国家科技计划项目汇交科技资源及成果信息（人口健康领域）

研究与实验报告:

【中文名称】听神经病的临床遗传机制研究
【英文名称】Clinical Genetic Mechanisms for Auditory Neuropathy
【研究起始时间】2005-03
【研究终止时间】2008-12
【中文关键词】听神经病; 候选基因法; 突变筛查; OTOF基因; GJB1基因;
【英文关键词】Auditory neuropathy; Candidate approach; Mutation screening; OTOF; GJB1;
【中文摘要】从上个世纪80年代开始,国内外临床听力学家、听觉生理学家、耳鼻咽喉科临床医生以及分子遗传学家们开始关注一种具有独特临床表现特征的听力疾病--听神经病。听神经病(Auditory neuropathy,AN)是一种表现为声音可以通过外耳、中耳正常的进入到内耳但是声音信号不能同步地从内耳传输到大脑的听功能异常性疾病,具体主要表现为诱发性耳声发射(Evokedotoacoustic emission,EOAE)正常、听性脑干反应(Auditory brainstem response,ABR)严重异常的一组听功能障碍症候群。 听神经病的病因至今尚未明确,迄今报道的病因有遗传、免疫、感染、中毒、代谢等。近年来关于听神经病致病基因学的研究引起越来越多的关注。应用分子遗传学研究手段对散发及家系神经病患者进行致病基因学研究,已成为目前国内外耳科领域研究的新的热点之一,对进一步了解和探讨听神经病致病因素具有重要的意义。 本研究以我院耳鼻咽喉科门诊及耳鼻咽喉研究所遗传资源收集网络收集到的听神经病的散发及家系病人为研究对象,对其临床听力学特征与遗传学特征进行分析,并进行了候选基因的突变筛查,以进一步了解听
【英文摘要】暂不公布

【中文名称】非综合征型遗传性听力损失家系致病基因定位克隆研究
【英文名称】 Mapping and Positional Cloning the Causative Genes in Chinese Pedigrees with Non-syndromic Hereditary Hearing Impairment
【研究起始时间】2006-03
【研究终止时间】2009-04
【中文关键词】遗传; 耳聋; 听力损失; 常染色体显性遗传; 定位克隆; 候选基因法; 连锁分析; 模块化方法; 突变筛查;
【英文关键词】Genetic; Deafness; Hearing loss; autosomal dominant; mapping; cloning; linkage analysis; modularization mutation;
【中文摘要】致聋基因的定位与克隆一直是全球遗传学和耳鼻喉科学学者共同致力研究的焦点。从1988年,第一个非综合征型耳聋基因位点被确定,截止至2008年5月,非综合征型遗传性耳聋的研究取得了巨大的成就,共定位了144个基因座位,克隆了49个基因。从1995年,第一个非综合征型耳聋基因被克隆,到2006年,耳聋基因的定位与克隆一直保持高速增长,平均每年定位8.3个位点,克隆4个基因。在这其中也包含了中国学者大量深入、细致的工作。早在1998年,夏家辉院士就克隆了GJB3基因——DFNA2基因座位的责任基因之一。到目前,中国学者共报告了13个基因座位(13/144,占9%),其中7个与国外报道的耳聋基因座位重合,6个是新的耳聋基因座位(6/144,4.2%)。遗传性耳聋基因的定位与克隆研究前景非常可观,有近2/3的基因座还没有找到责任基因,还有更多的新的耳聋基因等待着人们去发现。然而机遇与挑战并存,从2007年开始,遗传性耳聋的研究工作遭遇瓶颈,耳聋基因定位与克隆的速度明显减缓,成功定位和克隆的耳聋基因的数量逐年减少,2007-2008两年间只发现了4个耳聋基因新座位,克隆了2个新耳聋基因。为探索打破瓶
【英文摘要】The mapping and cloning of deafness genes is a hot focus that geneticists and otolaryngologists.The great progress of the research on hereditary non-syndromic deafness has been made since the first non-syndromic deafness locus was mapped in 1988.Until May 2008,144 loci are located,from which and 49 genes are cloned.The mapping and cloning on of deafness genes grew rapidly since the first gene of non-syndromic deafness was cloned in 1995.On average, 8.3 loci and 4 genes were identified every year,from 1995 t...

【中文名称】纳米铁协载阿霉素加用体外磁场增强抗肿瘤效果
【英文名称】Magnetic Nanocarrier of Doxorubicin with Simple External Magnetic Fields Enhances Antitumor Activity
【研究起始时间】2008-03
【研究终止时间】2010-09
【中文关键词】磁性纳米颗粒，抗肿瘤活性，体外磁场，PLGA
【英文关键词】Magnetic nanoparticles, anti-tumor activity, external magnetic fields, PLGA

【中文摘要】纳米铁经PLGA包裹阿霉素药物（Fe3O4-PLGA-Dox）在体外可增强对肿瘤细胞的凋亡作用，在体内，经瘤内注射，Fe3O4-PLGA-Dox增强了杀伤肿瘤作用，高于单用阿霉素，在加用体外磁场时进一步增强了杀伤作用，具有显著性差异，同时，在体外磁场作用下铁盐未在体内任何器官存留，对各脏器均无毒副作用。

【英文摘要】Drug delivery , selectively penetration and accumulate into neoplastic cells are critical for the effectiveness of chemotherapy for solid tumors. We incorporated Magnetic nanoparticles(MNPs) Fe3O4 and doxorubicin (Dox) into poly-lactic acid/glycolic acid (PLGA) to form a micelle-encapsulated Fe3O4 and Dox complex (Fe3O4-PLGA-Dox). In vitro, Fe3O4-PLGA-Dox increased the apoptosis of mouse Lewis lung cancer (LLC) cells . In vivo, 60 BALB/C mice bearing LLC cell tumors were treated by Fe3O4-PLGA-Dox with or without external magnetic fields. The mice treated by Fe3O4-PLGA-Dox with external magnetic field displayed significant reductions in tumor volume and metastases incidence and prolonged survival rate compared with free doxorubicin or Fe3O4-PLGA-Dox without external magnetic fields. No detectable lesions in heart, lung, liver and kidney in mice treated by Fe3O4-PLGA-Dox with external magnetic field. In contrast, the iron oxide was deposited in tubules of kidney in a few mice which was not applied external Magnetic Fields. This targeted drug delivery modality may provide a new strategy for the design of cancer therapies.

【中文名称】老年性聋治疗的疗效评价系统的研究

【英文名称】Evaluation of Diagnosis of Presbyacusis

【研究起始时间】2006-12

【研究终止时间】2010-12

【中文关键词】老年性聋、治疗、评价

【英文关键词】presbycusis、diagnosis、evaluation

【中文摘要】老年性聋是老年人口中常见的疾病现象，据世界卫生组织估计，全球约有2.5亿人患有重度以上的听力损失，其中2/3在发展中国家。特别是随着当前社会经济形势的高速发展，占世界人口总数1/5的我国正在迅速地进入老龄化社会，因此，深入研究老年性聋的治疗显得比以往任何时候都要迫切。对老年性聋应当实施配助听器，一些药物如维生素、微量元素、血管扩张剂对老年性聋的治疗无确切效果。针对这种现状，我科就治疗方法进行2×2析因设计的临床实验研究。旨在对临床常用的治疗方法进行疗效评价，以提出更科学的治疗方法。另外，围绕老年性耳聋的主题，我们相继研究了相关的领域。1.人工耳蜗植入患者电诱发听神经复合动作电位（ECAP）的阈值及其临床意义2.应用三维建模方法定量分析C57BL/6J小鼠耳蜗内毛细胞带状突触的数量。3耳蜗内毛细胞突触对氨基糖苷类药物毒性的反应特性。以上相关研究旨在通过研究过程及生成的相关数据能够更加深入的了解老年性耳聋并且为老年性耳聋治疗的疗效评价提供科学依据。

【英文摘要】Presbycusis is....

【中文名称】胚胎干细胞在药物损伤的大鼠内耳的迁移和分化

【英文名称】7.　Migration and differentiation of mouse embryonic stem cells transplanted into mature rat cochlea with aminoglycoside-induced hearing loss.

【研究起始时间】2008-03

【研究终止时间】2009-07

【中文关键词】胚胎干细胞; 毛细胞; 耳聋; 移植

【英文关键词】embryonic stem cells; hair cell; hearing loss; transplantation

【中文摘要】各种原因造成的人类和哺乳动物的内耳毛细胞一旦受损丢失就无法再生，从而造成永久性感音神经性耳聋。理论上讲胚胎干细胞具有特定环境中分化为任何组织和细胞的特性，因此，利用胚胎干细胞替代损失的内耳毛细胞具有很大潜力。我们实验目的是探讨胚胎干细胞在受损的哺乳动物内耳能否替代丢失的毛细胞。将胚胎干细胞通过鼓阶底转转打孔途径植入正常和氨基糖苷类抗生素作用的大鼠内耳，结果发现在胚胎干细胞可以在毛细胞损伤的内耳存活并且从鼓阶迁移至中阶和前庭，并且可以表达毛细胞标记物。毛细胞损失的模型中胚胎干细胞更易迁移至损伤的部位并向毛细胞分化。

【英文摘要】Sensory neural hearing loss in human is currently incurable because the hair cell that transduces acoustic signals into electrical responses is unable to regenerate. Stem cell transplantation is one of the strategies that may have the potential to replace the lost hair cells to restore hearing. We explored the possibility of transplanting EGFP-expressing wood mouse embryonic stem cells into the cochlear scala tympani of rats with and without amikacin sulfate-induced hearing loss. Results showed that the stem cells transplanted in the amikacin sulfate-damaged cochlea could survive in the microenvironment of the cochlea and migrate into the scala media and the vestibular cisterna. They were also able to differentiate into hair-cell-like cells and supporting cells in the organ of Corti in

two weeks. For the first time, the grafted stem cells were noticed to form the cellular structure resemble to that of the Organ of Corti. These results suggest that embryonic stem cells are able to migrate to the site where hair cells were injured and may have the potential to treat hearing loss caused by hair cell damage.

【中文名称】Fgf19对耳蜗毛细胞发育调控机制的研究
【英文名称】Developmental regulation of Fgf19 gene on cochlear hair cell
【研究起始时间】2008-09
【研究终止时间】2010-11
【中文关键词】毛细胞分化；调控机制
【英文关键词】RNAi（RNA interference）；Fgf19 (Fibroblast growth factors 19)；Bmp4 (bone morphogenetic protein 4)
【中文摘要】目的:研究 Fgf19、Bmp4.在耳蜗毛细胞发育调控中的作用,为基因导入或/和干细胞导入诱导耳蜗毛细胞再生治疗感音性耳聋提供理论基础。方法: 首先比较选择鸡胚背景染料、摸索最佳条件，内耳发育过程标本连续切片，了解正常形态特点，采用离体培养与活体基因干扰（RNAi）与过表达来研究耳蜗毛细胞发育区内依次出现的Fgf19、Bmp4与毛细胞发育的关系. 结果：目前完成背景染料选择、部分连续切片，正常耳囊离体培养，基因干扰（RNAi）病毒载体制备与活体注射条件的摸索. 结论 国产鸵鸟墨水作为鸡胚背景染料效果好，部分连续切片显示耳蜗形态发育过程特点，正常耳囊离体培养可存活7-10天，病毒载体活体注射后，胚胎存活率下降，Fgf19、Bmp4.在耳蜗毛细胞发育调控中的作用正待展开实质性工作。
【英文摘要】To investigate the developmental regulation of FGF-19 gene on cochlear hair cell

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【中文名称】超声引导经皮微波消融治疗机器人系统的研发和实验研究
【英文名称】Development and empirical study of robotic system for ultrasound-guided percutaneous microwave ablation
【研究起始时间】2006-04
【研究终止时间】2008-03
【中文关键词】机器人；消融；微波；超声引导；定位
【英文关键词】robotic; ablation; microwave; ultrasound-guided; localization
【中文摘要】近十年来的大量研究结果表明超声引导经皮微波消融治疗肝肿瘤是一项微创、安全、有效的治疗方法，为进一步推进该技术的规范化应用，使之建立在更加客观和可预见性的基础上，便于该技术的普及应用，需解决治疗前的科学规划、治疗中的准确定位、稳定穿刺及对治疗过程的量化评估等问题。我们试图通过研制机器人辅助治疗系统来解决相应的问题。机器人辅助治疗系统是一种计算机集成治疗系统。治疗前机器人辅助治疗系统将患者的影像资料及其它信息建立为个体化的模型，辅助医生在此模型上制定最优的治疗方案；治疗中系统将治疗前的数据与治疗时的患者实体及治疗器械匹配到同一个空间中，然后通过影像导航和机器人辅助医生精确地完成治疗方案；治疗后系统还可以对治疗过程中的各项数据进行进一步的分析处理，用以科学的量化评估治疗及系统规划模型自身的不断完善。从治疗技术及需求方面而言，超声引导经皮微波消融治疗适合应用机器人辅助治疗系统，通过科学规划、实时导航和监视、精确植入等一系列方法使该治疗更加科学、可控和规范。我们相信通过机器人辅助治疗系统可以极大的提高超声引导下微波消融治疗的准确性、有效性和安全性。目前国内外尚无商品化的可以应用于超声引导
【英文摘要】Ultrasound-guided percutaneous microwave ablation is an ideal setting to make use of robotic system. Improved real-time guidance for planning, delivering, and monitoring the ablative therapy would provide the missing tool needed to allow accurate and effective application of this promising therapy. It is believed that robotic system can ultimately make these procedures significantly more accurate, more effective and safer. Currently, no commercial Robotic system is applied in ultrasound-guided ablation therapy. Such systems only exist in the academic domain. So build a full robotic system would be of significant benefit to the broad community of scientists, engineers and doctors who develop these systems and use them to improve patients ’ lives.In this dissertation we first present the underlying theory for the robotic system. This theoretical foundation provides the ability to fully specify the technologies required for the system. Building on this foundation, we design a robotic system for ultrasound-guided percutaneous microwave ablation. And then we make some initial experiments using phantoms to verify and determine the accuracy of the system. A whole work-flow of the robotic system for ultrasound-guided percutaneous microwave ablation was completed and a passive robot was designed and a series of empirical studies were made in this study. This project demonstrates that the efficacy of ultrasound-guided percutaneous microwave ablation could be enhanced with the use of robotic system and this technique may become a stable and precise method of operation for clinical therapy.

【中文名称】基于超声影像导航的肝癌消融机器人系统精度研究
【英文名称】Research on the System Accuracy of the Ultrasound-guided Robot for Liver Cancer Coagulation Therapy
【研究起始时间】2006-03
【研究终止时间】2007-07
【中文关键词】误差传递模型；三维超声；血管配准；标定；定位精度
【英文关键词】 error propagation model; three-dimension ultrasound; vessel registration; calibration; position accuracy
【中文摘要】系统定位精度是基于超声影像导航的肝癌消融机器人系统最重要的指标之一，它是由众多因素引起的。为了分析影响系统定位精度的主要因素，本文首先建立了系统的误差传递模型。在此基础上，对其中的关键技术进行了研究，对产生误差的主要环节进行了标定。最后，对系统的整体定位精度进行了测试和验证。因此，本论文的主要目标是建立系统误差传递模型和提出提高系统精度的方法，论文完成的主要工作有：(1)分析了影响机器人系统定位精度的因素，依据手术流程和空间坐标变换将众多因素分为两大类：第一类为引起靶点映射误差的因素，第二类是引起机器人定位误差的因素。其中第一类误差因素还可以分为引起三维重建误差的因素，引起图像配准误差的因素和引起定位装置和机器人坐标变换误差的因素。运用概率统计模型和李群运动理论，建立了系统误差传递公式，系统误差的协方差矩阵是上述两类误差协方差矩阵之和。(2)分析了基于标志点的配准算法原理，在传统奇异值分解算法基础上，提出利用扩展卡尔曼滤波算法进一步提高配准精度的方法，并对此进行了仿真试验，验证了该算法可以大幅度提高配准精度。(3)分析了FreeHand扫描方式的三维超声重建算法流程，对比了
【英文摘要】System position accuracy is one of the most important specifications of the ultrasound-based robotic system for hepatic cancer. However, system position inaccuracy is caused by many sources. In order to analyze the principal factors impacting the system position accuracy, the error propagation model of the robotic system is deduced at first. Based on the model, the key techniques of the robotic system are studied and the principal parts where the errors arise from are calibrated. At last, the position accuracy of the whole robotic system is tested and verified. So the aim of this dissertation is to establish the error propagation model and to improve the position accuracy of the robotic system. The main contents of this dissertation are described as follow:(1)The factors that cause the position error of the robotic system are analyzed. These factors can be classified into two kinds according to surgery process and coordinate frame.(2)The registration algorithm based on markers is studied. The conventional method is singular value decomposition. The simulation is performed, which proved that the extended kalman filter can greatly improve the registration accuracy.(3)The three-dimension ultrasound reconstruction based on FreeHand scan is analyzed and the reconstruction accuracy of different interpolation algorithms is compared. The experiment results prove that the method described above is effective and accurate.(4) The ‘ N ’ phantom which is easy to manufacture is developed to calibrate the three-dimension ultrasound. The automatic feature extracting algorithm improves the calibration accuracy.

【中文名称】“ 预防性I型糖尿病反义肽疫苗的中试和临床前研究 ”项目研究报告
【英文名称】The pilot and pre-clinical study of Preventive antisense peptide vaccines of type I diabetes
【研究起始时间】2006-12
【研究终止时间】2008-12
【中文关键词】I型糖尿病，反义肽，疫苗
【英文关键词】type I diabetes，antisense peptide ，vaccine
【中文摘要】 本项目建立了I型糖尿病反义肽疫苗细菌发酵系统的技术程序，并使之用于I型糖尿病反义肽疫苗相应的制备生产。争取在项目结束时，具备年产1021pfu纯化I型糖尿病反义肽疫苗产品的生产能力（该因子的有效剂量为1011-1012pfu/人/次）。建立了I型糖尿病反义肽疫苗的纯化技术程序，并使之用于制备生产，争取通过本研究将产物纯化得率稳定保持在85%以上，产品纯度控制在95%。建立了I型糖尿病反义肽疫苗制备生产及产品效力检测的质量控制体系及相应有效的各项技术质量指标。完成了疫苗三批中试产品的制造。
【英文摘要】 This project have set up the program of culturing the bacteria for producing the antisense peptide vaccines of type I diabetes . For the end of the project, it is capable of producing 1021 pfu purification vaccines (the effective dose of the vaccine is 1011-1012 pfu/person/times). And the purification technology of the vaccine have been set up .The Purification yield remained steady at 85% above, and the purity was 95% in the control. The vaccines preparation and the product quality control system was set up ..And three Three batch of finished products of the vaccine have been produced..

【中文名称】三七病害无公害防治技术研究
【英文名称】没有

【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】三七；病害；无公害防治
【英文关键词】没有
【中文摘要】以三七的主要根病和黑斑病为对象，开发新型三七种子种苗微生物和化学处理剂、研发土壤无公害消毒技术和生物防治技术；明确三七黑斑病发生流行与气候因子关系，确定防治关键期；建立以生物防治为主要手段的三七主要根病和黑斑病无公害综合防治技术体系，为促进我国三七中药材产业的可持续发展和保护环境提供技术支撑。
【英文摘要】没有

【中文名称】黄连重要土传病害无害化控制关键技术研究
【英文名称】没有
【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】黄连；土传病害
【英文关键词】没有
【中文摘要】（1) 调查黄连土传病害发生及防治的实际现状；观察病原生物学及病理学特性；并对拟采用的防治方法和技术进行初试选择，以加强防治技术的针对性和有效性。（2) 结合整地、面土、培土、施肥对土壤基质进行无害化消毒处理，研究无害化控制土壤基质中病菌源的技术。（3) 在种子采收、储藏、播种过程中，通过对种子无害化消毒处理，研究控制种子带病菌的技术。（4) 在移栽过程中对秧苗进行无害化消毒处理，研究无害化控制秧苗带病菌的技术。（5）研究生防菌剂对在地黄连成株进行无害化保护的应用技术。（6）在上述单项技术研究的基础上进行技术集成，总结出黄连土传病害的无害化控制技术。
【英文摘要】没有

【中文名称】龙胆的关键病害防治技术研究
【英文名称】没有
【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】龙胆；病害；防治
【英文关键词】没有
【中文摘要】在明确龙胆关键病害发生规律的基础上，从龙胆生产全过程及作物生态系统整体出发，根据龙胆药材叶部病害发生规律及特点，重点围绕龙胆斑枯病的发生关键因子，进行预测预报和防治指标研究，开展病害综合防治技术研究（包括种子带菌检验和处理技术、农业防治技术、无公害化学防治技术、中药抗菌提取物防治病害），构建龙胆中药材地上部病害无公害防治技术体系，整体提升龙胆药材病害的防治水平，提出药用植物叶部病害防治共性技术。
【英文摘要】没有

【中文名称】人参根病生物防治技术研究
【英文名称】没有
【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】人参；根病；生物防治
【英文关键词】没有
【中文摘要】从人参根际筛选对人参根病菌具有明显拮抗活性的微生物，通过对人参根腐病菌的拮抗作用研究，阐明拮抗微生物对人参根腐病的拮抗作用机理。开展根系分泌物对人参致病菌及拮抗微生物的生长的影响研究、拮抗微生物在参地土壤环境的定殖及群体长期保持研究，建立以生物防治为中心的人参根病综合防治措施，并建立相应的技术标准，为中药材根部病害的防治提供共性技术。
【英文摘要】没有

【中文名称】栝楼的种子贮存、栽培生产、商品流通等环节的病虫害防治技术研究
【英文名称】没有

【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】栝楼；病虫害；防治
【英文关键词】没有
【中文摘要】以常用大宗中药瓜蒌、瓜蒌子、瓜蒌皮和天花粉的基原植物——栝楼为对象，全面调查病虫害发生规律和为害特点，根据病虫害发生的特点及难点，重点围绕果实贮藏和流通期间的害虫和田间栽培生产过程中的害虫，开展以生物防治、气调防治和化学农药防治为主的病虫害综合防治技术研究，构建无公害的防治共性技术体系，为整体提升中药材病虫害的防治水平进行示范性的研究。
【英文摘要】没有

