髓间充质干细胞 (bmMSCs) 来源于骨髓组织, 由于其低免疫原性以及多向分化潜能, 近年来受到广泛的关注。有研究显示, bmMSCs过表达胰岛 β 细胞相关转录因子能实现其向胰岛素分泌细胞分化。为了发掘新的参与胰岛素分泌的转录调控因子, 本研究中我们使用DNA亲和沉淀结合液相色谱 - 质谱技术 (LC-MS) 鉴定了转录因子: NRF2, 其可以特异性结合到胰岛素启动子区, 负调控启动子的活性。通过干扰bmMSCs中NRF2表达, 能够重新编程bmMSCs为胰岛素分泌细胞。分化的细胞表达胰岛的内分泌细胞特异性标志物, 如INS1, INS2, Pdx1, ISL-1, GLUT2和Pax6。诱导的细胞能够响应葡萄糖刺激释放C-肽和胰岛素, 双硫腺染色阳性。动物实验显示, 能提升糖尿病鼠体内胰岛水平, 降低血糖。因此通过干扰bmMSCs中NRF2的表达, 同时过表达MafA, 能促进其向胰岛素分泌细胞分化, 用于对 I 型糖尿病 (T1D) 的干细胞治疗。

MiR-136 modulates TGF- β 1-induced proliferation arrest by targeting PPP2R2A in keratinocytes

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Abstract:

Keratinocytes proliferation is critical for the capacity to heal wounds and accumulating evidences have proved that dysregulation of microRNAs is involved in proliferation of keratinocytes. However, the molecular mechanisms remain to be completely elucidated. Here, we show that miR-136 was significantly decreased by TGF- β 1 treatment in HaCaT cells and Normal Human Epidermal Keratinocytes (NHEK). By cell proliferation assay and cell cycle analysis, we found that re-introduction of miR-136 by transfection, as well as PPP2R2A silencing counteracted TGF- β -induced proliferation arrest in HaCaT cells. Further, PPP2R2A was verified as a direct target of miR-136 by Western blotting and Dual-luciferase reporter assays. These data suggest that miR-136 may play an important role during TGF- β 1-induced proliferation arrest by targeting PPP2R2A in keratinocytes, which might represent a potential target for improving skin wound healing.

In vitro toxicity of PEI-coated Fe₃O₄ nanoparticles in HaCaT cells

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Abstract:

Fe₃O₄ based nanoparticles are widely used in biomedical applications, including magnetic resonance imaging, drug delivery, and hyperthermia. However, their properties conducive to clinic use may potentially induce toxicity. Therefore, the purpose of this study was to investigate the cytotoxicity of PEI-coated Fe₃O₄ nanoparticles on HaCaT immortalized human keratinocyte cells. Nanoparticles were characterized by transmission electron microscopy. Then HaCaT cells were incubated with the nanoparticles at 0, 2, 20 or 200 ng/ml for 24 h, multiple assays had been adopted to analyze the cell toxicity subsequently, including Prussian blue staining, CCK-8 assay, cell cycle analysis and LDH release assay. In the results, the PEI-coated Fe₃O₄ nanoparticles were almost uniform and their size was 12 ± 7 nm. The nanoparticles at more than 2 ng/ml were sufficient for labeling HaCaT cells and cellular uptake was dose-dependent. The results showed that when the HaCaT cells were incubated with over 20 ng/ml PEI-coated Fe₃O₄ nanoparticles, the cell viabilities showed a significant reduction, the cell population in S phase decreased and the nanoparticles induced significant LDH release. Moreover, these manners were dose-dependent. In summary, exposure to PEI-coated Fe₃O₄ nanoparticles at above 20 ng/ml resulted in a dose-dependent cytotoxicity in HaCaT cells. Thus, the PEI-coated Fe₃O₄ nanoparticles at proper concentration are suitable for biomedical applications.

Dynamic expression of microRNAs in fetal Keratinocytes contributes to scarless wound healing

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Abstract:

Background

Early- to mid-gestational fetal mammalian skin wounds heal rapidly and without scarring. The main cause is Fibroblasts (FBs) which differ in many respects, such as the ability to migrate, synthesis of collagen and hyaluronic acid. Keratinocytes (KCs) have significant effects on the regulation of FBs. The advantages in early- to mid-gestational fetal KCs could lead to fetal scarless wound healing.

Methods

KCs from six human fetal skin samples were divided into mid- and late-gestational group. RNA extracted from KCs was used for the next-generation sequencing (NGS). The bioinformatical analyses were used to uncover potential novel microRNA (miRNAs) and the targets of miRNAs. The expression levels of the miRNAs were further confirmed by real-time quantitative RT-PCR.

Results

A total of 61.59 million reads were mapped to known human miRNAs. We further uncovered 106 potential novel miRNA candidates which have higher probability of being novel human miRNAs. A total of 110 miRNAs, including 22 novel miRNA candidates, were differently expressed between mid- and late-gestational fetal KCs. Thirty-three differently expressed miRNAs and miR-34 family members are found to be correlated with the transforming growth factor- β (TGF- β) pathway which is the key to cutaneous scarless wound healing.