【中文名称】玄参重要病虫生物学及无害化治理集成技术研究
【英文名称】没有
【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】玄参；病虫害；生物学特性；防治
【英文关键词】没有
【中文摘要】通过系统调查玄参田间生长期及储藏过程中的病虫害种类，明确蚜虫、红蜘蛛、印度谷螟、白绢病、叶斑病等病虫害对玄参的危害特性；研究对玄参经济学产量和质量有重要影响的1-2种病虫害的生物学特性和发生危害规律；重点开展南方小花蝽或捕食螨的人工繁殖及其控害作用研究、麦蛾茧蜂的人工繁殖及对印度谷螟的控制作用研究；筛选研究能有效控制白绢病等病害的新型生防菌剂；筛选出高效、低毒化学农药及生物制剂；优化、集成玄参主要病虫害的无害化防治技术体系。
【英文摘要】没有

【中文名称】五味子主要病害无公害防治技术体系研究
【英文名称】没有
【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】五味子；病害；无公害防治
【英文关键词】没有
【中文摘要】本子课题以生产上发生危害最重的五味子叶斑病及白粉病、茎基腐病为主要研究对象，兼顾研究其他五味子病虫害，重点达到以下研究目标：明确五味子叶斑病及白粉病、茎基腐病病原种类及其病原生物学特性；探索五味子叶斑病及白粉病、茎基腐病发生流行规律和预测预警技术；明确五味子种苗带菌情况和检测处理技术；探索五味子农药无公害减量使用技术；检测农药残留及对五味子药材质量的影响；形成五味子主要病害无公害配套防治技术体系。
【英文摘要】没有

【中文名称】化橘红重要害虫无害化治理技术研究
【英文名称】没有
【研究起始时间】2006-10
【研究终止时间】2009-10
【中文关键词】化橘红；害虫；无害化治防治
【英文关键词】没有
【中文摘要】以化橘红生产过程中发生危害严重的蛀茎性害虫天牛类、吉丁虫类等为研究对象，通过系统调查和研究，明确化橘红重要害虫生物学特性及发生危害规律，通过应用天敌产品、高效低毒化学农药、农业及物理等无公害综合防治技术研究，安全有效控制化橘红重要害虫的危害，保证化橘红药材的产量及质量。
【英文摘要】没有

【中文名称】人骨髓及脐带间充质干细胞修复与再生汗腺的基础与临床研究
【英文名称】Experimental and clinical researches of repairing and restoration of sweat gland by cultured human bone marrow-/umbilical cord-derived mesenchymal stem cells

【研究起始时间】2009-03
【研究终止时间】2011-06
【中文关键词】汗腺,骨髓,间充质干细胞,再生,脐带
【英文关键词】sweat glands, bone marrow, mesenchymal stem cells, regeneration, umbilical cord
【中文摘要】大面积深度烧、创伤造成的正常皮肤结构和功能的严重毁损会导致皮肤丧失正常的屏障作用及体温调节功能。为了能够修复与重建患者的排汗功能，围绕汗腺再生的各项基础与临床研究逐渐成为当前组织修复与再生研究领域的研究热点。本实验主要由以下三部分内容组成：一、快速分离获取人汗腺细胞方法的建立及其对汗腺细胞生物学特性影响的实验研究。本实验研究中发现：①快速分离法较常规分离法分离、获取汗腺细胞的时间明显缩短，有效提高了汗腺细胞的获取效率；②快速分离获取的汗腺细胞与常规方法分离的汗腺细胞具有相同的抗原表达特性，其抗原表达率之间的差异无统计学意义；③通过与常规汗腺分离法做比较，发现快速分离法对汗腺细胞的各项生物学特性（细胞增殖活性）无明显影响，此方法获取的细胞能够保持其各项生物学特性的稳定性。因此，快速分离法在提高分离、获取汗腺细胞效率的同时，对汗腺细胞的各种生物学特性未产生明显影响，可以为后续的汗腺再生研究中获取丰富汗腺细胞资源提供了可靠的技术支持。二、诱导自体骨髓间充质干细胞（BM-MSCs）在体修复与重建损伤汗腺的多中心临床研究。在汗腺再生的多中心临床研究中，①患者骨髓中可以分离提取得到的B
【英文摘要】The study was composed of three sections as follows:1.Establishment of quick isolation of sweat gland cells(SGCs) in vitro and analysis of its impact on their biological characteristics.①the quick isolation-group could shorten the period of harvesting SGCs;②SGCs isolated in quick isolation-group possessed the similar characteristics as regular group;③SGCs harvested in quick isolation-group could obtain enough SGCs.2.Experimental and multi-center clinical trial of repairing and restoring sweat glands by inducing autologous BM-MSCs into sweat gland like cells.① BM-MSCs could be harvested from human bone marrows, expressed the mesenchymal markers, and possessed the multi-differentiation potential. ②Differentiation of sweat gland-like cells could be obtained from BM-MSCs, which were positive for sweat gland markers. Sweat gland like-BM-MSCs could succeed in repairing and regenerating the damaged sweat glands.③The application of sweat gland like-BM-MSCs in the clinical trials could provided positive effects for repairing and restoring damaged sweat glands.3.Differentiation of sweat gland like-cells from human umbilical cord-derived mesenchymal stem cells(hUC-MSCs) and its potency in the study of sweat gland regeneration. ①hUC-MSCs could easily be obtained from human umbilical cords, and possess the similar properties of MSCs; and the multi- differentiation potential.②The sweat gland-induction medium could help hUC-MSCs differentiate into sweat gland like cells. The sweat gland-like hUC-MSCs could maintain the basic proliferative ability of cells, and possessed a new differentiation potential. ③Sweat gland like-hUC-MSCs could repair and re-establish the function and structure of the damaged SGs at the corresponding sites like normal sweat glands in the animal models. In summary， results in this study indicated that these stem cell therapies could give an alternative choice to repair destroyed sweat glands in future.

【中文名称】表皮细胞去分化形成表皮干细胞的基础研究
【英文名称】Basic Research of the Induction of Human Epidermal Cells to Dedifferentiate into the Epidermal Stem Cells
【研究起始时间】2005-09
【研究终止时间】2008-06
【中文关键词】表皮细胞；表皮干细胞；诱导；去分化；皮肤创伤修复
【英文关键词】skin; epidermal cell; keratinocyte; stem cells; dedifferentiation
【中文摘要】目的：从建立表皮细胞去分化模型入手，比较去分化来源的表皮干细胞和机体自身来源的表皮干细胞在功能和生物学特性等方面的异同点，为实现无延迟、无瘢痕完美修复及皮肤组织的再生提供新的实验参考。方法：采用免疫组织化学的方法探寻胎儿皮肤中的表皮干细胞（epidermal stem cells，ESCs），研究不同发育时期ESCs在胎儿皮肤中分布与迁移。采用改良的IV型胶原铺板选择黏附法分离培养人ESCs，观察其形态及增值分化的特点，并进行细胞免疫组织化学鉴定。同时，提取小鼠胚胎发育中期组织液，模拟表皮干细胞壁龛微环境，采用免疫组织化学、免疫荧光染色、流式细胞检测及RT-PCR技术研究表皮干细胞在此环境中的表型变化，探讨表皮干细胞周围生长微环境在表皮干细胞“命运”决定过程中的作用。此外，本研究在前期的工作基础上，建立表皮细胞去分化研究的体内、体外实验模型，采用免疫组织化学、MTT法、免疫荧光染色、流式细胞技术、扫描及透射电镜检测技术、RT-PCR、Western-blot及TRAP法再次验证表皮细胞通过去分化途径形成机体内源性去分化来源的表皮干细胞，参与皮肤组织的创伤修复与再生。同时，从细胞表型、超微
【英文摘要】Here we report on the dedifferentiation of human epidermal keratinocytes into their precursor cells in vitro with basic fibroblast growth factor (bFGF) but not external gene intervention. After incubation of human terminally differentiating keratinocytes, some of the surviving keratinocytes reverted from a differentiated to a dedifferentiated state, as evidenced by re-expression of some biological markers of native keratinocyte stem cells (nKSCs), including β1-integrin, CK19 and CK14. Moreover, these

dedifferentiation-derived KSCs (dKSCs) showed an ability for high colony-formation correlated with cell cycle analysis showing an marked accumulation in S phases, acquired a similar regional distribution of both α6-integrin and CD71 expression at the ultrastructural level, and had a increased proliferative capacity by releasing telomerase from nucleolar sites to nucleoplasmic distribution. However, on comparing dKSCs with nKSCs, 2 points seem noteworthy: (1) the proportion of transit amplifying cells in dKSCs treated with bFGF is much higher than that in nKSCs and (2) regional differences exist in the subcellular localization of telomerase in nKSCs and dKSCs. Most nKSCs showed a prominent nucleolar concentration of human telomerase reverse transcriptase expression, whereas most dKSCs showed a more diffuse intranuclear distribution of telomerase or even signal depletion at nucleoli relative to the general nucleoplasm. These results indicate that bFGF could induce the terminally differentiating epidermal keratinocytes to convert into their precursor cells. Although the dKSCs were more likely to be transient amplifying cells (the daughter cells of KSCs), reprogramming somatic keratinocytes into the precursor stage of epidermal lineage with bFGF rather than gene induction offers a new approach for generating residual healthy stem cells for wound repair and regeneration.

【中文名称】基于含汗腺结构工程化皮肤模型的汗腺再生研究

【英文名称】Sweat Gland-Regenerative Research Based on in vitro Constitution and in vivo Implantation of Engineered Skin with Sweat Glands

【研究起始时间】2009-02

【研究终止时间】2011-02

【中文关键词】皮肤；汗腺；修复；再生；组织工程；生物材料

【英文关键词】Skin; Sweat glands, Repair, Regeneration; Tissue engineering, Biomaterials

【中文摘要】汗腺再生能恢复创伤修复后皮肤对环境的适应能力和排汗功能，因此开展汗腺再生研究将提高创伤救治和愈合的质量，具有重大的临床需求。目前汗腺再生研究受限于缺乏合适、稳定的汗腺发生发育模型。在对汗腺发生发育基本规律以及对不同阶段汗腺形态结构认识的基础上，本项目进一步建立基于控释微载体的汗腺细胞扩增技术和构建含汗腺的工程化皮肤模型，从组织形态和分子水平考察体外模型中汗腺的发育能力，评价骨髓间充质干细胞（MSC）形成汗腺组织的关键途径，建立在体移植模型，选取可靠的标记、免疫表型、生化和功能指标观察和评价创面愈合中汗腺组织的再生。开展汗腺再生的体外模型研究不仅为揭示汗腺发生发育的过程及机制提供了新的策略，同时也为构建具有皮肤附属器的全功能组织工程皮肤奠定了理论基础，对创烧伤后排汗功能的恢复具有重要的理论意义和应用价值。具体研究内容分三个部分：一、基于微载体的汗腺细胞扩增和含汗腺工程化皮肤的构建研究获取人汗腺细胞种植于用明胶构建并复合生长因子微球载体上，接种于利用工程化方法构建三维皮肤模型，观察皮肤模型的结构、汗腺细胞分布和腺体形态发生情况，通过关键指标筛选、优化含汗腺组织工程皮肤的构建方案

【英文摘要】The presence of skin appendages such as sweat glands in repaired skin is of major clinical importance for maintaining skin homeostasis and regulating body temperature. However, because of poor intrinsic healing capacity, skin appendages cannot be successfully repaired by traditional treatment after severe skin injury. Hence, sweat gland-regenerative research plays key roles in improving the quality of wound healing after deep burns and various skin-related disorders. Currently, one of the main issues in limitation of this research is the lack of suitable and stable study models. Based on acknowledgement of basic developmental rules and morphological structure of sweat glands at different phases, we attempted to establish a novel engineered skin model with sweat glands which simulates a skin-specific microenvironment for investigating sweat gland-regenerative capability on the organization forms and molecular level as well as critical functions of mesenchymal stem cells (MSCs) in healed wounds. Furthermore, excisional wounds were established on both the back and the paws of hind legs in a murine model for vivo transplantation. This study indicates the feasibility of constituting an engineered skin construct incorporating sweat glands in vitro for sweat gland-regenerative research. The in vivo results demonstrate that this novel engineered skin construct could improving the quality of skin repair and maintaining homeostasis during skin regeneration and wound healing process in an athymic murine model. To a certain extent, greater knowledge of sweat glands development has been further recognized. Despite its imperfections, our novel engineered skin model is still a pioneering protocol of constructing engineered skin with skin appendages in vitro and a valuable strategy for skin regeneration.

【中文名称】人脐带间充质干细胞增强全反式维甲酸对HL-60细胞的诱导分化作用

【英文名称】Enhancement of all-trans retinoic acid-induced HL-60 leukemia cell differentiation by human umbilical cord mesenchymal stem cells

【研究起始时间】2009-09

【研究终止时间】2010-05

【中文关键词】脐带间充质干细胞；HL-60；全反式维甲酸；诱导分化；中性粒细胞；增殖
【英文关键词】umbilical cord mesenchymal stem cells; HL-60 cells; all-trans retinoic acid; differentiation; neutrophils; proliferation
【中文摘要】间充质干细胞（MSC）是一种具有自我更新能力和多向分化潜能的成体干细胞，它存在于多种组织中，如胎儿肝脏、胎血、胎儿骨髓、胎肺、脐血、胎盘、脐带、成人骨髓和脂肪等，已经成为组织工程和再生医学细胞治疗的主要候选干细胞之一。其中研究比较广泛的是骨髓间充质干细胞（BMMSC），但骨髓间充质干细胞需要进行骨穿才能得到，对供者有一定的损伤还有感染的可能。人脐带间充质干细胞（hUCMSC）与其他来源的间充质干细胞相比，更容易获得和在体外扩增，并且被病毒感染的概率明显降低，因此hUCMSC是众多来源间充质干细胞中更具有应用价值的种子细胞。急性早幼粒白血病（APL）不同与其他急性髓系白血病，具有独特的病理特征。在全反式维甲酸（ATRA）应用于治疗APL以前，病人极容易因大量出血而死亡。由于APL细胞具有因染色体易位产生的PML/RARA融合基因，因此早幼粒细胞不能向成熟的单核细胞或粒细胞分化。为了深入研究APL和其他的白血病，研究者从病人体内分离或对正常细胞进行分子生物学操作得到了多种白血病细胞系，如：HL-60、NB-4、KG-1a和K562等。HL-60细胞是从M-2型病人体内分离得到的早幼粒细
【英文摘要】This study was aimed to investigate the enhancement of all-trans retinoic acid-induced HL-60 leukemia cell differentiation by umbilical cord mesenchymal stem cell. In addition, we also investigate the effects of hUCMSCs on the HL-60 differetiation induced by 1,25(OH)2D3. When treated by 1,25(OH)2D3, we use flow cytometry to test the expression of CD11b and CD14 on the HL-60 cells. After co-culturing on the hUCMSC, there is an enhancement of CD11b on the HL-60 cells, but there is no significant change of the expression of CD14. In some degree, hUCMSCs also can enhance the differentiation effects of 1,25(OH)2D3, while 1,25(OH)2D3 can induce HL-60 cells to neutrophil like cells rather than macrophage cells on hUCMSCs.

【中文名称】《公众健康知识整合技术研究与应用》课题研究报告
【英文名称】null
【研究起始时间】2009-09
【研究终止时间】2010-12
【中文关键词】公众健康知识 知识整合 Mashup 门户 知识库
【英文关键词】null
【中文摘要】“公众健康知识整合技术研究与应用”是国家十一五科技支撑计划“公众健康普及技术筛选与评价研究”项目中的一个课题。课题研究健康知识整合技术和方法的应用，旨在集成不同类型、不同来源和不同载体的健康知识，通过公众健康信息服务的普及和深入，达到提高公众健康知识素养以及获取和利用健康知识的能力的目的。课题分析对比了国内外公众健康知识服务门户资源建设模式和服务手段，调研了国内公众对健康知识的需求状况和获取途径，构建了健康知识加工系统，建设了公众健康知识库，并开发了为公众提供集内容发布、浏览导航和在线咨询等功能为一体的一站式信息服务的公众健康知识服务门户。本课题研究内容主要包括如下几个方面：（1）资源整合的技术与方法。针对资源整合的基于链接的整合和基于知识的整合的两个层次，梳理了资源整合中常见的技术和方法，如网络信息采集、GIS、虚拟现实等，并利用成熟的方法整合不同来源、不同类型和不同载体中的健康知识，研究自然语言处理技术，分析和处理自然语言的提问和文档信息内容，支持语词、语义及语用层面健康知识的组织、标引等功能，辅助不同类型知识库内容的关联与集成，并将其运用于知识加工系统和服务门户的建设中
【英文摘要】null

【中文名称】FW-II型轴流泵体内血检形成实验报告
【英文名称】Report of in vivo thrombosis of FW-II axial blood pump
【研究起始时间】2010-01
【研究终止时间】2010-09
【中文关键词】心室辅助装置，轴流血泵，动物实验，血栓形成
【英文关键词】ventricular assist device; axial blood pump; animal model; thrombosis
【中文摘要】目的：对FW-II轴流泵短期辅助的抗血栓性能进行评价，为后期临床应用提供安全性依据。 方法：3只成年小尾寒羊，建立心室－泵－降主动脉旁路通道，FW-II轴流泵辅助循环2周，对羊的生命体征和泵的运转情况进行常规监测。实验结束后观察轴流泵各组成部分有无血栓形成，取材观察心、脑、脾、肾大体和镜下病理表现。结果：3只羊全部存活到实验结束，各项生理指标正常，轴流工作平稳。实验结束后拆分泵，仅泵轴根部有少量血栓形成，叶轮、泵管及前、后导叶无血栓形成，心、脑、脾、肾等主要脏器大体和镜下观察均无血栓形成及缺血梗死表现。结论：FW-II型泵抗血栓性能良好，可用于短期循环辅助。

【英文摘要】Objective: To evaluate in vivo anti-thrombosis property of optimized FW-II axial blood pump and provides evidence for future clinical use. Methods: A left ventricle-pump-descending aorta bypass model was established in three healthy sheep and the circulation of these sheep was assisted by FW-II axial blood pump for 2 weeks. Both the sheep and pumps were monitored routinely. Immediately after termination of the experiment, FW-II axial blood pumps were explanted and each part was inspected for thrombus formation. Macroscopic and histological examinations were performed on heart, brain, kidney and spleen, respectively for thrombosis. Results: All 3 sheep survived the experiments with normal condition. And there was no thrombus at other components (flow straighter, impeller and pump housing) except the minus thrombus in the front and rear hub of the pump rotor. There were no macroscopic and histological thrombosis or ischemia in heart, brain, kidney and spleen either. Conclusion: FW-II axial blood pump can be used to assist left ventricular circulation for 2 weeks with a satisfactory anti-thrombosis property.

【中文名称】中药材DNA条形码鉴定研究
【英文名称】Applying DNA barcoding to identify medicinal plants
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】中药材；DNA条形码；鉴定；ITS2
【英文关键词】herbal medicines; DNA barcoding; identification; ITS2
【中文摘要】研究目的：采用DNA条形码（DNA barcoding）技术建立中药材鉴定平台，促进中药鉴定研究的国际合作和中药鉴定方法的标准化。研究方法：应用生物信息学方法确定4个分子标记DNA序列（rDNA ITS，rpoB，rbcL和trnH-psbA），用于中药材PCR通用引物的设计并进行PCR扩增；考察各序列间的种间、种内差异情况，并采用Wilcoxon检验验证所得结论，最后采用“ Barcoding gap ”图示出各序列的优异情况。研究结果和结论：确定以ITS2序列为主，trnH-psbA序列为辅的一百种中药材的DNA 条形码复合鉴定体系。构建了一百种中药材样本信息数据库、引物序列数据库以及一百种中药材DNA条形码鉴定技术平台和标准，解决中药材鉴定的重大科技难题，促进合作基地建设。
【英文摘要】The objectives: To obtain DNA barcoding sequences of medicinal plants and to authenticate them by DNA barcoding sequences. To promote international collaboration and standardization for authentication of medicinal plants. The contents: Trade of Chinese herbs is largely increasing on the international markets which require specialists and methods for authenticating species of medicinal plants. In this project, methods for identifying species of medicinal plants by using short DNA barcoding have been proposed. According to references, we propose internal transcribed spacer of the nuclear ribosomal DNA (ITS), the whole chloroplast trnL(UAA) intron, plastid rbcL and trnH-psbA intergenic spacer as potentially usable DNA markers to medicinal plants. DNA barcoding sequences of one hundred medicinal plants would be obtained through polymerase chain reaction amplification and DNA sequences analysis. Then, Neighbour-joining analysis, implemented in MEGA3, will be employed to examine phylogenetic relationships among one hundred species of medicinal plants. Specialists will be trained in this project to be familiar with authentication of Chinese herbs by DNA barcoding. The Conclusions: To construct a synergistic identification system of DNA barcoding for one hundred medicinal plants, which consists of ITS2 as main locus and trnH-psbA as complementary locus.[Keywords] herbal medicines; DNA barcoding; identification; ITS2

【中文名称】急性 T 淋巴细胞白血病发病过程中正常与恶性造血细
【英文名称】Competition between leukemic cells and normal
【研究起始时间】2009-03
【研究终止时间】2010-06
【中文关键词】：急性T淋巴细胞白血病, Notch1,白血病微环境, 龛，造血干细胞,造血祖细胞，基因芯片，细胞因子芯片，双光子荧光显微镜
【英文关键词】T-ALL, Notch1, leukemic environment, hematopoietic stem cell, hematopoieticd progenitor cells, stem cell Niche， miroarray,cytokine array
【中文摘要】实验目的: 白血病是起源于造血干或祖细胞水平的一种恶性克隆性造血系统疾病，其发病率在各种肿瘤中占第六位，严重威胁着人民的生命健康。但由于具体发病机制至今尚不完全清楚，因此治疗效果仍然不尽如人意。本研究拟通过建立并优化非照射的白血病小鼠模型，系统深入的研究正常造血干/祖细胞（hematopoietic stem cell/Progentior stem cell,HSC/HPC）在急性 T 淋巴细胞白血病（acute T lymphoblastic leukemia，T-ALL）发病过程中的动力学变化及受抑规律，通过基因组学和生物信息学方法，提出白血病发生中正常造血受抑的可能机制；并对在此异常的白血病环境下，白血病细胞的迁徙和定位进行追踪，最终揭示并阐明白血病发病过程中，正常HSC/HPC 与LSC的相互消长变化规律，以及二者竞争性生长的可能机制，为白血病病程预测和有效干预提供新的科学依据和治疗策略。

【英文摘要】Background: The biological mechanisms on the development of leukemia still remain nebulous. Our recent study demonstrated that different effects of T-ALL leukemic environments on normal hematopoietic stem (HSCs) or progenitor cells (HPCs) in the irradiated model (Hu X, et al. Blood 2009). Moreover, a previous publication showed that the leukemic cells created bone marrow niches and disrupted the behavior of normal HSCs/HPCs (Sipkins DA et al, Science 2008). To further understand the actual effects of the leukemic environment on normal HSCs and HPCs in a more clinically-relevant model, we have introduced a non-irradiated mouse model to better mimic the physiological condition. We investigated the dynamic and function of HSC and HPC in the leukemic environment using this non-irradiated mouse model.

【中文名称】ERCC1和XPF功能性遗传变异与肺癌易感性及铂类药疗效相关
【英文名称】Functional ERCC1 and XPF Variants Are Associated with Susceptibility to Lung Cancer but Resistance to Platinum-Based Chemotherapy
【研究起始时间】2006-06
【研究终止时间】2008-04
【中文关键词】ERCC1；XPF；遗传变异；肺癌；小细胞肺癌
【英文关键词】ERCC1, XPF, genetic variant, lung cancer, small cell lung cancer
【中文摘要】结果 DNA测序发现ERCC1基因存在5个单核苷酸多态，分别位于启动子区（－433T>C）、5′非翻译区（262G>T）、外显子（3525C>T）、内含子（4855C>T）和3′非翻译区（14443C>A）。生物化学实验表明262G>T变异影响其所处DNA序列与转录因子的结合；－433T>C变异影响该位点的甲基化。－433C等位基因与肺癌发病风险升高相关（OR＝1.84，95% CI＝1.37－2.45，P＜0.0001）。－433C等位基因、262GG基因型与吸烟三者间交互作用显著增加肺癌发病风险。小细胞肺癌铂类药预后分析表明262GG基因型携带者比GT或TT基因型携带者拥有更长的中位生存时间[30个月（95% CI＝27－49）比19个月（95% CI＝15－22）或17个月（95% CI＝14－24），P值分别为0.025或0.005]。Cox模型分析结果表明，与ERCC1 262GG基因型携带者相比，262GT与TT基因型携带者校正的死亡风险分别是1.58（95% CI＝0.96－2.62，P＝0.074）和1.98（95% CI＝1.13
【英文摘要】Five ERCC1 genetic variants, located in the promoter region (－433T>C), 5′UTR (262G>T), exon (3525C>T), the intron immediately 3′ to the exon 3 (4855C>T), and 3′UTR (14443C>A), respectively, were identified. The 262G>T was proved altering the surrounding sequence′s ability of binding nuclear proteins and then impacting the ERCC1 mRNA levels, while －433T>C was involved into the methylation regulation of CpG island. Multivariate logistic regression analysis showed that subjects with the －433CC or TC genotype had a 1.84-fold (95% CI＝1.37－2.45, P＜0.0001) increased risk for developing lung cancer compared with those with the －433TT genotype. A supermultiplicative joint effect between the －433T>C, 262G>T and smoking was observed. In contrast, the analysis of chemotherapy outcome of SCLC patients revealed that the 262GG genotype is associated with longer survival time compared with the 262GT or TT genotype [30 months (95% CI＝27－49) versus 19 months (95% CI＝15－22) or 17 months (95% CI＝14－24), P＝0.025 and 0.005, respectively]. Cox proportional model analyses showed that the adjusted hazard ratios of death for the 262GT and 262TT genotypes were 1.58 (95% CI＝0.96－2.62, P＝0.074) and 1.98 (95% CI＝1.13－3.47, P＝0.017), respectively, compared with that of the 262GG genotype, indicating that this variant may be an independent prognostic factor. Besides, three functional variants in an absolute linkage disequilibrium located in the XPF promoter, －673C>T, －357A>C and －30T>A, were proved affecting XPF expression. The case-control analysis showed that the －673TT genotype is associated with a decreased susceptibility to lung cancer (OR＝0.62, 95% CI＝0.42－0.91, P＝0.015), but not with the SCLC prognosis.

【中文名称】FEN1基因的遗传学和表观遗传学调控及其与多种肿瘤发生发展的关系
【英文名称】Differencial Expression of FEN1 Caused by DNA Genetic and Epigenetic Changes Is Associated with Multiple Cancers
【研究起始时间】2006-06
【研究终止时间】2008-04
【中文关键词】FEN1；单核苷酸多态；DNA甲基化；肿瘤易感性；肿瘤预后
【英文关键词】FEN1; single nucleotide polymorphisms; DNA methylation; caner susceptibility; cancer progression
【中文摘要】方法：以全基因策略分析FEN1遗传变异；用一系列生物化学实验研究遗传变异对基因功能的影响。以彗星实验(Comet test)测定携带不同基因型焦炉作业工人白细胞DNA损伤修复程度。以重亚硫酸盐-DNA测序法分析FEN1启动子甲基化改变，实时定量PCR检测FEN1 mRNA表达量。以cDNA芯片和组织芯片技术检测FEN1在多种肿瘤标本中的表达情况。以病例-对照研究方法分析遗传变异与肿瘤易感性的关系，相关程度以多因素logistic回归计算的比值比(odds ratio, OR)及其95%可信区限(confidence interval, CI)表示。所有统计检验均为双测检验。结果：DNA测序发现FEN1基因存在两个高度连锁的单核苷酸多态，即－69G/A和4150G/T多态。位于启动子区的－69A＞G改变可能增加抑制性转录因子结合

从而降低FEN1转录活性，而4150G　T改变增加FEN1表达。在焦炉作业工人中，携带FEN1　69G或4150G等位基因者DNA损伤程度显著高于携带　69A或4150T者。含1,013例肺癌和1,131例对照的病例-对照分析显示，－69GG或4150GG基

【英文摘要】Methods: DNA samples from 30 individuals were sequenced to search for SNPs in FEN1, and the function of the SNPs was investigated by a series of biochemical assays. The association between the FEN1 genotypes and the ln-transformed Olive tail moment (Olive TM) values were tested in coke-oven workers, and the association between the genotypes and lung cancer susceptibility were examined in a case-control panel consisting of 1,013 lung cancer patients and 1,131 controls.The odds ratios and their 95% confidence intervals were estimated by logistic regression. The promoter methylation was identified by sequencing of sodium bisulfite-treated DNA and mRNA levels were determined by quantitative real-time RT-PCR. FEN1 expression was detected in BD Clontech™ Cancer Profiling Array I and Cybrdi™ Breast Carcinoma Progression Tissue Arrays.Results: Two SNPs (－69G/A and 4150G/T) were identified and the －69G and 4150G alleles were associated with reduced expression of FEN1 in vitro and in vivo. The higher ln-transformed Olive TM values of coke-oven workers and significantly increased risks for developing lung cancer were associated with the FEN1 －69G or 4150G allele compared with the －69A or 4150T allele, respectively. A multiplicative joint effect between smoking and FEN1 polymorphisms in intensifying lung cancer risk was detected. FEN1 mRNA was overexpressed in multiple cancers compared with matched normal tissue. In breast cancer, FEN1 expression was inversively correlated with the degree of tumour differentiation. Moreover, we identified two CpG islands in the FEN1 promoter region and showed that hypomethylation of CpG island 2 is important in regulating overexpression of the FEN1 gene in tumors.

【中文名称】表皮干细胞多向分化潜能特征的发现及其相关研究

【英文名称】The discovery of the multipotency of epidermal stem cells and related research

【研究起始时间】2009-02

【研究终止时间】2011-02

【中文关键词】表皮干细胞；CD34；未分化角质细胞；驯化诱导；转分化；上皮－间质化；去分化；诱导的多潜能干细胞

【英文关键词】epidermal stem cell; CD34; undifferentiated keratinocytes; acclimatization; epithelial－mesenchymal transition; dedifferentiation; induced pluripotent stem cells

【中文摘要】目的：1. 探讨表皮干细胞 (epidermal stem cells, ESCs) 潜在亚群及分析其解剖分布特点；2. 试图建立ESCs转分化诱导方法，拓展ESCs多向分化潜能；3. 明确ESCs体外培养表达谱特征，初步建立ESCs非转基因重编程为诱导的多潜能干细胞 (induced pluripotent stem cells, iPSCs) 实验体系。方法：1. 应用免疫组织化学的方法检测不同解剖部位皮肤组织CD34的表达。从mRNA及蛋白水平检测包皮来源表皮基底层细胞CD34 分子表达情况，并从蛋白水平研究ESC特异性标记β1整合素, p63与CD34双标记的情况。2. 分别采用直接血清诱导法、直接定向诱导培养基诱导法和驯化诱导法进行诱导。检测成脂相关mRNA及油红O染色证实脂肪系列转分化，检测成肌相关mRNA及SMA免疫荧光染色证实肌肉系列转分化，检测成神经相关mRNA水平及nestin, 3-tubulin, GFAP免疫荧光染色证实神经系列转分化。建立小鼠损伤模型，选取不同时间点利用免疫荧光技术检测创伤局部角质细胞细胞类型转变。3. mRNA水平检测体外培养ESCs

【英文摘要】Objective: 1: To explore the potential subpopulation of epidermal stem cells (ESCS) and analyze its characteristic of anatomical distribution; 2. To establish a method for transdifferentiation of ESCS, and to expand the multi-lineage differentiation potency of ESCS; 3. To identify the expression profile of cultured ESCS and set up an experimental system for producing induced pluripotent stem cells (iPSCs) from ESCS by non-transgenetic reprogramming. Methods: 1. Double-label immunofluorescence was used to detect the expression of CD34 and either of the two well documented ESC markers β1 integrin and p63. 2. UKs were induced by either serum or lineage-committed medium or acclimatized induction. 3. ESCs were reprogrammed by means of transgene through transfection of OCT4, SOX2, KLF4 and c-Myc, or induced for reprogramming directly under embryonic stem cells culture condition. Results: 1.We observed the expression of CD34 with all three epitope types specifically at the epidermal basal layers derived from human scalp and foreskin, but not trunk skins. The results of double immunofluorescence studies demonstrate that almost all CD34-positive cells are also positive for either of the two well documented epidermal stem cell markers β1 integrin and p63. 2. Serum acclimatization can induce UKs to produce a large number of smooth muscle cells and myofibroblasts and fewer of adipocytes and neurocytes within 3 weeks. 3. Immunofluorescence showed that these clones were positive for pluripotent transcription factors -- OCT4, SSEA1 and NANOG, and simultaneously expressed CD29, a marker specific to ESCs. Conclusion: 1. The study shows that CD34 may represent a subpopulation of ESCs in scalp and foreskin tissues, and the unbalanced expression of CD34 further confirmed the heterogeneity of stem cells. 2. The data of this study shows that human UKs possess multipotency in vitro. 3. In this study, we obtain iPSCs-like clones by means of transgenetic or non-transgenetic.

【中文名称】3.0T MR动态增强扫描对正常胰腺及胰腺癌定量分析研究
【英文名称】Quantitative analysis of normal pancreas and pancreatic adenocarcinoma with dynamic contrast-enhanced MR imaging on a 3.0T system
【研究起始时间】2008-03
【研究终止时间】2008-12
【中文关键词】胰腺；胰腺癌；磁共振成像；动态增强

【英文关键词】Pancreas, Pancreatic adenocarcinoma, Magnetic resonance imaging (MRI), Dynamic contrast enhanced (DCE)
【中文摘要】目的：利用3.0T MR快速三维动态增强扫描序列所得数据，对正常胰腺及胰腺癌的灌注过程进行定量分析研究，探讨其对胰腺癌诊断的临床应用价值。材料与方法：对43例经病理证实的胰腺癌患者（胰腺癌组）及37例非胰腺疾病患者(对照组)行全胰腺LAVA九期动态增强序列扫描，将所得数据传至ADW 4.2工作站处理，分别测量对照组胰腺的头、体、尾及胰腺癌组病变区域及非病变区域的30 s强化率（SER30）、90 s强化率（SER90）、曲线下面积（PEI）、达峰时间（TTP）及最大强化斜率（MSI），并使用SPSS 11.5统计软件进行组内及组间各项参数的比较。结果：对照组胰腺头、体、尾的SER30、SER90、PEI、TTP及MSI差异均无统计学意义。胰腺癌组病变区与非病变区的SER30、PEI、TTP、MSI均有显著性差异，SER90不具有统计学差异。胰腺癌组非病变区与对照组对应区域的SER90及TTP有统计学差异，两组的SER30不具有统计学差异。结论：正常胰腺的不同部位间无灌注差异。胰腺癌病变区域与非病变区域的灌注差异可以反映癌组织浸润范围。胰腺癌非病变区域与正常胰腺间TTP的差异
【英文摘要】Purpose: To quantify the perfusion parameters of normal pancreas and pancreatic carcinoma with three-dimension (3D) fast spoiled gradient echo dynamic contrast enhanced (DCE) MRI on 3.0T MR system, and to assess the value of 3D DCE-MRI in the diagnosis of pancreatic carcinoma. Materials and methods: Forty-three patients with pathology verified pancreatic carcinoma and thirty-seven control subjects with normal pancreas (without pancreatic diseases) underwent DCE-MRI with 3D LAVA sequence of ten phases. The data were processed on ADW4.2 workstation. The perfusion parameters of the head, body and tail of normal pancreas, together with lesion and non-lesion area of pancreatic carcinoma were measured and statistically analyzed, including signal enhancement ratio at 30 seconds after injection (SER30), signal enhancement ratio at 90 seconds after injection(SER90), positive enhancement integral (PEI), time to peak (TTP) and maximum slope of increase (MSI). Results: There was no significant perfusion difference among head, body or tail of normal pancreas. The difference of SER30, PEI, TTP and MSI between lesion and non-lesion region of carcinous pancreas was significant. The TTP between normal pancreas and the non-lesion region of carcinous pancreas was significantly different. Conclusion: Normal pancreas has no regional perfusion difference. The data from DCE-MRI provide reliable information for the diagnosis of pancreatic cancer, and for the assessment of the invasion of pancreatic carcinoma. The difference in TTP between the normal pancreas and non-lesion region of carcinous pancreas suggest the existing of potential lesions.

【中文名称】3.0T MR在体氢质子波谱分析对正常胰腺及胰腺癌
【英文名称】The metabolic analysis of normal pancreas and pancreatic adenocarcinoma by in vivo proton magnetic resonance spectroscopy at 3.0 T
【研究起始时间】2008-03
【研究终止时间】2008-12
【中文关键词】胰腺；胰腺癌；磁共振成像；波谱分析

【英文关键词】 Normal pancreas, Pancreatic adenocarcinoma, Magnetic Resonance Spectroscopy (MRS)
【中文摘要】目的：利用3.0T MR在体氢质子波谱分析技术，分析正常胰腺及胰腺癌的代谢特征。材料与方法：选取29例经病理证实的胰腺癌患者（胰腺癌组；胰头癌19例，胰体尾癌10例），其中男14例，女15例，中位年龄55岁；27例非胰腺疾病患者(对照组)，其中男15例，女12例，中位年龄56岁。采用GE公司的3.0 T磁共振扫描仪，分别对胰腺癌组的病变区与非病变区及对照组的胰头和胰体尾设定感兴趣区，并行单体素1H-MRS，将所得数据传至ADW 4.2工作站处理，分别测得胰腺癌组及对照组的各感兴趣区的脂肪酸（FA, 5.4 ppm）、总胆碱复合物（t-Cho, 3.2 ppm）、脂肪（Lip, 1.3 ppm）及内生水（InW, 4.7 ppm）的曲线下面积，并计算各感兴趣区的FA/InW、t-Cho/InW及Lip/InW的比值，使用SPSS 11.5统计软件对组内及组间所得各项比值进行比较。结果：① 对照组胰头区和胰体尾区FA/InW及Lip/InW的比值差异无

统计学意义，t-Cho/InW的比值胰头区小于胰尾区，且有显著差异。② 胰腺癌组病变区与非病变区的FA/InW及Lip/InW的比值

【英文摘要】Purpose: To analyze metabolic features of normal pancreas and pancreatic adenocarcinoma by in vivo proton MRS at 3.0 T.Materials and methods: 27 control subjects with normal pancreas (without pancreatic diseases) and 29 patients with pathology verified pancreatic adenocarcinoma and matching age and sex underwent single-voxel 1H-MRS on a 3.0T MR system (GE Healthcare, HDxt) with 8-channel body coil. Breath-hold PRESS with TE/TR = 35ms/1500ms was used. The peaks area at 1.3 (lipid, Lip), 3.2 (total choline, t-Cho) and 5.4 (fatty acids, FA) ppm of the head and body-tail in normal pancreas, together with lesion and non-lesion area in pancreatic carcinoma were measured by SAGE and their ratio to the peak area of none saturated (internal water, InW) at 4.7 ppm was calculated. Statistic analysis was made between different locations.Results:1) In normal pancreas, there were no statistical differences in the ratios of FA/InW and Lip/InW respectively, but t-Cho/InW of body-tail area was greater than that of head. 2) In the pancreatic carcinoma, there was significant difference of the ratios in FA/InW and Lip/InW between lesion and non-lesion region respectively. There was no difference in the ratios of t-Cho/InW between lesion and non-lesion region in pancreatic body-tail cance. But in pancreatic head cancer, the ratio of t-Cho/InW in carcious region was smaller than that in non-lesion region. 3) There were no statistical differences in the ratios of FA/InW、t-Cho/InWand Lip/InW between normal pancreas and non-lesion region in pancreatic cancer (head vs head, body-tail vs body-tail). Conclusion: The metabolic features of the pancreatic carcinoma including: a) in normal pancreas, t-Cho of body-tail was greater than that of head. b) the FA, t-Cho and Lip were decreased in the carcious region. c) no difference can be found between the normal pancrease and the non-leision region of pancreatic cacinoma.

【中文名称】数字化乳腺x线摄影与超声检查对乳腺癌诊断价值的比较研

【英文名称】Comparative Study of Digital Mammography and Ultrasonography for the Diagnosis of Breast Carcinoma

【研究起始时间】2007-12

【研究终止时间】2008-12

【中文关键词】乳腺癌，数字化x线乳腺摄影，超声

【英文关键词】 breast neoplasm, digital mammography, ultrasonography

【中文摘要】目的：比较数字化乳腺x线摄影、超声对乳腺癌的诊断价值；分析年龄、激素水平、腺体密度、病理类型、病理分期及是否钙化对诊断的影响；并评价BI-RADS分类的临床应用价值。材料及方法：自2007年12月至2008年12月，对我院有临床症状或乳腺癌高危人群均进行数字化乳腺x线摄影及超声检查，随访截止2009年12月，符合病例诊断标准者共1432例患者。所有患者随机先后接受x线摄影和全乳腺超声检查。对两种检查的结果进行BI-RADS分类，与病理作对照，评价并比较两种方法的诊断效能及相关影响因素。利用卡方检验及ROC曲线进行统计分析。结果：1432例患者，共1500个病灶，良性737个，恶性763个。1、数字化x线摄影及超声检查的敏感性分别为90.0%和95.4%，特异性为83.0%和84.8%，准确性为86.6%及90.2%。超声检查的敏感性、特异性及准确性优于x线检查（P<0.05）。x线及超声联合检查可提高对乳腺恶性疾病诊断的敏感性（98.4%）。2、乳腺腺体密度类型对x线的敏感性有影响，但不影响超声诊断。对于致密性腺体或年龄小于等于50岁患者，超声敏感性均高于x线（P<0.

【英文摘要】Purpose: To (a) determine the performance of digital mammography (DM) and ultrasonography (US), (b) analyze the in fl uence of age, hormonal status, breast density, pathological type, T stage, and calcification or not; (c) assess the value of BI-RADS categories.Materials and Methods: Between December 2007 and December 2008, the suspected and risk patients with breast carcinoma received DM and US examination. Until December 2009 follow-up ended, 1432 female were rolled in this study who had complete medical history and definite diagnosis. Results: In 1432 patients, 1500 lesions including 737 benign and 763 malignant were found. 1. Sensitivity, speci fi city, and accuracy of mammography were 90.0%, 83.0%, and 86.6%, respectively; and those of US, 95.4%, 84.8%, and 90.2%, respectively. There was significant difference between DM and US performance. DM and US together had signi fi cantly higher sensitivity (98.4%) than a single modality (P<0.05). 2. Mammographic sensitivity declined signi fi cantly with increasing breast density (P <0.05), but not for US. There was no sensitivity difference for both modalities in patients older than 50 years or with fat and scattered fibroglandular density, or with the same pathological T stage. The sensitivity of both modalities was higher for invasive ductal carcinoma (IDC) than ductal carcinoma in situ (DCIS). The sensitivity of DM for DCIS and IDC were 74.6% and 92.2%, those of US were 79.1% and 98.4%. US had higher sensitivity for IDC or palpable lesions than DM (P=0.000). DM was more sensitive for lesions with calcification (97.0% VS 95.1%, P=0.001) or pure calcification (91.5% VS 85.1%, P=0.016).Conclusion: US has shown better performance than DM for clinic patients. Combined exams improve the sensitivity. BI-RADS categories are useful for predicting the presence of malignancy.