Conclusions

Our results provide compelling evidence supporting the existence of 106 novel miRNAs and the dynamic expression of miRNAs that extensively targets the TGF- β pathway at different gestational ages in fetal KCs. MiRNAs showing altered expression may contribute to scarless wound healing in early- to mid-gestational fetal KCs, and thus be new targets for scar therapies.

MR-378b Promotes Differentiation of Keratinocytes through NKX3.1.

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Abstract:

MicroRNA (miRNA) is a kind of short non-coding RNA, involved in various cellular processes. During keratinocyte differentiation, miRNAs act as important regulators. In this study, we demonstrated by microarray assay that the expression of miR-378b significantly increased during keratinocytes differentiation. Our findings showed that miR-378b could inhibit proliferation, migration and differentiation in keratinocytes. Luciferase reporter assays showed that miR-378b directly target NKX3.1. Silencing of NKX3.1 could coincide with the effects of miR-24 overexpression. In conclusion, our results demonstrate miR-378b promote keratinocytes differentiation by targeting NKX3.1. Manipulation of miR-378b may afford a new strategy to clinic treatment of skin injury and repair.

MicroRNA-149对皮肤无瘢痕愈合作用机制的研究

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摘要: 目的探讨microRNA-149对无瘢痕愈合的作用, 为microRNA作为一种新型治疗手段应用于临床创伤修复提供科学理论基础。方法通过高通量测序得到在人胚胎早中期(28周前)和晚期(28周后)microRNA-149显著差异表达, 并通过qRT-PCR的方法对胚胎早中期和晚期的皮肤样本进行验证。并且通过双荧光素酶报告基因的方法验证microRNA-149的靶基因。将microRNA-149的模拟物瞬时转染人永生化表皮细胞系(HaCaT), 观察其对HaCaT的生物学作用。以及通过与人真皮成纤维细胞共培养检测其对成纤维细胞增殖、迁移以及无瘢痕愈合相关基因的表达的情况。结果人胚胎早中期的皮肤样本中microRNA-149的表达为晚期的1.8倍($p < 0.05$), 并且qRT-PCR验证此结果。将

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microRNA-149与含有IL-6 3'UTR的重组质粒报告载体共转染HaCaT, microRNA-149可以下调IL-6的表达。转染microRNA-149模拟物的HaCaT通过与人真皮成纤维细胞共培养后, 划痕实验证实转染模拟物组可以促进成纤维细胞迁移; 同时, qRT-PCR检测到共培养后成纤维细胞中促进皮肤无瘢痕愈合的TGF β -3和Collagen3表达量升高约1.5倍 ($p < 0.05$)。结论microRNA-149可以通过调控其靶基因白介素-6的表达, 而调控成纤维细胞无瘢痕愈合相关因子TGF β -1, TGF β -3, Collagen1和Collagen3的表达, 从而参与皮肤创伤愈合的过程。

人羊膜间充质干细胞促进皮肤创伤愈合的机制研究

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摘要: 目的: 探讨hAMSC促进皮肤创伤愈合的机制。方法: 体外培养hAMSC, PEI-SPIO标记后皮内移植小鼠皮肤创伤模型并于移植后3,7, 10天进行创面观察、组织学检查创面愈合情况。通过transwell将hAMSC与hFB共培养, 检测hFB增殖, 迁移, 生长因子VEGF, bFGF的分泌, 探讨hAMSC促进创面愈合机制。结果: 创伤后3d起移植组创面逐渐缩小 ($P < 0.05$), 组织学检查移植组重上皮化明显。体外实验各组的hFB增殖均无显著性差异, hAMSC共培养组hFB迁移, 生长因子分泌明显优于对照组 ($P < 0.05$)。结论: hAMSC能促进小鼠皮肤创伤愈合, 其机制是通过旁分泌作用促进hFB生长因子VEGF, bFGF的分泌从而促进其迁移。

脂肪间充质干细胞联合普罗布考对糖尿病小鼠皮肤创伤愈合的作用

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摘要: 目的: 探讨脂肪间充质干细胞 (Adipose mesenchymal stem cells, ADSCs) 联合普罗布考对糖尿病小鼠皮肤创伤愈合的作用。方法: 建立糖尿病小鼠皮肤创伤模型并随机分为 4组: ① ADSCs移植组; ②ADSCs移植组联合普罗布考组糖尿病小鼠ADSCs移植组; ③普罗布考组; ④空白对照组。分别以皮内注射方式将3代ADSCs的细胞混悬液移植到小鼠创面四周, 空白对照组注射生理盐水, 于伤后14d观察创面愈合情况; 通过western blot检测伤后14d创面组织Bcl-2和血管内皮生长因子 (VEGF) 蛋白表达; 通过试剂盒检测伤后14d创面组织ROS含量。结果: 与ADSCs移植组相比, 联合组创伤后14d伤口的愈合率均明显提高, ($P > 0.05$), 联合组创伤后14d伤口创面组织Bcl-2和VEGF表达水平明显提高, ($P > 0.05$), 联合组创伤后14d伤口创面组织ROS水平明显降低, ($P > 0.05$)。结论: 普罗布考联合脂肪间充质干细胞移植能明显改善糖尿病小鼠皮肤创面的氧化应激和生长因子含量, 从而更能促进创面愈合。

Tendon-derived Stem Cells Undergo Spontaneous Tenogenic Differentiation.