【中文名称】3.0T磁共振波谱成像预测乳腺癌NAC疗效的价值
【英文名称】 The Predictive Value of NAC Efficacy with 3.0T MRS
【研究起始时间】2009-03
【研究终止时间】2011-01
【中文关键词】乳腺癌；新辅助化疗；磁共振成像；磁共振波谱成像
【英文关键词】Key words:neoadjuvant chemotherapy; magnetic resonance imaging; magnetic resonance spectroscopy
【中文摘要】目的：通过前瞻性研究探讨乳腺癌NAC前、中（第一、二个疗程结束后）、后（全部疗程结束后）病灶磁共振波谱成像（Magnetic resonance spectroscopy, MRS）得到稳定谱线的成功率、成功谱线中胆碱峰的出现率以及谱线中胆碱峰/水峰峰高比、峰下面积比等预测NAC疗效的价值。资料和方法：应用3.0 T MR对90例经核芯针穿刺病理证实为浸润性乳腺癌且临床进行NAC的患者行乳腺扫描（NAC前、第一疗程后、第二疗程后、全部疗程结束后等4次扫描中的至少一次），扫描序列包括常规平扫、DWI成像及VIBRANT多期动态增强扫描。对其中23位自愿接受乳腺MRS 的患者，在增强扫描后2~12小时内进行3.0TMRS。以横轴T2WI 、矢状位VIBRANT增强前蒙片图像作为定位像，确定ROI范围，采用单体素扫描序列，扫描时间约4.8 min，扫描方向为横轴面。采集MRS 数据前进行常规自动预扫描，包括自动匀场和抑制水信号，本组线宽为6～13，抑制水信号程度达92%～98 %。扫描结束后利用ADW 4.2 工作站中Functool SAGE 后处理软件对MRS进行后处理分析，得出相应
【英文摘要】 Objective: To investigate the MRS achievement ratio and the frequency of cholineIn the lesion of breast cancer before NAC, during NAC(post-first or second cycle) and after NAC(all cycles are over); To investigate the predictive value of NAC efficacy With choline/water hump height ratio and the area under hump ratio. Materials and Methods: 90 patients pathology confirmed invasive breast cancer with core needle puncture biopsy undergone at least one time breast MR scans at before NAC, post-first cycle, post-second cycle, or after NAC. The scan series includes: routine plain scan, DWI and VIBRANT dynamic contast enhanced scan. 23(of 90) patients voluntary accepted the braest MRS scan. Results: For normal breast tissues and lesions before NAC, post-first cycle treatment, after NAC, the MRS achievement ratio are all 100%(13/13, 5/5, 7/7)and the frequency of choline are respectively 85%(11/13), 60%(3/5), 28.6%（2/7）. For lesion before NAC, choline/water hump height ratio and the area under hump ratio in MHR group(4 sides) and NMHR(9sides) are respectively 0.113±0.080, 0.236±0.283(P=0.420) and 0.061±0.069, 1.467±3.862(P=0.492).Conclusion: the MRS achievement ratio are all 100% at three check point and the frequency of choline decrease in turn. For the lesion, Neither choline/water hump height ratio nor the area under hump ratio can not actively predict the MP efficacy statisticly, just there are the tendengcy that choline/water hump height ratio and the area under hump ratio is higher in NMHR.

【中文名称】18F-FDG PET-CT对NSCLC术前T分期的应用价值
【英文名称】18F-FDG PET-CT in the Presurgical T Staging of Non-Small Cell Lung Cancer
【研究起始时间】2006-10
【研究终止时间】2009-03
【中文关键词】肺肿瘤；肿瘤分期；体层摄影术，发射型计算机；体层摄影术，X线计算机；脱氧葡萄糖
【英文关键词】Lung neoplasm; Neoplasm staging; Tomography emission-computed; Tomography, X-ray computed; Deoxyglucose

【中文摘要】目的　探讨正电子发射计算机体层成像-CT（PET-CT）在非小细胞肺癌（NSCLC）患者术前原发肿瘤分期（T分期）方面的价值。资料与方法　90例手术病理证实的NSCLC患者均于原发肿瘤切除术前行18F-脱氧葡萄糖（FDG）PET-CT扫描，由两名有PET-CT诊断经验的影像医师采用双盲法分别根据CT和PET-CT图像对肿瘤行T分期。以手术病理结果作为金标准，对CT和PET-CT的分期结果进行比较和评价。T分期定义参照美国癌症联合会（AJCC）修订的第7版分期手册。结果　手术病理结果显示90例NSCLC中T1期22例，T2期42例，T3期14例，T4期12例，CT正确分期69例，PET-CT正确分期75例。8例中心型肺癌合并阻塞性肺改变，CT正确分期3例，PET-CT正确分期6例；5例同侧肺内转移，CT正确诊断2例；PET-CT正确诊断4例；6例胸膜转移，CT正确诊断3例，PET-CT正确诊断4例。CT和PET-CT对T分期的符合率分别为76.7%和83.3%，两者差异无统计学意义（P=0.063）。Kappa检验结果表明CT、PET-CT与病理T分期均有较好一致性（K=0.59
【英文摘要】Objective To evaluate the diagnostic value of integrated positron emission tomography and computed tomography (PET-CT) with fluorine 18 fluorodeoxy- glucose (18F-FDG) in preoperative primary tumor stage (T stage) of non-small lung cancer (NSCLC). Materials and Methods Ninety NSCLC patients underwent curative surgical ressection after integrated 18F-FDG PET-CT examination and then breathhold CT examination from Oct 2006 to Mar 2009. Two blinded experienced radiologist staging all primary

tumors in consensus by CT and PET-CT images. Surgical and histopathologic results served as the “ golden standard ” for determing the staging value of CT and PET-CT. T stage was assigned on the basis of image analysis by using American Joint Committee on Cancer staging systems.Results According to pathological result, there are 22 patients in T1 stage, 42 in T2, 14 in T3, 12 in T4. CT and integrated PET-CT classified T stage accurately in 76.7% (69 of 90 patients) and 83.3% (75 of 90 patients), respectively (P =0.063). CT and PET-CT classified accurately 3 and 6 patients respectively in 8 patients of central cancer with atelectasis, diagnosed accurately 2 and 4 metastases respectively in 5 patients at the ipsilateral lung, 3 and 4 pleural metastases respectively in 6 patients.Conclusions Describing the size, modality, and infiltrative region of primary tumor in NSCLC distinctly, CT is the main imaging method for T stage. 18F-FDG PET-CT has unique value in differentiating center cancer with atelectasis, and diagnosing pulmonary or pleural metastasis.

【中文名称】18F-FDG PET-CT对NSCLC术前N分期的应用研究
【英文名称】18F-FDG PET-CT in the Preoperative N Staging of Non-Small Cell Lung Cancer
【研究起始时间】2006-10
【研究终止时间】2009-03
【中文关键词】肺肿瘤；肿瘤分期；体层摄影术，发射型计算机；体层摄影术，X线计算机；脱氧葡萄糖
【英文关键词】Lung neoplasm; Neoplasm staging; Tomography emission-computed; Tomography, X-ray computed; Deoxyglucose

【中文摘要】目的 探讨18F-FDG PET-CT在非小细胞肺癌（NSCLC）患者术前区域淋巴结分期（N分期）方面的应用价值，以及CT密度和双时相显像在淋巴结性质判定方面的作用。资料与方法 80例手术病理证实的NSCLC患者均于术前行18F-FDG PET-CT扫描，由两名有PET-CT诊断经验的影像医师采用双盲法分别对CT和PET-CT图像进行分析。对CT图像，根据淋巴结大小判断性质，淋巴结短径≥1.0cm诊断为恶性。对PET-CT常规显像图像采用两种方法分析。（1）FDG摄取法：CT作为解剖定位图像，根据18F-FDG摄取情况判断淋巴结性质，摄取增高者诊断为恶性，无摄取增高者诊断为良性；（2）摄取＋CT密度法：结合CT密度和FDG摄取情况判断淋巴结性质，摄取增高者若合并有钙化或者密度高于主动脉者诊断为良性，否则诊断为恶性。FDG摄取标准通过目测法和半定量分析法结合判定，淋巴结摄取高于纵隔或最大标准摄取值（SUVmax）≥2.5为摄取增高。双时相显像的储留指数（RI）>10%为延迟相摄取升高。N分期参照美国癌症联合会修订的第7版分期手册。以病理检查作为金标准对所得结果进行统计学分析。结果
【英文摘要】Purpose To evaluate the diagnostic value of integrated positron emission tomography and computed tomography (PET-CT) with fluorine 18 fluorodeoxyglucose (FDG) in preoperative regional lymph nodal stage (N stage) of NSCLC, especially the additional value of CT attenuation and the dual-time-point imaging in determining the status of lymph nodes in China where tubercular granulomatous disease is epidemic.Materials and Methods Eighty NSCLC patients underwent curative surgical resection after integrated 18F-FDG PET-CT examination from Oct 2006 to Mar 2009. The CT and PET-CT images were analyzed by two blinded radiologist. For CT scan, the status of lymph nodes was diagnosed by their size. For PET-CT scan, the initial scan images were analysed by two methods. Results A total of 265 nodal groups were sampled, of which 51 nodal groups were malignant according to pathological result. On per-nodal-station (group) basis, the diagnostic sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were 45.1%, 92.5%, 83.4%, 58.9% and 87.6% respectively by CT; 66.7%, 89.7%, 85.3%, 60.7% and 91.9% respectively by method 1 of PET-CT; 64.7%, 96.7%, 90.6%, 82.5% and 92.0% respectively by method 2 of PET-CT. The sensitivity beween CT and method 1 had statistically significant difference (P<0.01). The specificity and accuracy between method 1 and 2 had statistically significant difference (P<0.01). Thirty-nine nodal groups with high uptake in the initial scan underwent dual-time-point imaging and the difference of ΔSUVmax and RI between benign and malignant groups both had no statistical significance (P>0.05). On per-patient basis, the accuracy was 67.5% by CT, 70.0% with PET-CT by method 1, and 76.2% by method 2. The accuracy for N2 staging between CT and PET-CT (method 2) had statistically significant difference.Conclusions 18F-FDG PET-CT has high diagnostic value in preoperative N staging of NSCLC patients.

【中文名称】非小细胞肺癌原发灶FDG摄取与病理分期及区域淋巴结转移的相关性研究
【英文名称】Relationship between 18F-FDG uptake of primary tumor at PET-CT and pathological stage, along with regional lymph nodal metastases in NSCLC
【研究起始时间】2006-10
【研究终止时间】2009-03
【中文关键词】关键词 肺肿瘤；病理学；肿瘤分期；体层摄影术，发射型计算机；脱氧葡萄糖

【英文关键词】Lung neoplasm; Pathology; Neoplasm staging; Tomography emission-computed; Deoxyglucose

【中文摘要】目的 研究非小细胞肺癌（NSCLC）原发灶18F-脱氧葡萄糖（FDG）摄取与病理分期（T和N分期）及区域淋巴结转移的关系；分析NSCLC区域淋巴结转移的影响因素以及原发灶FDG摄取在预测淋巴结转移中的作用。资料与方法 80例有完整病例资料的NSCLC的病人，均行术前18F-FDG PET-CT检查、肿瘤切除并淋巴结清扫手术，均有术后病理分期。不同病理分期的NSCLC进行肿瘤FDG摄取的比较并进行相关性分析；淋巴结转移的影响因素采用单因素和多因素分析。肿瘤FDG摄取采用最大标准摄取值（SUVmax）来表示。结果 原发肿瘤大小和FDG摄取存在整体线性相关（r=0.591, P=0.000），≤3.0cm组肿瘤大小与SUVmax有相关性；>3.0cm组肿瘤大小与SUVmax无相关性。不同T或N分期间原发灶SUVmax差异均有统计学意义（F=5.701, P=0.005；F=4.124, P=0.023）。相关分析表明T和N分期均与原发灶SUVmax呈正相关（r=0.378，P=0.001；r=0.438，P=0.000）。区域淋巴结转移影响因素的单因素分析表明变量X4（血清TM）、X
【英文摘要】Objective To investigate the relationship between 18F-FDG uptake of primary tumor and pathological stage (T and N stage) of NSCLC. Furthermore, we analyzed the possible risk factors for regional lymph nodal metastases and determine whether the degree of 18F-FDG uptake of the primary tumor is an independent predictor of nodal metastases in patients with NSCLC.Materials and Methods Eighty NSCLC patients underwent curative surgical resection after integrated 18F-FDG PET-CT examination were enrolled, with their disease thoroughly pathological staged. Results A positive correlation was found between SUVmax and size of primary tumor (r=0.591, P=0.000). The difference in SUVmax of primary tumor among different T staging groups and the correlation between SUVmax and T stage both had statistical significant(F=5.701, P=0.005; r=0.378, P=0.001). Similarly, the SUVmax of primary tumor was significantly associated with N stage (F=4.124, P=0.023; r=0.438, P=0.000). In the study of the risk factors which may affecting the nodal metastases, tumor size, histological grade, blood tumor marker level and SUVmax of primary tumor were factors significantly associated with lymph node involvement in univariate analysis. Logistic multivariate analysis showed that SUVmax of primary tumor and blood tumor maker level was both significant predictive factors for lymph nodal metastases in NSCLC patients.Conclusion There are significantly relationships between the SUVmax of the primary tumor and pathological stage (T and N stage) of NSCLC. 18F-FDG uptake by the primary tumor may be an independent predictor of regional lymph node metastases in patients with NSCLC.

【中文名称】室性心律失常的计算机三维仿真研究
【英文名称】computerized dimensional modelling of ventricular arrhythmia
【研究起始时间】2007-07
【研究终止时间】2010-06
【中文关键词】计算机三维仿真，室性心律失常，心内膜标测
【英文关键词】computerized dimensional modelling, ventricular arrhythmia, endocardial mapping
【中文摘要】目的：建立符合我国患者发病特点的各种室性心律失常的计算机三维仿真模型，进而探讨其发病机制。方法：首先建立基于离子通道的计算机三维仿真模型，在此基础上，调整模型参数，并与临床获得的标测结果相互验证.结果：成功在生理条件下心肌细胞内钙波演变过程的建模仿真，提出了一种高效的三维心肌兴奋传播仿真算法，建立了一个真实结构和心肌纤维旋向的三维计算机心脏模型。结论: 舒张期[Ca2+]i升高、Km减小，都会增加自发性钙波发生概率,计算机仿真结果与心内标测系统的实测结果相吻合。
【英文摘要】无

【中文名称】心脏性猝死高危患者预测模型研究
【英文名称】prediction model of high-risk sudden cardiac death patients
【研究起始时间】2007-06
【研究终止时间】2010-06
【中文关键词】心脏性猝死，预测模型，室颤，室速
【英文关键词】sudden cardiac death,prediction model,ventricular fibrillation, ventricualr tachycardia
【中文摘要】目的：通过对器质性心脏病患者及恶性室性心律失常患者进行无创心电学指标筛查和随访，以求发现心脏性猝死(SCD)高危患者并建立心血管病患者SCD风险预测模型，以便对器质性心脏病患者进行SCD风险评估及预测并及时预防SCD的发生。方法：多中心、前瞻性队列研究。主要终点为SCD（定义为各种心脏原因引起的以意识丧失为先导的自然死亡；死亡发生在症状出现后1小时内）和全因死亡。次要终点为心脏骤停或首次发生持续性室颤(VT)。 结果：随访期间共发生139例死亡，心脏性猝死38例，占27.34%。经cox 回归分析显示年龄、体质指数(BMI)、既往发生室颤和持续性室性心动过速、纽约心功能分级以及超声心动图指标对死亡有预测价值。而无创心电指标中除HRV中的窦性心

搏RR间期标准差（SDNN），和相邻心搏间期差的均方根（RMSSD）有轻度预测价值外，其余指标无预测价值。而血脑型利钠肽（BNP）、C反应蛋白（CRP）和高敏CRP对死亡有明显的预测价值。 结论：年龄、BMI、既往发生室颤和持续性室性心动过速、纽约心功能分级以及超声心动图指标对死亡有预测价值。
【英文摘要】无

【中文名称】粘质沙雷氏菌发酵生产2,3-丁二醇及其代谢工程研究
【英文名称】Research on 2,3-butanediol production by Serratia marcescens H30 and its metabolic engineering
【研究起始时间】2006-09
【研究终止时间】2009-12
【中文关键词】粘质沙雷氏菌；2,3-丁二醇；发酵调控；基因改造；2,3-丁二醇合成调控机制
【英文关键词】S. marcescens; 2,3-butanediol; fermentation regulation; gene modification; regulatory mechanism of 2,3-butanediol biosynthesis
【中文摘要】2,3-丁二醇(2,3-butanediol, BD)是一种重要的生物基化学品，广泛用于化工、食品、航空航天燃料等领域，可用来制备聚合物、油墨、香水、熏蒸剂、增湿剂、软化剂、增塑剂、药物手性载体等。本论文以粘质沙雷氏菌H30(Serratia marcescens H30)为出发菌株，通过传统的发酵调控方法结合现代代谢工程手段对生物法制备2,3-丁二醇开展了以下研究工作：1. 发酵条件和发酵培养基的优化通过摇瓶实验，确定了粘质沙雷氏菌H30生长及2,3-丁二醇合成的最佳培养条件和最优发酵培养基组成。最佳培养条件为：初始pH值为7.0，过程pH值控制为6.0，培养温度为30℃，接种量为5%，250mL三角瓶最适装液量为50mL。在此基础上通过单因素实验、Plackett-Burman Design实验和Response Surface Methodology实验对粘质沙雷氏菌H30的发酵培养基组分进行了优化，获得了培养基的最优配方为：蔗糖 90g/L，安琪酵母粉 33.36g/L，柠檬酸钠 10g/L，乙酸钠 4g/L，硫酸锰 0.1g/L，硫酸镁 0.3g/L，磷酸二氢铵 1g
【英文摘要】2,3-butanediol is an important biobased bulk chemical due to its extensive industrial application. It has been shown to have potential applications in the manufacture of printing inks, perfumes, fumigants, moistening and softening agents, explosives and plasticizers, and as a carrier for pharmaceuticals. In this current thesis, 2,3-butanediol production by Serratia marcescens H30 was studied by using traditional fermentation regulatory methods and modern metabolic engineering technique. The detailed work was introduced as following:1. Optimization of fermentative conditions and medium compositionsThe optimization of flask fermentation conditions and cultural medium compositions for 2,3-butanediol production by Serratia marcescens H30 was investigated. The results showed that the optimal fermentation conditions included initial pH of 7.0, process controlled to pH 6.0, cultivation at 30°C, inoculum size of 5% (v/v) and 50mL medium in 250mL flask. On the basis of the above fermentation conditions, the concentrations of medium components were optimized in shake flask fermentations by using single factor experiment, Plackett-Burman design and Response Surface methodology. And the optimal medium (g/L) (sucrose 90; yeast extract 33.36; sodium citrate 10; sodium acetate 4; MnSO4 0.1; MgSO4 0.3; NH4H2PO4 3) was obtained. It could improve 2,3-butanediol production from 15.93 g/L to 44.7g/L and shorten fermentation period from 48h to 15h. Fed-batch experiments in flask showed residual sucrose concentration of 15-30g/L favored 2,3-butanediol production.2. The experiments in 3.7L bioreactor and scale up in 50L-5000L bioreactorsThe fermentation experiments were firstly carried out in 3.7L bioreactor. Several feeding and regulatory strategies, including pulse fed batch, constant feed rate fed batch, constant residual sucrose concentration fed batch with respiratory quotient (RQ) control and pH self-control with constant residual sucrose concentration fed batch and RQ control, were compared for improving the production of 2,3-butanediol. The obtained 2,3-butanediol concentrations were 115.5g/L, 117.14g/L, 139.92g/L and 130.65g/L, respectively. Ultimately, a suitable control strategy which combined the RQ control with the constant residual sucrose concentration fed batch was developed. Using this strategy, the DCW (Dry Cell Weight) of 16.05g/L with the 2,3-butanediol productivity of 3.34g/L • h and the yield of 94.67% was obtained. Then we performed fermentation scale up experiments in 50L-5000L bioreactors using the above strategy. The 2,3-butanediol concentrations obtained in 50L-5000L bioreactors were over 130g/L, and in 5000L bioreactor the 2,3-butanediol concentrations of 130.2g/L was achieved.3. Construction of the swrw mutant encoding a biosurfactant synthase in S. marcescens H30Biosurfactant synthesis by S. marcescens H30 during the fermentation process for 2,3-butanediol producton results in a lot foam formation, which is harmful to the fermentation process due to microbial pollution. In addition, excessive anti-foam agent added would influence the microbial activity and emulsify fermentation broth. So we amplified and cloned the swrw gene encoding the biosurfactant synthase in S. marcescens H30. A swrw mutant by mutagenesis with the suicide vector was constructed successfully. The flask experiment results of the swrw mutant on the basis of optimized medium showed that the swrw inactivation had no effect on the growth and 2,3-butanediol production. In 3.7L bioreactor, the swrw mutant was performed fermentation experiments using constant residual sucrose concentration fed batch-RQ control strategy. The maximum 2,3-butanediol concentration of 152g/L was obtained at 57h.4. Cloning, characterization and expression of the genes involved in 2,3-butanediol pathway from S. marcescens H30Based on the genome sequence of Serratia genus, we successfully cloned the genes involved in 2,3-butanediol pathway from S. marcescens H30. The

sequencing result showed the budA, budB and budR genes, encoded α-acetolactate decarboxylase (α-ALDC), α-acetolactate synthase (α-ALS) and a LysR type regulatory factor, located in one operon designated acetoin operon. While the budC gene encoded 2,3-butanediol dehydrogenase (acetoin reductase) exsited in another position of the genome. Search of the knowledge database comfirmed that this was the first report of the genes involved in 2,3-butanediol pathway from S. marcescens H30. Bioinformatics analysis showed that the strengths of the budA, budB and budC genes were 780bp, 1686bp and 786bp respectively, and encoded proteins of 259, 561 and 261 residues. Their molecular weights and isoelectric points were 28.96kD and 5.48, 60.7kD and 5.88, 27.43kD and 5.51. They were acidic proteins judged from the calculated pI values. Expression products of the genes with pET28a system exhibited comparable molecular weights using SDS-PAGE analysis.

【中文名称】药物先导化合物发现和优化技术
【英文名称】New Principles in Drug Design
【研究起始时间】2006-12
【研究终止时间】2010-12
【中文关键词】药物设计，集中组合库，基于活性碎片的药物设计，从头设计
【英文关键词】Drug design，focused library design，fragment-based drug design，de novo drug design
【中文摘要】发展了三种全新的药物先导化合物发现和优化技术，即集中组合库设计程序、基于活性碎片的新化合物设计程序和活性分子从头设计程序。其中，应用活性分子从头设计程序，针对免疫抑制药物靶标亲环素A，在国际上首次发现了全新结构的纳摩尔水平抑制剂，研究成果发表在本领域主流期刊《美国药物化学杂志》（J. Med. Chem. 2009, 52, 5295-5298）；应用集中组合库设计程序，针对抗疟疾靶标半胱氨酸蛋白酶Falcipain-2，发现了新颖结构的抑制剂，部分抑制剂表现出与现有药物氯喹相当的体内活性，部分研究成果发表在本领域主流期刊《美国药物化学杂志》（J. Med. Chem. 2009, 52, 4936-4940）；应用活性碎片组装方法，分别针对抗艾滋病靶标CCR5受体和抗肿瘤药物靶标VEGFR-2，发现了多个新颖结构的先导结构。以上三种发展的技术极大的提高了药物先导化合物发现的速度和成功率，并得到了实验验证。相关技术可以作为示范，广泛应用于各种重大疾病靶标先导化合物的发现研究。目前，共发表SCI文章27篇，申请发明专利8项。
【英文摘要】Three new Principles in Drug Design have been developed, including focused library design,fragment-based drug design,and de novo drug design.

【中文名称】中药分期序贯方案治疗轻中度溃疡性结肠炎的临床研究
【英文名称】Clinical research of Traditional Chinese medicine staging sequential treating mild or moderate ulcerative colitis
【研究起始时间】2006-10
【研究终止时间】2010-10
【中文关键词】中药；溃疡性结肠炎；临床研究
【英文关键词】Traditional Chinese medicine；ulcerative colitis；Clinical research
【中文摘要】背景：中医药是我国溃疡性结肠炎患者广泛采用的治疗方法之一，但由于方药运用杂乱，研究设计欠规范，其临床疗效及安全性有待于进行科学系统的评价。方法：按照多中心、随机、对照的临床研究，将224例轻、中度溃疡性结肠炎患者采用中药分期序贯治疗或者阳性对照药物(美沙拉嗪肠溶片)治疗，观察治疗第2周、第4周、第8周、第12周、第16周、第20周和第24周的症状变化和临床缓解情况，并对用药安全性以及生存质量进行评价，对于进入缓解的患者随访6个月，观察其复发情况。结果：入组224例患者中，试验组115例，对照组109例；其中全分析集（FAS）223例，试验组115例，对照组108例；符合方案集（PPS）199例，试验组106例，对照组93例。治疗24周结束时，试验组证候总有效率92.45%，缓解率64.15%，黏膜愈合率78.89%；对照组的证候总有效率90.32%，缓解率51.61%，黏膜愈合率75.00%。而随访6个月内，试验组复发率13.24%，对照组的复发率14.58%。安全性监测显示，试验组不良反应发生率3.5%，对照组不良反应发生率2.8%，差异无统计学意义。
【英文摘要】Methods: Clinical trial according to the principle of multicenter, randomized and controlled. 224 cases of mild and moderate patients with ulcerative colitis appear by the traditional sequential treatment or positive control drugs (mesalazine) treatment . Observe the symptom change and clinical ease of second week, 4 weeks, 8 weeks, 12 weeks, 16 weeks and 24 weeks . Then evaluate the drug safety and survival quality. To patients with ease, followed up for 6 months and observe their recurrence.Results: The group of 224 patients, 115 cases of experimental group and 109 cases of control group. Full analysis set (FAS) in 223 cases, 115 cases of experimental group and 108 cases of control group. The project set (PPS) in 199 cases, 106 cases of experimental group and 93 cases of control group. After the treatment of 24 weeks , in experimental group , the syndrome effective rate was 92.45%, the response rate was 64.15%, and the mucosa healing rate was 78.89%. In control group , the syndrome effective rate was 90.32%, the response rate was 51.61%, and

the mucosa healing rate was 75.00% . In followed up for 6 months, the recurrence rate of experimental group was 13.24% , and 14.58% of control group. Safety monitoring showed that adverse reaction rate of experimental group was 3.5%, and 2.8% of the control group. The differences were not statistically significant.Conclusion: Patients of mild or moderate ulcerative colitis who accept Chinese medicine staging sequential therapy , can reduce the symptoms faster and induced illness to alleviate. The clinical curative effect non-inferior effect in mesalazine.

【中文名称】新型口蹄疫基因工程疫苗
【英文名称】Novel genetic engeneering vaccine for FMDV
【研究起始时间】2007-07
【研究终止时间】2010-11
【中文关键词】口蹄疫病毒；疫苗；佐剂；腺病毒；表位；抗原
【英文关键词】FMDV;vaccine;adjuvant;adenovirus;epitope;antigen
【中文摘要】新型口蹄疫基因工程疫苗项目针对目前口蹄疫基因工程疫苗研制的三个重要方面进行研究，即：1）抗原表位和病毒抑制性RNAi序列的筛选：通过模拟表位筛选等技术筛选了多个能诱导中和抗体活性的口蹄疫模拟表位；筛选到了能在细胞水平抑制FMDV病毒增殖的RNAi序列。2）基因工程疫苗佐剂及载体研究：BCG佐剂及构建的含佐剂分子的新型核酸疫苗载体能有效提升免疫效果；以FMDV病毒表位构建的HBc类病毒颗粒能在实验动物中诱导保护性免疫；采用自身抗原表达最低化的gutless腺病毒载体降低了腺病毒载体自身的中和抗体，并能延长外源抗原的表达时间。3）对新型基因工程FMDV核酸疫苗进行了中试研究，对疫苗生产工艺、质控及安全性环节进行了分析。上述研究成果有望发展成为新型口蹄疫基因工程疫苗预防猪、牛等FMDV的流行。
【英文摘要】In the present study, three important aspects in the field of FMDV genetic vaccines were studied. i) Antigen epitopes and RNA interference sequences: several mimic epitopes were identified with ability of inducing neutralizing antibody and some short interference RNA were identified to inhibit virus reproduction. ii) Adjuvants and vectors for genetic vaccine: BCG DNA and novel vector including molecular adjuvant could effectively improve immune response. HBc VLP could induce protective immune response and reconstructed gutless adenovirus vector could reduce the neutralizing antibody against vector and prolonged the time course of expression. iii) During the semi-work production of FMDV DNA vaccine, producing craft, quality control and safety were analysed. The results in the study will be with the perspect for developing a novel genetic vaccine to control the epidemic FMDV infection.

【中文名称】精子功能相关蛋白质与疾病
【英文名称】protein related sperm function and desease
【研究起始时间】2006-09
【研究终止时间】2010-10
【中文关键词】精子发生，精子功能，蛋白质
【英文关键词】spermatogenesis,sperm function,protein
【中文摘要】围绕课题目标，本课题组开展了一系列的工作，具体如下：（一）结合蛋白质组学技术，运用蛋白质组高通量策略及功能法策略，构建了一系列与男性生殖生理及其疾病相关的蛋白表达谱系。（二）对精子运动、精子获能、顶体反应、精卵识别和精卵融合等一系列事件中的相关精子功能蛋白开展研究.（三）本课题组在前期对附睾基因和蛋白功能研究的基础上，开展了与MicroRNA相关的一些工作.
【英文摘要】We did many works. (1) construction of proteome profile of male reproductive phisyology and pathaology using proteomics technique.(2)further functional research of proteins involved in sperm motility/capacitation/acrosome reaction/sperm-egg recognition and fusion.(3)some work about MicroRNA.

【中文名称】艾迪康唑的研究与开发
【英文名称】Research and Development of Iodiconazole
【研究起始时间】2006-12
【研究终止时间】2010-12
【中文关键词】艾迪康唑，抗真菌，临床试验
【英文关键词】Iodiconazole, Antifungal, Clinical trial
【中文摘要】本课题主要完成了抗真菌创新药艾迪康唑的I期、II期和部分III期临床试验。I期临床结果显示，本品在健康志愿者耐受性良好，艾迪康唑主要在皮肤局部发挥疗效，吸收入血液非常少。探索并完成了我国首例人体皮肤药代研究，建立了人体皮肤药代“胶带粘贴”取样和分析模型，证实艾迪康唑在人体皮肤表层以高浓度形式储存，并维持24小时

以上，为临床用药方案制定了依据。完成了240例多中心、随机、双盲和安慰剂对照的IIa期临床试验，考察了1%，2%，4%和6%四种浓度和安慰剂的临床疗效。研究证实，2%艾迪康唑乳膏安全有效，与安慰剂存在显著性差异。在此基础上完成了216例多中心、随机、双盲和阳性药对照的IIb期临床试验，考察一日用药一次和一日用药二次两种给药方案。IIb临床研究结果证实，艾迪康唑一日用药一次的痊愈率，一日用药两次的有效率和痊愈率均明显优于目前市售最佳药物联苯苄唑。全面开展了多中心、随机、双盲和阳性药物对照的III期临床试验，目前已经完成200例。

【英文摘要】Phase I, phase II and part of phase III clinical trials of iodiconazole, a novel antifungal agent, were finished in the present study. The results of phase I clinical trial indicated that iodiconazole had good tolerance for healthy volunteers and mainly functioned at skin. Only a small portion of iodiconazole can be absorbed into blood. The first study of skin pharmacokinetics in china was finished. The ‘ adhesive tape ’ model was built for sampling and bio-analysis. The results of skin pharmacokinetics revealed that iodiconazole could be accumulated in epidermis with high concentration and long time (> 24h), which provided useful information for dosage regimen. A randomized, double-blind, multicentre, placebo-controlled phase IIa trial of iodiconazole was performed for 240 patients. The clinical efficacy of four kinds of formulations, namely 1%, 2%, 4% and 6%, were evaluated. As a result, 2% iodiconazole cream is effective and safe, whose efficacy is significantly better than that of placebo. In the following randomized, double-blind, multicentre, positive drug-controlled phase IIb trial, flexible dosing regimens (once a day and twice a day) were evaluated. The results of this comparative clinical trial showed that the cure rate of treatment with 2% iodiconazole twice a day is significantly higher than that of bifonazole. A randomized, double-blind, multicentre, and comparative phase III trial of iodiconazole is in progress.

【中文名称】多囊肾病治疗药物先导化合物的设计、合成和药理研究
【英文名称】无
【研究起始时间】2007-06
【研究终止时间】2010-11
【中文关键词】新型PPAR-γ 激动剂，多囊肾病，治疗药物，药物代谢，安全评价
【英文关键词】无
【中文摘要】通过课题组的集体努力，设计合成了全新结构的系列PPAR 激动剂，进行了化合物抗肿瘤及抑制多囊肾上皮细胞活性的体外筛选，构效关系分析，完成初步药代试验，完成化合物的在体筛选工作，确定了五种优选化合物，并完成放大合成。与瑞士苏黎世大学合作，开展优选化合物的体内药效学实验，完成了化合物的安全性研究，并初步阐明了化合物对多囊肾病细胞模型中 -catenin信号通路的作用及其机制。至2010年，本课题发表SCI论文8篇（IF合计22.6），申请国际专利1项，获得国家专利1项。培养博士研究生4名、硕士研究生2名。
【英文摘要】无

【中文名称】新型免疫融合蛋白佐剂的临床前研究
【英文名称】New immune adjuvant fusion protein in preclinical studies
【研究起始时间】2006-12
【研究终止时间】2010-12
【中文关键词】Osteopontin;Monoclonal antibody; Humanization
【英文关键词】骨桥蛋白;单克隆抗体;人源化
【中文摘要】本项目利用基因工程的手段，将全人源的抗体恒定区与FL融合表达，组成融合蛋白免疫佐剂，将该融合蛋白佐剂与HBsAg一起融合表达，组成新型的复合疫苗；在乙肝疾病模型中检验该佐剂打破免疫耐受，提高融合疫苗诱发免疫应答的能力。该融合蛋白免疫佐剂与抗原一样，均为蛋白质，可在基因水平融合形成一个蛋白分子，同时具备了各自的功能，使大规模表达和纯化成为可能，同时由于成分单一，简化成品的质量控制标准。更为重要的是，在该蛋白免疫佐剂融合基因的基础上，更换合适的前述强免疫逃逸病毒的抗原基因，在合适的动物模型体内，也能够达到打破免疫耐受的目的。
【英文摘要】The project expressed the Fc fragment of human antibody fused with FL as the fusion protein adjuvant. This adjuvant was fused with HBsAg to form a new compound vaccine. The ability of adjuvant to break immune tolerance and to induce immune responses in hepatitis B disease model was tested. The fusion protein as immune adjuvant and antigen, are both proteins. They could be fused on the gene level and expressed as a protein molecule. They also have their own functions. This characteristic makes it possible to prepare it in large-scale. Because of its simple component, the quality control is simplified. More importantly, on the base of the adjuvant fusion protein gene, it is more suitable to replace the antigen gene of strong immune escaping virus, and can also achieve the purpose of breaking immune tolerance in appropriate animal models in vivo.

【中文名称】口服长效促胰岛素激素超产菌的构建及应用
【英文名称】The construction and application of Oral long-acting insulinotropic hormone high-yielding strains
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】口服长效 毕赤酵母 GLP-1 糖尿病
【英文关键词】oral long acting,Pichia pastoris,GLP-1,diabetes
【中文摘要】本研究采用十拷贝串连重复基因表达策略，构建高表达口服长效促胰岛素的毕赤酵母超产菌株，进行200L-5吨规模发酵试验，完成发酵工艺、分离纯化、制定剂型，研制口服长效促胰岛素片剂、胶囊和注射用针剂样品，以糖尿病大鼠为动物模型研究其降血糖活性、促胰岛素作用、抑制β细胞凋亡、半衰期以及免疫学活性等，为研制具有“治标治本”特殊疗效的口服降糖药物和其产业化奠定基础。
【英文摘要】In this study, ten tandem repeats gene expression strategy was used to construct oral long-acting insulin high expression Pichia pastoris strains. Furthermore， we proceeded the 200L-5 tons scale fermentation tests, complete the fermentation, purification, formulation development, and the development of oral long-acting insulin tablets, capsules and injection sample injection. We also chose diabetic rats as animal model to study the hypoglycemic activity of insulin, inhibition of β-cell apoptosis, immunological activity and the half-life.This study laid the foundation for the development of oral hypoglycemic drugs and their industrialization.

【中文名称】Illumina Goldengate 384k 高通量耳聋基因筛查芯片的设计、研发及其对遗传性耳聋家系的检测
【英文名称】Designing and development of Illumina Goldengate 384k high-throughput BeadArrey for deafness gene mutations screening, and screening for patients in deafness pedigrees
【研究起始时间】2008-09
【研究终止时间】2011-03
【中文关键词】耳聋；基因；基因芯片；突变；筛查
【英文关键词】Deafness; gene; BeadArrey; mutation; screen
【中文摘要】目的：设计、制备Illumina Goldengate 384K高通量耳聋基因筛查芯片，采用此芯片以期在更广的范围内对已知耳聋突变位点进行筛查和对耳聋大家系进行已定位耳聋位点的排除定位。方法：芯片设计原则：由于芯片的引物探针需间隔60bp以上才能确保准确的杂交，故我们在找出所有已知耳聋相关突变位点的基础上，首先挑选出目前文献报道有2篇以上的突变位点，再依据60bp距离尽可能多的将剩余的突变位点设计在芯片上，一共选取了240个耳聋相关突变位点，包括77个显性突变位点及163个隐性突变位点。另外，我们在亚洲人群中报道的已克隆耳聋相关基因中，选取了144个SNP位点，整张芯片共384个检测点。该芯片可进行已知耳聋相关突变位点的高通量筛查和耳聋相关家系的初步排除定位。我们通过对465例DNA样本进行Illumina GoldenGate 384K高通量耳聋基因芯片筛查，统计芯片Call rate、对其准确性进行了验证、对芯片中144个SNP位点的等位基因频率进行了统计分析及对芯片的排除定位连锁分析进行了验证。对90个耳聋家系的135例DNA样本的芯片检测结果进行分析。结果：1.芯片总的
【英文摘要】Objective: Designing and development of Illumina Goldengate 384k high-throughput BeadArrey. Screen for patients in deafness pedigrees and exclude locus for large deafness pedigrees by use of the BeadArrey.Methods: Design principles: Interval of 60bp for primer probe was needed to ensure accurate cross over on BeadArrey. So we selected mutations which have been reported twice, and then put the other mutations on the BeadArrey according the design priciple. Totally 240 mutations were selected, including 77 dominant mutations and 163 recessive mutations. On the other side, we selected 144 SNPs in deafness genes which were reported in Asian populations. Therefore, the BeadArrey we designed could screen for the deafness gene mutations and exclude locus for large deafness pedigrees. We conducted a call rate statistics and accurate verification for the BeadArrey. An allele frequency analysis of the 144 SNPs and exclusive location analysis were carried on. Finally, we analyzed the test results of BeadArrey for 135 DNA samples of 90 deafness pedigrees which were collected by ENT clinic of Xiangya Hospital and State Key Laboratory of Medical Genetics in 1997-2010.Results: 1. Total Call rate of the BeadArrey was 96.32%, 110 of 384 test points’ Call rate were 100%. 2. False negative rate was 3 / 97 (3.1%) and false positive rate was 0 for test point GJB2_235delC. 3. Minimum allele frequencies of 19 SNPs in 8 genes were less than 0.1 (10%). 4. The region located by BeadArrey was similar to which was located by traditional micro-satellite scan. 5. We detected 31 mutations of 12 genes in the BeadArrey screening for 135 patients. 189 mutations which might be the rare mutations in Chinese deafness were not detected. Detection rate of GJB2_1_BP_DEL_235C and SLC26A4_IVS7-2A>G were the same as previous reports. But mutations like PJVK(DFNB59)_1_ BP_DEL_988G（57.36%） and SLC26A4_Gly497Ser（7.14%）which were not the hot mutations had a high detection rate.Conclusions: Illumina Goldengate 384k high-throughput BeadArrey could test more mutations for the patients and exclude locus for large deafness pedigrees. PJVK(DFNB59)_1_BP_DEL_988G（57.36%） and

SLC26A4_Gly497Ser（7.14%）et al which were not the hot mutations had a high detection rate. To find the reason whether they are snps or the low accuracy, in the next step, we will conduct a accurate verification for more test point and remove the points with low call rate , mutation frequency and accuracy, add in the other mutation points which did not add in the BeadArrey as a result of the principle of 60bp Interval. We will remove the SNPs which allele frequencies are less than 10% and add in the other SNPs in the similar position.

【中文名称】基因芯片技术在散发非综合征性耳聋基因诊断中的应用
【英文名称】Application of DNA Chips in Clinical Genetic Testing for Sopratic genetic Deafness
【研究起始时间】2008-09
【研究终止时间】2011-03
【中文关键词】非综合征型耳聋，突变，基因，GJB2(或CX26)，大前庭水管综合征(EVAS或LVAS)，SLC26A4(或PDS)，mtDNA，PE，DHPLC，基因芯片，X-连锁，母系遗传
【英文关键词】non-syndromic hearing loss(NSHL)，mutation，gene，GJB2(or CX26)，enlarged vestibular aqueduct syndrome(EVAS)，SLC26A4(or PDS)，mtDNA，PE，DHPLC, gene chips, x-linkage, maternally inherite
【中文摘要】基因芯片技术在散发非综合征性耳聋基因诊断中的应用第一章　基因芯片技术应用于耳聋基因检测的可行性研究目的：分析基因芯片技术应用于非综合征性耳聋基因检测的准确性，为建立新的基因检测方法提供依据。 方法：通过对122例散发的非综合征性耳聋患者进行芯片及测序的双盲检测实验，验证GJB2_235delC在这些散发样本中的分布情况 结果：随机选取的122例样本的GJB2_235delC的芯片检测与测序结果完全吻合，该法的准确率达100%。结论：该款芯片具有快速、高通量、高准确性、等特点，适合于大样本量遗传性耳聋的基因检测。第二章 基因芯片检测技术在散发非综合征性耳聋患者中的应用目的：应用Goldengate耳聋基因芯片检测散发非综合征性耳聋患者，研究散发非综合征性耳聋的热点突变基因及关联分析，为建立新的基因检测方法提供依据及模型。 方法：对389例散发DNA样本（其中正常人DNA样本102例，散发非综合征性耳聋患者的DNA样本287例）进行芯片检测，应用关联分析研究耳聋及所选位点的相关性 结果：6个位点WFS1_Leu829Pro、GJB3_Arg32Trp、OTOF_IVS5+
【英文摘要】Application of DNA Chips in Clinical Genetic Testing for Sopratic genetic DeafnessChapter I：Feasibility Investigation of DNA Chips Applied in Clinical Genetic Testing for Sopratic genetic DeafnessObjectives: To investigate the feasibility of DNA Chips, and to found a new genetic detecting technology, we use the Illumina Goldengate gene chips in this part. Methods: In order to test the feasibility of DNA Chips, we detected the GJB2_235delC mutation in 122 sporadic NSHL individuals through DNA Microarray and DNA sequencing at the same time. Results: The results get from the DNA Chips is the same as the traditional methods of sequencing. The detecting rate is 100%. Conclusion: Illumina GoldenGate DNA Chips appears to have some inherent advantages in genetic diagnosis of NSHL, such as low time consuming, high performance and accuracy, which make it fit to be used in clinic practice. Chapter II：Clinical Application of DNA Chips in Rapid Genetic Testing of Sopratic Non-Syndromic Hearing LossObjectives: To detect the hot genes in sporadic NSHL patients and the association analysis between these genes and genetic deafness. Methods: 389 sporadic patients were collected and detected by Illumina GoldenGate DNA Chips . Results: WFS1_Leu829Pro, GJB3_Arg32Trp, OTOF_IVS5+1, TMIE_IVS2_2, PCDH15_3_BP_DEL_5601_5603aac and SLC26A4_Gly497Ser appeared negative correlation with NSHL; While rs4809261、rs7421943、MYH14_Arg726Ser、 TMPRSS3_ PRO404LEU、rs878042、COCH_MET512THR、 MYO3A_IVS7_2、TMC1_Tyr259Cys、GJB2_Arg165Trp、rs10515535、rs568619、rs7600176、rs3664、WHRN(DFNB31)_IVS2+1、rs4679155及COL9A3_ 9_BP_DEL_541_549ggtccccca appeared positive correlation with NSHL Conclusion: The Illumina GoldenGate DNA Chips dependent new technique could be well applied for mutation detecting of deafness genes and confirmed the high genetic heterogeneity of genetic deafness.

【中文名称】非核苷类抗乙肝病毒候选药物W28F的临床前研究
【英文名称】non-clinical research of Non-nucleoside compound W28F
【研究起始时间】2008-10
【研究终止时间】2010-12
【中文关键词】非核苷类药物，W28F，临床前研究
【英文关键词】Non-nucleoside compound， W28F，non-clinical research
【中文摘要】异噻氟定（Isothiafludine），W28F，是中科院上海药物研究所科研人员基于海洋天然产物Leucamide A罕见的双杂串联结构单元，经深入系统的构效关系（SAR）研究，获得的具有全新结构的非核苷类抗乙肝病毒（HBV）病毒候选药物，其全面的临床前研究工作已经完成，已申报SFDA临床研究。
【英文摘要】Isothiafludine (W28F), a non-nuclioside compound, was obtained from leucamide A. Through SAR analysis and bioactivity test, Isothiafludine was identified as a drug candidate for the treatment of HBV infection. All Non-clinical studies have been

completed. SIMM has submitted the application to commence clinical trials.