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Abstract:

Tendon-derived stem cell (TDSC) is a subpopulation of residing stem cells within the intact tendon tissues, with the capacities of self-renewal, clonogenicity, and three-lineage differentiation. Compared with bone marrow derived mesenchymal stem cells (BMSCs), TDSCs are superior for tendon injuries repair as they remain some tendon tissue-specific differentiation properties. In the present study, TDSC was found to undergo spontaneous tenogenic differentiation in which the expression of tenogenic markers were increased while the expression of stemness markers decreased with time in TDSCs culture (without tenogenic induction medium). After a longer period of culture, the monolayer of TDSCs formed a "3D" layers with rich extracellular matrices of typical tendon tissues. In addition, the key tenogenic transcription factors, such as Scx, Mlx, Egr1 and Eya1 were all up-regulated in this process. Finally, we compared the spontaneous tenogenic differentiation with TGF- β 1-induced tenogenic differentiation of TDSCs, and the results showed that the spontaneous tenogenic differentiation of TDSCs was general character of TDSCs, similar to but weaker than the effect of TDSCs under tenogenic induction. Taken together, the present study identified that TDSCs had the potential of spontaneous tenogenic differentiation, which may be a better cell source for the treatment of tendon injury.

骨搬移治疗下肢慢性缺血性疾病的基础及临床研究

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摘要:

目的:

在动物身上模拟人体下肢慢性缺血性疾病, 研究骨横向搬移技术治疗下肢慢性缺血性疾病的相关原理。为骨横向搬移技术在临床上的应用给予理论指导。研究骨搬移技术在临床上的治疗效果。

方法:

18只实验用杂种犬(雌雄不限, 体重15-18kg), 随机分为A、B、C三组, 每组各6只。A组犬作为正常对照组, 不做干预处理。B组和C组实验动物左、右两侧后肢均采用腹股沟区沿股动脉走行方向手术切口, 股动脉及其主要分支双重结扎、切断的方法制作肢体缺血模型。B组所有犬右后肢(BR)不做其它处理, 左后肢(BL)实施胫骨横向搬移手术, 安装横向骨搬移外固定架并以1mm/d(分2次)的速度进行横向搬移; C组所有犬右后肢(CR)不做其它处理, 左后肢(CL)实施同B组相同操作的骨搬移手术, 但不上外固定架, 不进行骨横向搬移。定期利用激光散斑血流监测视频系统检测肢体远端皮肤组织血液灌注量。分期取肢体远端趾长伸肌肌肉组织行组织学检查, 定期行骨X线检查。总结临床病例, 分析临床治疗效果。

结果:

单纯的行骨搬移手术, 不进行骨横向搬移, 与缺血组比较, 无论是皮温还是血液灌注量, 均无明显差异。接受了骨横向搬移治疗的缺血肢体与单纯的缺血肢体相比较, 皮温的升高和血液灌注量

的升高经过统计学分析都是有显著差异的。经过骨搬移治疗的患者，远端溃疡创面愈合速度明显增快，远期效果满意。

结论：

股动脉及其分支的结扎法，可以作为慢性下肢缺血性疾病模型的制作方法。骨横向搬移不仅能够促进局部骨以及软组织的再生，对于改善远端组织的血液循环也是有效的。单纯的骨瓣切开法对于改善远端血运是无效的。骨横向搬移法适用于下肢慢性缺血性疾病的治疗。临床应用胫骨骨横向搬移法治疗糖尿病足157例，获得了良好的临床效果，71.5%的患者静息痛消失，11%的患者静息痛减轻，17.5%的患者静息痛无变化。85%的患者下肢远端血运都有不同程度的改善，15%的患者血供无变化。

蛆虫疗法修复严重感染创面的应用体会

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目的 探讨蛆虫疗法用于修复严重感染创面的应用体会。方法 采用丝光绿蝇蝇卵灭菌和幼虫（3天龄）消毒两种方法进行处理，证实幼虫体表及体内无细菌病毒生长且幼虫的活力存在。将消毒灭菌的蛆虫50~100只放入创面，无菌盐水敷料覆盖，外罩尼龙网，隔日更换蛆虫及敷料一次。结果 1999年至2014年，我们将蛆虫疗法用于修复严重感染创面的患者400例，平均治疗7天，所有创面坏死组织均清除干净，有大量新鲜的肉芽组织生长，创面表面培养无细菌生长，创面经皮片植皮后痊愈，效果满意。结论 蛆虫疗法是一种修复严重感染创面安全有效的生物扩创疗法。

交通图示

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