【中文名称】多功能热化疗纳米载药材料的制备
【英文名称】Preparation of multifunctional hot chemotherapy nanometer materials
【研究起始时间】2009-07
【研究终止时间】2009-10
【中文关键词】Fe3O4，氨基修饰，PNIPAM
【英文关键词】无
【中文摘要】实验目的：制备Fe3O4@Au@PNIPAM多功能热化疗纳米材料。方法：采用化学沉淀法制备Fe3O4@Au@PNIPAM粒子，通过扫描电镜分析其形态，粒径仪分析其粒径分布及所载电荷，磁滞回线图分析其磁性。结果：所得纳米粒子形态均匀，粒径分布稳定，磁性好。结论：制得良好的Fe3O4@Au@PNIPAM多功能热化疗纳米材料。
【英文摘要】无

【中文名称】多功能热化疗纳米载药材料载药性能的研究
【英文名称】Function of drug-carried Multifunctional nano materials hot chemotherapy
【研究起始时间】2009-10
【研究终止时间】2010-03
【中文关键词】载药
【英文关键词】drug carrier
【中文摘要】实验目的：多功能热化疗纳米载药材料载药性能的研究。方法：HLPC方法检测PBS中紫杉醇浓度，近红外线对纳米载药系统进行照射以控制紫杉特尔的释放，制定药物释放曲线。结果：得到药物检测方法及释放曲线。
【英文摘要】无

【中文名称】CGD免疫学机制及干预研究
【英文名称】research on the immunogical mechanism and intervention of chronic graft dysfunction
【研究起始时间】2003-01
【研究终止时间】2008-12
【中文关键词】器官移植；慢性失功；存活率；纤维化；免疫抑制剂；缺血再灌注
【英文关键词】organ transplantation; chronic dysfunction; survival rate; immunosuppressant; ischemia/reperfusion
【中文摘要】从特异性免疫学因素、非特异性免疫学因素和非免疫因素出发，结合二次研究和原始研究，揭示CGD免疫学机制，探讨新的干预方法，取得了系列阶段成果：1）基于全球近29.6万余例各种实体器官不同时间存活率的统计数据，综合利用分层聚类和森林图等方法，首次发现边缘供肾移植可作为划分高低存活率移植器官的标准；单独胰腺、小肠、肺和肾移植后胰肾、心肺联合移植是高发早发CGD器官。2）系统评价了HTK和UW液对供肝贮存的影响及HLA配型对不同术式移植胰腺存活率的影响；3）发现IRI可致小鼠肝细胞两种MIC分子上调表达，参与肝脏CGD的发生发展。4）发现CsA可抑制肾小管上皮细胞对糖的吸收，形成高糖环境，从而促进NRK52E 细胞纤维化相关因子的表达，提示免疫抑制剂可致纤维化。5）发现免疫抑制剂致CGD主要通过调节受者激活Smads和抑制性Smads，影响移植肾组织TGF-β1信号通路；CsA、FK506可上调Smad2表达和下调Smad7表达；TGF-β1表达增高促使CGD发生；MMF和Rapa则相反，可延缓和减轻CGD发生；小剂量CsA和MMF联合应用综合效果最好。6)发现中药益生注射液可以下调IRI诱导
【英文摘要】This study has some series findings from three points including specific immunological factor, nonspecific immunological factor and nonimmunological factor: 1) The graft survival rates in different solid organ transplantations changed regularly and the graft loss had organ specificity. The organs of lower graft survival were DD-ECDK, PTA, PAK, In, DD-Lu and H-Lu; 2)performed systematic review to evaluate the effect of HTK & UW solution on the liver graft and the effect of HLA typing on the outcome of transplanted pancreas of different surgery; 3)Ischemia/reperfusion injury could induce the expression of MIC in the mice liver and contribute to the progress of liver CGD; 4)CsA could inhibit the sugar absorption of renal tubular epithelial cells and thereby promote NRK52E cell expression of fibrosis-related factors, suggesting that immunosuppressive drugs can cause fibrosis; 5) YM injection could down regulate the MIC expression induced by IRI; 6) Using single-chain antibody recognized by activated T cells specifically, built the selective removal molecules targeted on the activated T cell molecules.

【中文名称】973计划项目总结报告

【英文名称】The Summary Report of 973 Plan projects
【研究起始时间】2007-08
【研究终止时间】2011-12
【中文关键词】重症肝炎；动物模型；诊断
【英文关键词】severe hepatitis;animal model;diagnosis
【中文摘要】课题组经过五年的研究，已经筛选出一批可用于提示重症肝炎发生、早期诊断、病情转归的分子靶标IFN-γ、TRAIL-R2和NGAL，在此基础上，初步建立定量RT—PCR技术、ELISA技术等能提示重症发生、早期诊断、病情监测和疗效评估的诊断方法，并通过临床标本研究这些方法用于重症肝炎早期诊断、病情监测和疗效评估的可行性。
【英文摘要】After five years study of research group, we have screened many molecular targets (e.g. IFN - γ , TRAIL-R2 and NGAL)which can be used to indicate severe hepatitis occurrence, early diagnosis and illness turnover.Based on this, we preliminarily established quantitative RT-PCR technology, ELISA technology and so on, which can suggest the diagnostic method of intensive occurrence, early diagnosis and condition monitoring and clinical assessment of efficacy. We study the feasibility of these methods used for early diagnosis of severe hepatitis, condition monitoring and clinical assessment of efficacy by the clinical specimens.

【中文名称】抗肿瘤创新药物——酪氨酸激酶抑制剂的研究
【英文名称】Research and development of tyrosine kinase nhibitor,molecular target anti-cancer drug
【研究起始时间】2005-01
【研究终止时间】2009-12
【中文关键词】酪氨酸激酶，抑制剂，筛选，评价
【英文关键词】Tyrosine kinase, inhibitor, screen, evaluation.
【中文摘要】围绕功能基因组中一个在细胞生长和分化中起着主要和关键调控作用的蛋白激酶家族——蛋白酪氨酸激酶家族及其信号通路为研究对象，开展并完成了药物筛选和机理研究两大方面的工作
【英文摘要】无

【中文名称】国家重点基础研究发展计划（973计划）
【英文名称】国家重点基础研究发展计划（973计划）
【研究起始时间】2003-12
【研究终止时间】2008-08
【中文关键词】慢性移植物失功 器官移植 CGD预警指标
【英文关键词】慢性移植物失功 器官移植 CGD预警指标
【中文摘要】本课题设计着眼于CGD早期相关免疫分子的动态变化规律、预警价值的研究，目前为止基本完成课题预定的计划任务，包括利用生物芯片技术筛选和验证CGD患者具有特异性和诊断价值的基因组学和蛋白组学的改变，建立CGD预警体系并进行临床组织病理学验证；通过一项多中心，前瞻性的临床研究筛选出尸体肾移植患者发生急性排斥反应 /移植肾功能延迟的各种高危因素，并建立一个量化的数学模型和评分系统；建立相关动物模型，针对特定CGD相关分子进行干预，验证干预疗效，进一步延长移植物存活时间。1）慢性移植物失功是影响移植物长期存活的主要原因之一，慢性移植物失功（慢性排斥反应）的早期诊断和鉴别诊断是临床器官移植最主要的问题。目前诊断慢性移植物失功主要是依据移植物穿刺活检的病理组织学变化，然而穿刺活检有较多的弊端。本课题建立了一种更为灵敏、可靠的检测手段来及早发现、诊断慢性移植物失功。2）分析肾移植患者发生移植肾功能延迟恢复的危险因素及建立风险预测评分系统）生物芯片确定CGD预警指标，建立预警体系3）干预筛选确定的兴趣分子和通路，验证对移植物功能的影响
【英文摘要】本课题设计着眼于CGD早期相关免疫分子的动态变化规律、预警价值的研究，目前为止基本完成课题预定的计划任务，包括利用生物芯片技术筛选和验证CGD患者具有特异性和诊断价值的基因组学和蛋白组学的改变，建立CGD预警体系并进行临床组织病理学验证；通过一项多中心，前瞻性的临床研究筛选出尸体肾移植患者发生急性排斥反应 /移植肾功能延迟的各种高危因素，并建立一个量化的数学模型和评分系统；建立相关动物模型，针对特定CGD相关分子进行干预，验证干预疗效，进一步延长移植物存活时间。1）慢性移植物失功是影响移植物长期存活的主要原因之一，慢性移植物失功（慢性排斥反应）的早期诊断和鉴别诊断是临床器官移植最主要的问题。目前诊断慢性移植物失功主要是依据移植物穿刺活检的病理组织学变化，然而穿刺活检有较多的弊端。本课题建立了一种更为灵敏、可靠的检测手段来及早发现、诊断慢性移植物失功。2）分析肾移植患者发生移植肾功能延迟恢复的危险因素及建立风险预测评分系统）生物芯片确定CGD预警指标，建立预警体系3）干预筛选确定的兴趣分子和通路，验证对移植物功能的影响

【中文名称】积极性优生途径－植入前胚胎基因诊断技术的临床应用和推广
【英文名称】Active eugenic---the application of preimplantation genetic diagnosis
【研究起始时间】2007-07
【研究终止时间】2010-11
【中文关键词】优生，植入前遗传学诊断
【英文关键词】Active eugenic；preimplantation genetic diagnosis
【中文摘要】植入前遗传学诊断(PGD)是借助体外受精，单细胞遗传学分析技术，从第三天的胚胎中活检一个细胞进行遗传学分析，再将无病胚胎移植回母体子宫，是一种将诊断时机前移到胚胎期的新型的产前诊断技术。相比于传统的产前诊断技术，PGD可避免绒毛活检、羊膜腔穿刺存在的感染风险和异常妊娠后选择性流产问题，是一种积极性优生的新途径。我们建立了单个卵裂球荧光原位杂交（FISH）、单细胞巢式/多重巢式PCR、扩增前引物延伸、简并寡核苷酸引物PCR以及全基因扩增结合巢式PCR等单细胞多基因多位点的分析技术。此外，我们还创建了可有效拓宽基因病和染色体病的诊断范围的单细胞比较基因组杂交技术和间期核转化技术。利用我们建立的单细胞染色体和单基因分析平台，我们完成了150余例的染色体病PGD,同时我们也进行了进行性肌营养不良（DMD）、囊性纤维病、家族性腺瘤性结肠息肉（FAP）、X连锁的无丙种球蛋白血症(XLA)等多个单基因遗传病的PGD.
【英文摘要】Preimplantation genetic diagnosis (PGD) is an alternative form of prenatal diagnosis in which the genetic testing is performed on one blastomere from a day 3 embryo. By combining IVF with single-cell genetic analysis at the preimplantation stages, PGD allows unaffected embryos to be identified and transferred to the uterus. Compared with the traditional prenatal diagnosis, PGD potentially avoids the use of therapeutic pregnancy termination and its potential complications including hemorrhage and infection after of Amniocentesis and chorionic villus sampling (CVS). With the establishment of single blastomere fluorescence in situ hybridization (FISH), single-cell nested / multiplex nested PCR, pre-amplification primer extension, degenerate oligonucleotide primers PCR, and whole genome amplification with nested PCR technology, we have developed single-cell chromosome and single gene genetic analysis platform. Furthermore, we estatblished the methods of single-cell comparative genomic hybridization and single-cell interphase nuclear conversion, With the genetic analysis platform, we have complete more than 150 cycles of chromosomal disease PGD, some single gene disorders such as Duchenne's muscular dystrophy DMD , familial adenomatous polyposis (FAP) ,X-linked agammaglobulinemia (XLA) PGD has been also attempted or successfully completed in our institute.

【中文名称】布鲁氏菌抗体cELISA检测试剂盒临床试验总结
【英文名称】Brucella antibody cELISA test kit clinical trials Summary
【研究起始时间】2010-04
【研究终止时间】2010-05
【中文关键词】布鲁氏菌cELISA检测试剂盒，临床试验，检测规程，总结
【英文关键词】Brucella cELISA kit, Clinical Trials, test procedures, summary
【中文摘要】中国农业科学院哈尔滨兽医研究所和中国兽医药品监察所联合研制了布鲁氏菌抗体cELISA检测试剂盒，制定了试剂盒制造与检验规程和质量标准草案。哈尔滨维科生物技术开发公司按拟定制造及检验规程（草案）进行中试生产。2010年4月~5月，生产5批（2010001，2010002，2010003，2010004，2010005）试剂盒。按着拟定试剂盒质量标准（草案），检验合格。在黑龙江省齐齐哈尔市兽医卫生防疫站、黑龙江省巴彦县兽医卫生防疫站和黑龙江省动物卫生监督所进行临床试验，结果表明试剂盒与试管凝集试验（SAT）和虎红平板凝集试验（RBPT）的符合率均为93%以上，与SAT的符合率最高，对羊符合率达96.4%，对牛的符合率达97.4%。
【英文摘要】Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences and the China Veterinary Drug Control jointly developed Brucella antibody cELISA test kit, developed a test kit manufacturing procedures and quality standards with the draft. Harbin Vico biotechnology development company by developing manufacturing and testing procedures (draft) for pilot production. April 2010 to May, producing five groups (2010001,2010002,2010003,2010004,2010005) kit. Kit according to the development of quality standards (draft), inspection. Qiqihar City, Heilongjiang Province, veterinary health and epidemic prevention stations, veterinary Bayan County, Heilongjiang Province and Heilongjiang Province Health and Epidemic Prevention Station of the animal health supervision for clinical trials, results showed that the kit and tube agglutination test (SAT) and rose bengal plate agglutination test (RBPT) compliance rates were 93%, the highest rate of compliance with the SAT, in line with rate of 96.4% for sheep, cattle line rate of 97.4%.

【中文名称】布鲁氏菌抗体cELISA检测试剂盒生产中间试制报告

【英文名称】Brucella antibody cELISA test kit production of intermediate trial report
【研究起始时间】2010-01
【研究终止时间】2010-05
【中文关键词】cELISA,试剂盒,试制
【英文关键词】cELISA,Kit, production
【中文摘要】应用提纯好的马耳他布鲁氏菌M5-90的sLPS包被商品化Costar的ELISA板,将单克隆抗体16C5冻干,制备的阳性血清,弱阳性血清和阴性血清,试制了5批共250个试剂盒,内参检测表明满足实验要求,达到标准。
【英文摘要】Application of good purification Brucella Melitensis sLPS M5-90 package is the commercialization of Costar ELISA plates, freeze-dried monoclonal antibody 16C5, prepared by the positive serum, a weak positive serum and negative serum, trial of five batches of 250 kit, internal reference testing that meet the test requirements, meet the standards.

【中文名称】经导管人工生物主动脉瓣膜置换动物实验
【英文名称】Transcatheter replacement of an aortic valve prosthesis：an animal feasibility study
【研究起始时间】2009-07
【研究终止时间】2010-12
【中文关键词】主动脉瓣膜置换；经导管；动物实验
【英文关键词】aortic valve prosthesis replacement；transcatheter；animal study
【中文摘要】目的：探索经导管人工生物主动脉瓣膜置换动物实验的可行性和安全性。方法：将自膨胀镍钛支架三叶式猪心包瓣膜装配入18F 导管输送系统，在X 线和超声引导下，经颈总动脉逆行性放置到8 只健康的实验用绵羊主动脉瓣膜位置。植入前、后即刻进行主动脉根部及左心室造影、超声心动图检查评估植入支架瓣膜的功能及对冠脉血流灌注及二尖瓣功能等的影响。结果：6 只实验动物植入支架瓣膜成形良好，无移位，冠脉血流未受影响，可见微量瓣周漏。因瓣膜位置放置不良导致2 只实验动物术中死亡，其中1 例因为瓣膜植入位置过深，影响到二尖瓣开放与闭合，引起急性心功能不全；另1 例因为瓣膜植入位置偏高，影响到冠状动脉血流，导致急性心肌梗死和恶性心律失常。结论：经颈总动脉逆行性植入支架式主动脉生物瓣膜动物实验取得初步成功，近期效果满意。
【英文摘要】Objective：To explore the feasibility and safety of transcatheter aortic valve prosthesis replacement in a sheep model. Methods：Under the guidance of fluoroscopy and echocardiography, the self-expanding nitinol stents integrated with porcine pericardialvalves were transcatheterly implanted at the native position of eight sheep through the common carotid artery using 18F delivery systems. Immediately after the procedure, the aortic-root angiogram, left ventriculargraphy and echocardiography were carried out to evaluate the function of the prosthetic valve and its influence on coronary flow or mitral valve. Results：Six animals were successfully implanted with the prosthesis without obstruction of the coronary artery orifice. The procedure failed in two sheep as a result of malposition. Lethal heart failture occurred in one sheep due to too inferior positioning of the prosthesis, and the other died of acute myocardial infarction related life-threatening ventricular arrhythmia with too superior positioning of the prosthesis. Conclusion：The aortic valve prosthesis consisted of self-expanding nitinol stent and porcine pericardial valve, and could be successfully implanted using a retrograde approach via the common carotid artery with gratifying immediate outcomes.

【中文名称】基于肝细胞生长因子受体C-Met的抗肿瘤先导化合物研究
【英文名称】The study of anti-tumor leading compounds targeting HGF receptor c-Met
【研究起始时间】2004-01
【研究终止时间】2009-09
【中文关键词】W014，HGF，C-Met抑制剂，抗肿瘤化合物
【英文关键词】W014, HGF, inhibitor of C-Met, anti-tumor drug
【中文摘要】肝细胞生长因子（Hepatocyte Growth factor，HGF）又称离散因子（SF），是一种具有多种重要生物学活性的细胞因子，其特异性膜受体是原癌基因c-met的表达产物。在多种肿瘤组织中已发现HGF/C-Met信号通路异常活化，这种异常活化参与并调控肿瘤的发生、发展或转移；阻断HGF/MET信号途径可有效抑制肿瘤细胞生长、侵袭和转移。HGF/MET已被国际公认为抗肿瘤的靶标。根据HGF/C-Met的生物学特性，我们建立了一套基于C-Met抗肿瘤先导化合物的高通量细胞筛选平台，通过对两千多种小分子化合物的筛选，发现多种可抑制HGF诱导细胞离散的活性化合物。进一步研究发现一种化合物W014在微摩尔水平能够有效地抑制C-Met的磷酸化，并阻断HGF诱导的C-Met下游的AKT活化。体外实验表明W014可抑制多种高表达C-Met肿瘤细胞的增殖，尤以对HepG2（人肝癌细胞）的作用最为显著。体内实验表明W014 可有效抑制HepG2细胞接种裸鼠肿瘤的生长。上述结果表明W014可作为针对C-MET抗肿瘤的先导化合物，为进一步的药物研究奠定基础。

【英文摘要】Hepatocyte growth factor (HGF), also known as scatter factor (SF), is a multifunctional cell factor which predominantly expressed in mesenchymal origin. C-Met tyrosine kinase is the only known high-affinity receptor for HGF. C-Met and HGF are dysregulated in human cancers and are also believed to contribute to the development， progression and metastasis of cancers . Preliminary studies show inhibiting the HGF/C-Met cell signal path will retrieve the growth, invasion and metastasis of tumor cells. HGF/MET have be represented a world-wide recognized target for cancer therapy. According to the biological characteristics of HGF/C-Met, we devised a platform to screen new drugs for cancer. Screened about 2000 compounds, we find one Compound named W014, which belong to derivate of indolin-2-one. W014 could inhibit the activation of HGF/C-Met cell signal path and PI3K cell signal path in the low nanomolar range. Although W014 can inhibitor the growth of many kinds of tumor cell, it brings more conspicuous result to HepG2. The results show W014 can be a lead compound for cancer therapy, and lay the foundation of new medicine.

【中文名称】抑郁严重程度功能核磁共振成像评估及临床应用
【英文名称】无
【研究起始时间】2008-01
【研究终止时间】2011-10
【中文关键词】抑郁症；功能核磁共振成像；临床应用
【英文关键词】无
【中文摘要】采用医学功能影像技术在体观察中国汉族抑郁症患者的脑功能状态，结合临床抑郁症状严重程度评定、神经心理测试结果，分析其间的相关性，提取新的抑郁症功能影像学信息诊断指标，该指标旨在为抑郁症提供早期干预；评测抑郁症脑功能恢复的状态，为抑郁症维持治疗的持续时间提供客观依据；研究自组织机制，设计决策支持系统的在线学习和优化机制，旨在以简洁的系统知识体系提供完善的诊疗方案，方便的融合病理药理上的新发展，并能进行快速的系统自调整使之适应当前具体患者的诊疗需要，使治疗方案根据治疗进展能够及时动态调整；追溯和临床跟踪患者病情发展，设计合理的数据库结构。
【英文摘要】无

【中文名称】血管生成素功能分析
【英文名称】Functional analysis of angiogenin
【研究起始时间】2009-03
【研究终止时间】2009-09
【中文关键词】血管生成素；核糖核酸酶；血管拟态；脐静脉内皮细胞
【英文关键词】angiogenin, Ribonuclease, vascular mimicry, Umbilical vein endothelial cells
【中文摘要】血管生成素（Angiogenin，ANG；亦称RNase A family 5）可以特异性地定位于血管内皮细胞及一些肿瘤细胞的细胞核，在血管新生和肿瘤发生中起重要作用，但其具体的作用机制尚未完全明了。microRNA是一类非编码小RNA，通过在转录后水平对基因表达的调控而影响生物学过程，包括血管生成及肿瘤形成等，但目前并不了解其与ANG的关系。为此，本论文从直接受ANG调控的microRNAs和直接靶向调控ANG的microRNAs 两个方面研究了ANG特异的microRNAs及其生物学功能。第一部分基础性实验主要包括1）脐静脉血管内皮细胞（HUVEC）的分离培养及鉴定；2）分离纯化的ANG蛋白活性检测，包括其核转位活性及核糖核酸酶活性；3）确定HT1080细胞为ANG的靶细胞；4）筛选合适细胞并建立多种体外血管生成功能分析模型；5）作为miRNAs 的对照，设计针对ANG基因的siRNA序列，并确定其在各种细胞中对ANG的干扰作用。
【英文摘要】Angiogenin (Angiogenin, RNase A family 5) is a critical factor involved in angiogenesis and tumorigenesis. It can translocate to the nucleus of HUVECs and bind to the genomic DNA, but the mechanism of ANG-induced angiogenesis or tumorigenesis is still unclear. MicroRNAs are small non-coding RNAs, which regulate gene expression post-transcriptionally and are considered to play important roles in many biological events, including angiogenesis and tumorigenesis. However, the microRNAs involved in ANG related biological processes have not identified yet. Thus, exploring both the ANG regulated microRNAs and the microRNAs targeting to ANG are two aspects of this thesis to elucidate the ANG-specific microRNAs and their biological functions.The first part of work includes: 1) isolation of HUVE cells, 2) isolation and purification of ANG protein, 3) identify HT1080 cell as a target cell of ANG, 4) screen appropriate model for angiogenesis, 5) effect of ANG knock-down by RNAi.

【中文名称】受血管生成素调控miRNA的筛选
【英文名称】Screening of miRNAs regulated by Angiogenin

【研究起始时间】2009-10
【研究终止时间】2010-09
【中文关键词】血管生成素；miRNA；芯片；启动子
【英文关键词】angiogenin, miRNA, array, promoter
【中文摘要】为探索受ANG影响和调控的microRNAs，本论文首先利用microRNA芯片筛选的方法，在血管内皮细胞中鉴定受ANG刺激后表达发生改变的microRNAs。通过筛选，共得到了26个在ANG刺激前后发生差异表达的microRNAs，包括17个上调和9个下调的microRNAs。生物信息学分析显示，这些microRNAs参与多种生物学过程，包括肿瘤发生和转移、血管生成、神经发育、细胞凋亡等。利用数据库MicroCosm，初步预测了这些microRNAs的靶基因。另一方面，本论文利用ChIP-on-Chip方法探索了ANG与microRNAs启动子区的结合情况，发现有121个microRNAs启动子区可能与ANG结合，其中有9个启动子控制的microRNAs与上述利用microRNA芯片筛选得到的受ANG直接调控的microRNAs相同，包括8个上调和1个下调的microRNAs。在此基础上，利用ChIP-QPCR的方法对所得到的部分microRNA启动子区做进一步验证，发现miR-149、miR-17、miR-378和miR-641等确实受ANG的调控，说明ANG具有转录因子的活性，可
【英文摘要】To explore the ANG regulated microRNAs, first we employed a microRNA Chip to screen the ANG-specific or ANG-regulated microRNAs in HUVECs. After ANG stimulation, the expressions of 26 microRNAs were altered in HUVECs, including 17 up-regulated microRNAs and 9 down-regulated microRNAs. The function and the potential targets of these microRNAs were analyzed by a bioinformatics approach. Overall, these microRNAs were reported to involve in many biological processes, including tumorigenesis and metabasis, angiogenesis, neural development, and apoptosis. The potential targets of these microRNAs were predicted with the MicroCosm Database. Furthermore, a ChIP-on-Chip assay was carried out to explore whether ANG can bind to microRNA promoters to regulate the transcription of certain microRNAs. Data showed that 121 microRNA promoters could be potentially bound by ANG, 9 of which were identified as ANG regulated microRNAs as well, including 8 up-regulated and 1 down-regulated microRNAs. Partial bindings were validated with a ChIP-QPCR assay, including the ANG bindings to miR-149, miR-17, miR-378, and miR-641 promoter regions, suggesting that ANG could up-regulate their transcriptions as a transcriptional factor.

【中文名称】靶向血管生成素的miRNA研究
【英文名称】Study of miRNAs targeting angiogenin
【研究起始时间】2009-03
【研究终止时间】2010-12
【中文关键词】血管生成素；miRNA；小鼠；结直肠癌
【英文关键词】angiogenin, miRNA, mice, colorectal cancer
【中文摘要】ANG是一个在血管内皮细胞和肿瘤细胞中高表达的蛋白质，本身也可能受到microRNAs的靶向调控。为此，本论文首先通过生物信息学方法预测得到8个可能靶向结合到ANG基因3’UTR的microRNAs，然后分析了它们对ANG mRNA和蛋白质表达水平的影响，发现miR-1208、miR-196b、miR-296、miR-409、miR-570和miR-641共六个microRNAs确实可以调节ANG的表达，并对靶细胞的增殖、迁移、粘附和管腔形成均有一定影响。在此基础上，本论文着重对miR-409进行了较深入的研究，发现miR-409不仅可以抑制内皮细胞的管腔形成和细胞增殖，也可以抑制肿瘤细胞HT1080的增殖及血管拟态；小鼠移植瘤实验也证明了miR-409可以抑制肿瘤的生长、血管生成和转移。进一步，本论文在结肠癌病人的组织中发现miR-409的表达较相应癌旁组织的表达下降，并且miR-409的表达与肿瘤的转移密切相关。以上结果说明ANG本身可以受多种microRNAs的调控，其中miR-409可以直接靶向下调ANG的表达，影响ANG在血管生成及肿瘤发生、发展中的作用。
【英文摘要】ANG was reported to be highly expressed in both vessel endothelial cells and tumor cells, suggesting itself might be a regulating target of microRNAs. In order to find the microRNAs targeting to ANG-3’UTR, bioinformatic analysis was employed to predict the potential candidates, and 8 microRNAs were chosen for further validation of their bindings to ANG-3’UTR. Among them, six microRNAs, i.e. miR-1208, miR-196b, miR-296, miR-409, miR-570, and miR-641 could inhibit ANG mRNA and protein expression and show various repression effects on cell proliferation, cell migration, cell adhesion and tubular formation. Especially, miR-409 was found not only to inhibit HUVECs cell proliferation and tubular formation, also inhibit vascular mimicry and cell proliferation of tumor cell HT1080. Furthermore, miR-409 could inhibit tumor growth, angiogenesis and metastasis in in vivo tumor xenografts in nude mice. In addition, the expression of miR-409 in colorectal cancer was lower than the corresponding tumor-adjacent tissues, meanwhile the clinical outcomes of the patients are related with miR-409 expression, expecially tumor metastasis. Thus, ANG could be regulated by different microRNAs, and miR-409 can affect angiogenesis, tumorigenesis and metastasis through negtively regulating ANG expression.

【中文名称】分子、细胞和整体动物水平的酪氨酸激酶抑制剂药物筛选模型的建立
【英文名称】无
【研究起始时间】2004-09
【研究终止时间】2009-09
【中文关键词】酪氨酸激酶、荧光偏振、细胞锚着、JAK/STAT信号通路、Met信号通路
【英文关键词】无
【中文摘要】根据目前国际上各大药厂所公认并采用的抗肿瘤药物分子靶点建立了一系列的分子水平的高通量药物筛选模型。这些模型的优势是易于高通量化，并且筛选得到的是靶点和机制都明确，并且针对性很强的激酶抑制剂。我们目前已经获得下列10种具有酪氨酸激酶活性的功能蛋白，建立了基于ELISA原理的稳定、高效、灵敏的分子水平评价模型：
【英文摘要】无

【中文名称】活性化合物的筛选和功能研究
【英文名称】无
【研究起始时间】2004-09
【研究终止时间】2009-09
【中文关键词】酪氨酸激酶、信号通路、血管生成、选择性抑制、EGFR、STAT-1
【英文关键词】无
【中文摘要】（1）来源于植物的活性化合物CCA9的作用机理研究（2）外源性糖链MdOS广谱抑制酪氨酸激酶，进而影响相关信号通路，抑制新生血管生成（3）小分子化合物BB选择性抑制EGFR酪氨酸激酶活性（4）小分子化合物AL3810的抗肿瘤作用研究（5）STAT-1信号通路调节剂Wed及其功能研究（6）STAT-3信号通路调节剂APC-003及其功能研究（7）Met抑制剂及其功能研究（8）强效特异的无磷酸拟肽Grb2-SH2抑制剂研究
【英文摘要】无

【中文名称】PGE2和LXR在糖尿病胰岛β细胞损伤中的作用和机制研究
【英文名称】The Roles and Mechanisms of PGE2 and LXR in Diabetes
【研究起始时间】2005-09
【研究终止时间】2009-07
【中文关键词】糖尿病；胰岛β细胞；PGE2；肝X受体；功能损伤
【英文关键词】Diabetes, Pancreatic β cell, PGE2, LXR, Dysfunction
【中文摘要】糖尿病是由于胰岛素绝对或相对不足引起的一种全身性代谢紊乱综合症。目前认为，胰岛β细胞功能障碍是1型和2型糖尿病发病的主要原因，但是其机制仍不清楚，本文将从以下方面对糖尿病胰岛β细胞损伤的机制进行探讨：一、PGE2在1型和2型糖尿病胰岛β细胞功能损伤中均发挥着十分重要的作用，但是其具体机制尚未阐明。本研究首次发现PGE2通过激活JNK信号通路，引起Akt和FOXO1去磷酸化，促使FOXO1入核，PDX1出核，最终导致β细胞胰岛素分泌障碍；二、在2型糖尿病发病过程中，血糖和血脂持续升高是胰岛β细胞数量减少和功能障碍的重要原因，但是其具体机制仍有争议。最近的一些研究显示葡萄糖和氧化固醇都是细胞内核受体肝X受体（Liver X Receptor, LXR）的内源性激动剂。我们推测随着2型糖尿病的发生发展，不断增高的血糖和血脂将引起LXR的异常激活，进而导致胰岛β细胞功能衰竭。本研究发现LXR激动剂能够剂量依赖性地抑制胰岛β细胞的增殖，而且，LXR是通过抑制SKP2介导的p27蛋白降解，上调细胞内p27蛋白水平，导致β细胞G1期到S期细胞周期阻滞和生长抑制，从而导致胰岛β细胞数量减少的，
【英文摘要】Diabetes is a chronic systematic syndrome caused by absolute and relative inadequancy of insulin. Pancreatic β cell dysfunction is the common cause of type 1 and type 2 diabetes. But the mechanism is not fully understood. The aim of this study was to explore the mechanisms of the pancreatic β cell dysfunction in the following aspects,First, accumulating evidence suggests that inflammatory cytokines, including prostaglandin E2 (PGE2), play an important role in β cell dysfunction in both types of diabetes, but the underlying mechanism is not clear. In this study, we reveal for the first time that PGE2-mediated JNK activation, through de-phosphorylation of Akt and FOXO1, leads to nuclear accumulation of FOXO1 and nucleocytoplasmic shuttling of PDX1, finally resulting in defective glucose-stimulated insulin secretion (GSIS) in pancreatic β cells.Second, under type 2 diabetic conditions, progressive increases in the levels of blood glucose and lipid are important reasons for the reduction in β cell mass and β cell insulin secretion. Recent studies indicate that both glucose and some kinds of lipids are the endogenous ligands of the Liver X receptor (LXR). We speculate that with the development of type 2 diabetes progressive increases of both blood glucose and lipid would lead to aberrant

activation of LXR, which might be involved in pancreatic β cell failure. In the present study, we find that the LXR agonist dose-dependently inhibits pancreatic β cell proliferation. Inhibition of SKP2-mediated degradation of p27 and upregulation of cellular p27 protein levels, resulting in cell cycle arrest from G1 to S phase, is involved in LXR activation mediated β cell growth inhibition. These observations suggest the involvement of aberrant LXR activation in β cell mass inadequacy, which is an important step in the development of type 2 diabetes.In summary, in the present study we investigate the mechanisms of pancreatic β cell dysfunction in diabetes in the areas of inflammatory cytokine signaling pathway, cell cycle regulation and cell energy metabolism. We report for the first time that PGE2-induced JNK-Akt-FOXO1-PDX1 signaling pathway and LXR activation mediated cell cycle arrest and cell energy metabolism impairment are important mechanisms of β cell failure in diabetes. Our findings contribute to the understanding of the molecular mechanisms of β cell dysfunction induced by cytokines, glucotoxicity as well as lipotoxicity, and provide potential new clues for the prevention and therapy of diabetes.

【中文名称】白藜芦醇对3T3-L1前脂肪细胞成脂分化以及TNF-α诱导的脂肪因子表达的影响

【英文名称】The effect of resveratrol on adipogenesis of 3T3-L1 preadipocyte and tumor necrosis factor-α (TNF-α) induced adipokines expression in adipocytes

【研究起始时间】2006-09

【研究终止时间】2008-07

【中文关键词】白藜芦醇；3T3-L1前脂肪细胞；Sirt1；肿瘤坏死因子-α；单核细胞趋化因子-1；核因子-κB

【英文关键词】Resveratrol; 3T3-L1 preadipocytes; Sirt1; Tumor necrosis factor-α; monocyte chemoattractant protein-1; Nuclear factor-κB

【中文摘要】目的：（1）观察白藜芦醇对3T3-L1前脂肪细胞成脂分化的影响；（2）探讨白藜芦醇对肿瘤坏死因子-α（TNF-α）诱导的脂肪因子表达的影响及其机制。方法：（1）通过CCK-8法检测Sirt1激动剂—白藜芦醇对3T3-L1细胞增殖活力影响，油红O染色法、甘油三酯GPO-POD酶法测定白藜芦醇对3T3-L1细胞脂肪含量增长的影响情况，借助于甘油含量测定试剂盒检测3T3-L1脂肪细胞脂质分解的情况；（2）分别以不同浓度白藜芦醇、核因子-κB（NF-κB）的抑制剂—BAY11-7082或Sirt1抑制剂—Sirtinol和TNF-α共同处理成熟3T3-L1脂肪细胞，用定量PCR技术、ELISA技术检测各条件下白介素-6（IL-6）、单核细胞趋化蛋白-1（MCP-1）以及脂联素基因转录、蛋白分泌情况；（3）分别以不同浓度白藜芦醇或Sirtinol和TNF-α共同处理转染含IL-6、MCP-1启动子的荧光素酶报告质粒的HEK293细胞，通过荧光素酶基因报告技术检测各组的荧光素酶活性；（4）TNF-α（10ng/ml）处理表达质粒（pcDNA-Sirt1或pCMV-IκBα）与荧光素酶报告质粒共

【英文摘要】Objective: (1) To determine the effect of resveratrol, a Sirt1 activator, on adipogenesis of 3T3-L1 preadipocyte. (2) To investigate the effect of resveratrol on tumor necrosis factor-α (TNF-α) induced adipokines expression in adipocytes.Methods: (1) The 3T3-L1 post-confluent preadipocytes and lipid-filled adipocytes were incubated with resveratrol (0 to 100 μM) for up to 48 hours. Viability was determined using the CCK8 cell proliferation assay. Post-confluent preadipocytes were incubated with resveratrol for up to 6 days during maturation, adipogenesis was quantified by measuring lipid content using triglyceride assay kit. The cells were also stained with Oil Red O for visual confirmation of effects on lipid accumulation. Mature 3T3-L1 adipocytes were incubated with resveratrol or TNF-α for 2h, lipolysis was quantified by measuring glycerine content in supernatant.(2) Differentiated 3T3-L1 adipocytes were pretreated with or without various concentrations of resveratrol for 6 h, and then were stimulated for 12 or 24h by the addition of 10ng/ml TNF-α. The mRNA expression levels of monocyte chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6) and adiponectin were detected by quantitative RT-PCR. The protein content of MCP-1, IL-6 and adiponectin in conditioned medium were measured by ELISA. (3) HEK293 cells were transfected with firefly luciferase reporter construct, pSV-βgal plasmid and expression vector（pCMV-IκBα or pcDNA-Sirt1). Twenty four hours after transfection, cells were untreated or treated with 10ng/ml TNF-α for 6 h. The luciferase and β-galactosidase activities were measured. (4) 3T3-L1 adipocytes were preincubated for 6 h with different concentrations of resveratrol (10-50 μM), followed by 1h incubation with 10ng/ml TNF-α. Nuclear extracts were prepared and then assayed for nuclear factor-κB (NF-κB) activation. (5) HEK293 cells were transfected with pcDNA-Sirt1 or pcDNA3.1 vector. Twenty four hours after transfection, cells were treated with or without TNF-a (10 ng/ml) for 1 h, and nuclear extracts were prepared and then assayed for NF-κB activation by electrophoretic gel mobility shift assay (EMSA).Results: (1) In post-confluent preadipocytes and mature adipocytes, resveratrol(≥75 μM) caused a time-related and dose-dependent decrease in viability. Resveratrol also inhibited adipogenesis of 3T3-L1 preadipocytes. Resveratrol (50 μM) mediated inhibition of adipocyte differentiation occurred during the early, intermediate stages of the differentiation process. Resveratrol (10~50 μM) did not increase the release of glycerol into the culture medium compared with control 3T3-L1 cells. (2) Resveratrol could attenuate the TNF-α induced IL-6 and MCP-1 expression and secretion in a dose-dependent manner, and partially recovered adiponectin expression and secretion which was suppressed by the addition of TNF-α in a dose-dependent fashion. (3) Overexpression of IκBα inhibited TNF-α-induced IL-6 and

MCP-1 promoter activities. (4) Resveratrol elicited dose-dependent inhibitory effects on TNF-α-induced DNA binding activity of the NF-κB complex. (5) Overexpression of Sirt1 inhibited TNF-α-induced NF-κB-dependent transcription activities, though no effect on TNF-α-induced DNA binding activity of the NF-κB complex was found.Conclusions: (1) Resveratrol can decrease fat cell mass by direct inhibition on cell viability and adipogenesis in 3T3-L1 cells. (2) Resveratrol attenuates the TNF-α induced adipokines expression and secretion in 3T3-L1 adipocyte by direct repression of NF-κB binding activity, and indirect inhibition of NF-κB dependent transcription activity through activation of Sirt1.

【中文名称】脂肪细胞与原代肝细胞共培养诱导肝细胞在细胞水平上发生胰岛素抵抗
【英文名称】Fat cells induces insulin resistance in primary hepatocytes
【研究起始时间】2005-09
【研究终止时间】2007-07
【中文关键词】3T3-L1脂肪细胞肝细胞；胰岛素抵抗；胰岛素受体底物-2；AKT
【英文关键词】Adipocytes; hepatocytes; insulin resistance(IR); IRS-2; AKT
【中文摘要】目的：研究不同分化阶段的脂肪细胞对肝细胞胰岛素抵抗的影响，对肥胖与2型糖尿病的关系作进一步的探讨。方法:体外诱导分化3T3-L1前体脂肪细胞，随着细胞内脂滴增加，逐步成为不同分化程度的脂肪细胞。采用不同分化阶段脂肪细胞（未分化Day0、中期分化Day4、接近完全分化Day8）与原代肝细胞共培养，用ELISA方法检测诱导分化的脂肪细胞、肝细胞、共培养细胞所分泌的细胞因子，以Western bolt方法检测共培养后肝细胞内胰岛素信号通路的反应性，借助于同位素标记葡萄糖方法检测肝细胞糖原合成能力。结果：与单独培养肝细胞相比，共培养后肝细胞内胰岛素受体底物-2酪氨酸磷酸化（Tyr612）（pIRS-2）水平及Akt磷酸化（Ser473）（pAkt）水平均显著下调；肝糖原合成也明显降低。结论：脂肪细胞可诱导肝细胞发生胰岛素抵抗，而且肝细胞胰岛素信号通路反应性的下调与脂肪细胞的分化程度呈正相关。
【英文摘要】Objective : To assess the effects of adipocyte on the development of hepatic insulin resistance. Methods : Hepatic cells were co-cultured with fat cells at various stages of differentiation and the effects of fat cells on insulin signal transduction and glycogen synthesis in hepatic cells were evaluated. Results : Insulin – induced tyrosine phosphorylation of IRS-2 was significantly inhibited. Insulin-related activation of Akt kinase and glycogen production in the hepatocytes were also reduced after co-culture, and the reduction was positively correlated with the differentiation of co-cultured fat cells. Conclusion: Adipocyte differentiation might induce insulin resistance in hepatocytes. To our knowledge, our data present firstly the direct evidence of interaction for insulin signaling event between the adipocytes and hepatocytes.

【中文名称】地塞米松部分通过Foxo1引起胰岛β细胞功能障碍
【英文名称】Dexamethasone Induces Pancreatic beta Cell Dysfunction Partially Through Foxo1 Transcription Factor
【研究起始时间】2005-09
【研究终止时间】2008-07
【中文关键词】糖皮质激素；地塞米松；胰岛β细胞功能障碍；Foxo1；PDX-1
【英文关键词】Glucocorticoid; Dexamethasone; Pancreatic β-cell dysfunction; Foxo1; PDX-1
【中文摘要】糖皮质激素类药物，在临床上广泛应用于治疗多种疾病，但长期、大量地使用会产生一些严重的副作用，包括类固醇性糖尿病(steroid diabetes mellitus, SDM)。类固醇性糖尿病发生的分子机制仍不十分清楚。FOXO蛋白家族作为胰岛素/胰岛素样生长因子（INS/IGF）信号通路中的关键调节因子，在胰岛β细胞功能障碍中可能发挥着重要作用。在本研究中我们探讨了糖皮质激素类药物地塞米松对胰岛β细胞系RINm5F内FOXO家族成员Foxo1表达及活性的影响。地塞米松能够诱导RINm5F细胞中Foxo1的表达，且该作用是糖皮质激素受体（GR）依赖性的。此外，地塞米松可以下调Foxo1的磷酸化水平及其上游磷酸化的AKT水平，并且PI-3kinase/Akt信号通路的激动剂IGF-1能够逆转该作用。然而，糖皮质激素受体竞争性拮抗剂不但不能拮抗地塞米松下调p-AKT及p-Foxo1水平的作用，而且还发挥了与地塞米松相似的作用。PDX-1作为Foxo1在胰岛β细胞内重要的靶基因，其表达水平下降与胰岛β细胞功能障碍相关。荧光素酶报告基因方法证明了地塞米松可以促进RINm5F细胞内Foxo1的转
【英文摘要】Glucocorticoids are widely used in clinical therapy and steroid diabetes is one of the side effects of glucocorticoid treatment. The molecular mechanisms involved in the process of steroid diabetes are not fully understood. The Foxo proteins, key transcriptional effectors of insulin and IGF signaling pathways could have important role in β-cell dysfunction. In this study, we investigated the role of synthetic glucocorticoid, dexamethasone in the expression and activity of Foxo family member Foxol in β-cells. Dexamethasone induced Foxo1 expression in pancreatic β (RINm5F) cells and this effect was glucocorticoid receptor (GR)-dependent. Additionally, dexamethasone decreased the phosphorylation of Foxo1 and the phosphorylation of AKT, upstream of

Foxo1, and stimulant of PI-3kinase/Akt signaling pathway revert this effect. However, GR competitive antagonist couldn't block this effect and played a same role as dexamethasone. The decrease of PDX-1, an important target gene of Foxo1 in β-cells, is involved in β-cell dysfunction. Luciferase reporter studies proofed that dexamethasone could increase Foxo1 transcriptional activity. Through RNA interference,we indicated that dexamethasone reduces PDX-1 expression partially by the increase of active Foxo1. Besides, our research indicated that dexamethasone could induce PDX-1 nuclear export by the increase of nuclear Foxo1.In conclusion, our research suggest that dexamethasone reduces PDX-1 expression partially by the increase of active Foxo1 and could induce PDX-1 nuclear export by the increase of nuclear Foxo1. This novel viewpoint will replenish the molecular mechanism of steroid diabetes and β-cell dysfunction induced by dexamethasone.

【中文名称】苗药有毒药材了哥王的特殊炮制技术研究
【英文名称】Wikstroemia indica (L.) C.A.Mey
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】了哥王；炮制工艺；质量标准；炮制机理
【英文关键词】Wikstroemia indica (L.) C.A.Mey.;Processing technology standardization; Quality standard;Processing mechanism
【中文摘要】提供不同地区了哥王炮制工艺的比较、验证情况；通过对炮制工艺及质量控制等方面的应用研究，确定炮制具体的工艺技术参数，制定和提供规范化的炮制工艺及工艺流程，建立炮制规范；按照《中国药典》的起草说明、起草格式等要求，完成质量标准及其起草说明。阐明了哥王的炮制机理等。
【英文摘要】blank

【中文名称】特需人群补碘方案的研究报告
【英文名称】Research on iodine supply programme for special needed population
【研究起始时间】2009-09
【研究终止时间】2011-01
【中文关键词】特需人群 补碘方案
【英文关键词】specially needed population iodine supply program
【中文摘要】目的：对不同程度缺碘地区的孕期和哺乳妇女口服碘油的时间、剂量、有效期以及对母婴可能产生的负面影响提供指导性意见，确保孕期及哺乳妇女适宜碘营养和胎儿、婴幼儿的正常发育。方法：在新疆生产建设兵团选择碘盐覆盖率不同的地区对孕妇和哺乳妇女在口服碘油丸前，口服后1个月、3个月、6个月和9个月不同时期跟踪上述调查对象的尿碘、盐碘、甲功及乳碘等。结论：对于缺碘的孕妇和哺乳妇女应采用碘油等进行补碘，无论200mg还是400mg均不至于引起病理反应，而对于不缺碘的孕妇和哺乳妇女不建议进行补碘，尤其是大剂量补碘，因为补碘会引起较大的代偿性血液指标波动。
【英文摘要】Objective:Providing guidance to time, dose and validity of oral iodine oil during pregnancy and breast-feeding women in the different iodine-deficient areas and to the negative effects of infant and mother.To ensure that the pregnancy and lactation women have appropriate iodine nutrition and normal development of fetal and infant. Methods: Choose different areas of the iodine salt coverage for pregnant women and nursing women in XinJiang production and construction corps.Before taking iodine oil pill and after 1 month, 3 months,6 months and 9 months in different periods of the object tracking the investigation urine iodine,salt iodine, the thyroid function and breast milk iodine. Conclusion:For pregnant women and nursing lack iodine women should supply iodine with iodine oil, whether 200 mg or 400 mg will not causing pathological reaction.We don't suggest supply iodine for pregnancy with sufficient iodine and lactation women, especially supply large dose of iodine. Because it can cause decompensated blood index volatility largely.

【中文名称】有毒傣药大黑附子的特殊炮制技术研究
【英文名称】Alocasia macrorrhiza (L.) Schot
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】海芋；炮制工艺；质量标准；炮制机理
【英文关键词】Alocasia macrorrhiza (L.) Schot;Processing technology; Quality standard;Processing mechanism
【中文摘要】对傣药有毒药材大黑附子的特殊炮制方法“借雅法”进行研究，通过文献调研及实地考察及化学、药效学、毒理学等方法，规范其炮制工艺，制定其质量标准，初步探讨其炮制机理，揭示民族药炮制的科学内涵。

【英文摘要】blank

【中文名称】我国部分地区孕妇和哺乳妇女适宜的尿碘参考值范围的研究报告
【英文名称】Research on adequate reference value of urinary iodine for pregnant and lactate women in different areas in China
【研究起始时间】2009-09
【研究终止时间】2011-01
【中文关键词】孕妇 哺乳妇女 适宜 尿碘参考值
【英文关键词】pregnant lactate adequate reference value of urinary iodine
【中文摘要】目的：建立我国正常孕妇和哺乳妇女适宜的尿碘水平范围，指导孕妇和哺乳妇女适量补碘，显得尤为重要。方法：采用横断面调查方式，采集不同地区至少50名孕妇和哺乳妇女的1次静脉血和3次随意尿，选择甲功正常的调查对象，检测其尿碘浓度。使用SPSS 13.0统计软件进行数据处理及统计分析。结果及结论：我国正常孕妇的尿碘参考值范围应为90-500μg/L，哺乳妇女的尿碘参考值范围应为70-450μg/L。
【英文摘要】Objective: To build the urinary iodine reference value of the “normal” pregnant and lactating women of our country, to guide the right iodine supplement in pregnant and lactating women are especially important. Method: The cross-section investigation was adopted to collect once venous blood and 3 times urine of at least 50 pregnant and lactating women, the subjects were selected by the thyroid function, the urinary iodine was determined. The data processing and statistic analysis was finished by SPSS 13.0. Conclusion: The urinary iodine reference value of normal pregnant is 90-500 μg/L, and it is 70-450 μg/L regarding lactating women.

【中文名称】充分补碘地区特需人群适宜碘摄入量的研究报告
【英文名称】Research on adequate iodine intake of special needed population in enough iodine supply areas
【研究起始时间】2009-09
【研究终止时间】2011-01
【中文关键词】充分补碘地区 特需人群 适宜 碘摄入量
【英文关键词】adequate iodine supply areas specially needed population adequate iodine intake
【中文摘要】目的：研究充分补碘地区特需人群的适宜的碘摄入量。方法：采用营养与食品卫生行业的摄入量参考值指标（生理需要量、平均需要量和推荐供给量等）进行估算和采用正常孕妇和哺乳妇女的尿碘反向进行推算等方法，确定特需人群适宜的碘摄入量。结论：孕妇、哺乳妇女、婴幼儿的适宜碘摄入量分别为300μg/d、250μg/d和90μg/d。
【英文摘要】Objective: To research on adequate iodine intake of special population in iodine sufficient areas. Method: They were adopted that the method of acceptable daily intake indicators (including physiological requirement, average requirement and recommended supplement) usually used in Nutrition and Food hygiene domain and method of reversal calculation by normal pregnant and lactating women urinary iodine to define the adequate iodine intake for special population. Conclusion: The adequate iodine intake for pregnant, lactating women and infant were 300 μg/d, 250 μg/d and 90 μg/d.

【中文名称】傣药有毒药材榄藤子仁的特殊炮制技术研究
【英文名称】Entada phaseoloides(Linn.)Merr.
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】榄藤子仁；炮制工艺；质量标准
【英文关键词】Entada phaseoloides(Linn.)Merr.;Processing technology ; Quality standard
【中文摘要】榄藤子傣医传统认为生品有毒，需炒熟后服用。按照任务书要求，主要对榄藤子展开文献调研、传统炮制原理、炮制工艺、质量标准、毒性药理、稳定性等研究，为临床提供用药参考。
【英文摘要】blank

【中文名称】PMirP：基于结构序列混合特征的pre-microRNA预测方法软件实验报告
【英文名称】Experimental Report on PMirP: pre-microRNA prediction based on structure sequence hybrid feature software
【研究起始时间】2009-07
【研究终止时间】2009-12
【中文关键词】前体小RNA 混合特征 预测
【英文关键词】pre-microRNA;hybrid feature;prediction

【中文摘要】在科技部863项目支持下,编写了基于结构序列混合特征的pre-microRNA预测方法软件PMirP,内容包括左三元局部编码的计算预测平台PMirP，从而可以根据输入的序列预测pre-microRNA。
【英文摘要】Under support of 863 project, we compile the pre-microRNA prediction software as PMirP which based on structure sequence hybrid feature, the content of which contains left three meta localized encoded computational prediction platform PMirP, that could predict pre-microRNA using input sequences.

【中文名称】基因表达数据的误标记样本检测软件实验报告
【英文名称】Experimental Report on gene expression mislabeled data detection software
【研究起始时间】2009-07
【研究终止时间】2011-07
【中文关键词】基因表达 误标记样本 回归分析
【英文关键词】gene expression;mislabeled sample ;regression analysis
【中文摘要】在科技部863项目支持下,编写了基因表达数据的误标记样本检测软件,内容包括CL-Stability、LOOSE-Sensitivity、CAPIV、PRAPIV等基因表达数据误标记样本检测算法，从而检测和分析基因的表达情况，以消除噪声的扰动。
【英文摘要】Under the support of 863 project, we compile the gene expression mislabeled data detection software, the contents of which includes CL-Stability, LOOSE-Sensitivity, CAPIV\PRAPIV algorithms which could used for gene expression mislabeled data, and then detect and analyze the gene expression, which aims eliminate the disturbing of noise.

【中文名称】基于交叉验证的SVM-RFE特征选择软件实验报告
【英文名称】Experimental Report on cross-validation based SVM-RFE feature selection software
【研究起始时间】2010-07
【研究终止时间】2011-07
【中文关键词】特征选择 支持向量机迭代特征消去法 交叉验证
【英文关键词】feature selection;SVM-RFE;cross-validation
【中文摘要】在科技部863项目支持下,编写了基于交叉验证的SVM-RFE特征选择软件,内容包括基于Bootstraps并得到交叉验证的SVM-RFE特征选择算法，从而从海量的基因芯片数据中挑选出特征基因集合。
【英文摘要】Under the support of 863 project, we compile the feature selection software which based on cross validation of SVM-RFE, the contents of which includes SVM-RFE feature selection algorithm based on bootstraps and validated by cross-validation, and that could select feature gene sets from gene expression microarrays.

【中文名称】基于芯片和新一代测序技术的小麦功能分析软件实验报告
【英文名称】Experimental Report on microarray and next sequencing technology based wheat function analysis software
【研究起始时间】2009-07
【研究终止时间】2011-09
【中文关键词】芯片 新一代测序 小麦 功能分析
【英文关键词】Microarray;next-generation sequencing;wheat;Functional analysis
【中文摘要】在科技部863项目支持下,编写了基于芯片和新一代测序技术的小麦功能分析软件,内容包括小麦功能分析数据库，基于microRNA靶基因表达的作物生物功能与互作网络分析数据库，从而为小麦功能分析和miRNA基因的进一步分析提供软件及其计算平台支撑。
【英文摘要】Under support of 863 project, we compile a suit of wheat function analysis software which based on microarray and next generation sequencing technology, the contents of which includes wheat function analysis database, plants function and interaction network analysis database which based on microRNA target gene expression, the aim of which supports the computation platform for further wheat function analysis and miRNA gene analysis.

【中文名称】土家药有毒药材隔山消的特殊炮制技术研究
【英文名称】Cynanchum auriculatum Royle ex Wight
【研究起始时间】2008-01
【研究终止时间】2010-12

【中文关键词】隔山消；炮制工艺；质量标准；炮制机理
【英文关键词】Cynanchum auriculatum Royle ex Wight;Processing technology; Quality standard;Processing mechanism
【中文摘要】针对土家药“隔山消”以前的米炒工艺进行了改进，对其关键炮制工艺指标进行了优化量化，如炮制温度，炮制时间，药材与炮制辅料的比例。系统地研究了隔山消在炮制前后的主要化学成分、药效（抗炎、促消化、抗肿瘤）、毒性的变化情况，初步揭示了土家药“隔山消”传统炮制工艺的科学内涵。完善了土家药“隔山消”生品饮片及其米炒炮制品的质量控制方法和质量标准，并系统地建立了HPLC指纹图谱。
【英文摘要】blank

【中文名称】不同地区加碘盐浓度的研究报告
【英文名称】Research on iodized salt level of different areas
【研究起始时间】2009-09
【研究终止时间】2011-01
【中文关键词】不同地区 加碘盐浓度
【英文关键词】different areas level of iodized salt
【中文摘要】目的：研究我国不同地区适宜的加碘盐浓度。方法：通过对我国不同地区（南方城市、南方农村、北方城市、北方农村、中部城市、中部农村）等地区的盐摄入量、盐碘含量、碘盐覆盖率、调味品碘摄入量和食品碘含量、水碘含量和居民饮食习惯的分析，得出适于我国不同地区适宜的加碘盐浓度。结果及结论：我国目前适宜采用的盐碘浓度为10-15mg/kg，允许波动范围为食用盐碘含量±30%。南方城市、北方农村地区的碘盐浓度可选择10 mg/kg；中部城市、北方城市、南方农村地区，可选择15 mg/kg的碘盐浓度；为防止居民碘营养水平偏低，中部农村的缺碘地区可选择15 mg/kg的碘盐浓度。
【英文摘要】Objective: To research the adequate iodine level of the salt in different areas. Methods: By investigation the salt intake, salt iodine content, coverage rate of iodized salt, iodine intake in condiment, food iodine, water iodine and residents ’ dietary habit in different areas (South city, South village, North city, North village, Central city and central village), finally obtain the adequate iodine level in salt. Conclusion: The adequate salt content we should take currently is 10-15mg/kg, which has a fluctuation range of salt iodine ±30 percent. The South city and North village should choose the 10 mg/kg, the Central city, North city and South village areas might choose 15 mg/kg, in case of the iodine deficient of residents, the iodine deficient areas in Central village might choose 15 mg/kg iodized salt.

【中文名称】彝药八角枫特殊炮制技术的研究
【英文名称】Alangium chinense(Lour.) Harms
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】八角枫；炮制工艺；质量标准
【英文关键词】Alangium chinense(Lour.) Harms;Processing technology;Quality standard
【中文摘要】探索八角枫的炮制工艺方法，制定八角枫规范化的炮制工艺。制定八角枫饮片质量标准。初步揭示八角枫特殊炮制方法的科学内涵，为临床安全合理用药提供建议。提高彝药的研究水平。
【英文摘要】blank

【中文名称】羌药有毒药材铁棒锤的特殊炮制技术研究
【英文名称】Aconitum pendulum Busch.
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】铁棒锤；炮制工艺；质量标准；炮制机理
【英文关键词】Aconitum pendulum Busch.; Processing technology; Quality standard;Processing mechanism
【中文摘要】结合文献研究和实地调查的方法对羌族地区铁棒棰炮制方法进行调研，并确定出羌医铁棒锤常用炮制方法。结合羌医传统炮制方法，建立了铁棒棰的规范化炮制工艺，并进行了7批中试研究。结合药效、毒性评价和化学成分研究明确了铁棒棰砂炒、蒸制、水煮的炮制减毒原理，并发现了5条减毒途径，其中2条为乌头类生物碱的新的减毒途径。
【英文摘要】blank

【中文名称】基于长链脂肪酸受体的抗糖尿病药物靶标研究
【英文名称】Anti-diabetic drug development on long-chain free fatty acids receptor
【研究起始时间】2007-07
【研究终止时间】2010-11
【中文关键词】GPR40；胰脂肪酶；FABP4；DGAT；糖尿病；靶标确证
【英文关键词】GPR40; pancreatic lipase; FABP4; DGAT; diabetes; drug target
【中文摘要】针对长链脂肪酸受体GPR40、GPR120、胰脂肪酶、FABP4、DGAT等抗糖尿病药物靶标进行了系列研究，开发出多系列小分子化合物成为抗糖尿病先导化合物。1，GPR40和GPR120靶标确认和小分子化合物研究；2，基于天然产物开发的胰脂肪酶抑制剂研究；3，FABP4的小分子抑制剂研究及靶标确认；4，DGAT靶标研究及其小分子抑制剂开发。
【英文摘要】As the receptors of long-chain free fatty acids, GPR40, GPR120, pancreatic lipase, FABP4 and DGAT are related to type 2 diabetes and other metabolism disease. As drug target of type 2 diabetes, the small molecule agonists or antagonists of these proteins could be effective to the therapy of metabolism disease including type 2 diabetes.1, GPR40 and GPR120 as anti-diabetic target;2, development of pancreatic lipase inhibitor;3, development of FABP4 inhibitor;4, development of DGAT inhibitor.

【中文名称】MMP-2抑制性结合肽筛选及其模拟化合物体内、外抗肿瘤作用的研究
【英文名称】Screening of MMP-2 Inhibitory Peptides and Anti-cancer Effects of Their Mimetic Compounds in Vitro and in Vivo
【研究起始时间】2005-09
【研究终止时间】2008-07
【中文关键词】MMP-2；噬菌体展示技术；MTT；荧光分析药物筛选；肿瘤动物模型；肿瘤生长/转移
【英文关键词】MMP-2; phage display technology; MTT; fluorescent assay drug discovery; tumor growth and metastasis
【中文摘要】目 的：1、采用噬菌体展示技术筛选MMP-2抑制性结合肽，观察该短肽体外抑制肿瘤细胞的侵袭作用；2、根据筛选短肽和MMP-2酶活性中心三维立体结构特征，借助生物信息学方法设计并合成系列化合物，经体内、外试验，筛选能够抑制肿瘤生长、转移的化合物。方 法：1. 采用噬菌体展示技术从噬菌体文库中筛选出对MMP-2具有较强亲和力的噬菌体单克隆；2. 用MMP-2的特异性荧光分析药物筛选试剂盒对所筛选的噬菌体单克隆进行再次筛查，找出对MMP-2具有抑制作用的噬菌体单克隆；3. 提取噬菌体DNA，测序，进行序列比对，找出噬菌体PIII末端表达的、与MMP-2结合的多肽的编码序列；4. 体外合成短肽；5. 用MMP-2特异性荧光分析药物筛选试剂盒测定该短肽对MMP-2酶活性的抑制作用；6. 采用Transwell技术，观察该短肽体外抑制肿瘤细胞侵袭作用；7. 根据所筛选短肽结构特点以及MMP-2酶活性中心三维立体结构，借助生物信息学技术设计并合成系列化合物，体外采用MTT法及MMP-2荧光分析药物筛选技术筛选出既可以抑制肿瘤生长又可以抑制MMP-2活性的化合物；8. 复制乳腺癌肿
【英文摘要】Objectives:1. To screen MMP-2 inhibitory peptides from phage display library and observe their effects on tumor cell invasion.2. To design and synthesis compounds using bioinformatics according to the conformation of the selected peptides and MMP-2 active domain.3.To observe the effects of the compounds on tumor cell proliferation in vitro， and tumor growth, invasion and metastasis in vivo.Methods:1. Phages with high affinity to MMP-2 enzyme were selected from phage display library.2. MMP-2 fluorescent assay kit for drug discovery was used to screen the selected phage clones and determine their effect on MMP-2 activity.3. Extracting single-stranded phage DNA and sequencing.4. Synthesizing the peptides in vitro.5. Determining the synthetic peptide effect on MMP-2 activity using MMP-2 fluorescent assay kit for drug discovery.6. Matrigel-coated transwell inserts were used to observe the effects of synthetic peptides on cancer cell invasion.7. According to the conformation of selected peptides and MMP-2 active domain, a series of compounds were designed using bioinformatics and synthesized. All compounds were assayed with MMP-2 fluorescent assay kit for drug discovery and MTT method to determine their effects on MMP-2 activity and cancer cell proliferation.8. Breast cancer nude mice model was made to observe their treatment effects in vivo.Results:1. 22 phage clones with high affinity to MMP-2 enzyme were obtained after screening of phage display library, and all of these clones could inhibit the activity of MMP-2 enzyme. 19 peptides were obtained after sequencing.2. Two peptides were obtained after screening of phage display library and MMP-2 enzyme activity inhibitory effect assay. Their sequences were as follows:M204C4：H W W Q W P S S L Q L R G G G SM205C4: H N W T R W L L H P D R G G G S3. Those two peptides M204C4 and M205C4 inhibited the activity of MMP-2 in the different effects and the inhibitory effects were dose dependent. The median effective inhibiting concentration (IC50) for M204C4 and M205C4 were 78.0 and 38.8 nmoml/L， respectively.4. M204C4 inhibited MMP-2 mediated invasion of the pancreatic cancer cell lines PANC-1 and CFPAC-1 with a dose dependent manner. High concentration (200 nmol/L) of M204C4 significantly inhibited the invasion of these two cell lines than the control (P<0.001). The other two concentrations 60 nmol/L and 20 nmol/L of M204C4 had similar inhibitory effects, but

milder than high concentration.5. M205C4 inhibited MMP-2 mediated invasion of the pancreatic cancer cell lines PANC-1 and CFPAC-1 with a dose dependent manner. The high and middle concentration (100 nmol/L and 30 nmol/L) of M205C4 could inhibit the pancreatic cancer cell invasion significantly. The low concentration (10nmol/L) could inhibit the pancreatic cancer cell invasion, but no difference was observed compared with the control group (P>0.05).6. 48 compounds were synthesized. According to the results of MTT assay and MMP-2 enzyme activity inhibitory assay, WB-1, WB-45 and WB-46 were selected to further investigate in vivo.7. No toxic reaction was observed between the control and the drug administration groups. In the control group, breast cancer metastases were observed in the lung pathologic section, but no metastasis in the WB-1 group. The average weight of the animals in WB-1 administration group was higher than the control group, but no difference was observed. The average tumor weight in the 200mg/kg group decreased to 24.7% of the control group, and the same phenomenon was observed between 100mg/kg and 10mg/kg groups. In the WB-45 and WB-46 group, tumor metastases were observed in almost all lung pathologic sections. In other organs, no metastasis was observed.8. The serum level of VEGF in the WB-1 group (100mg/kg and 10mg/kg) were lower than that in the control group, and a statistical difference was observed between 100mg/kg and the control group (P<0.05).9. The serum levels of pro- and active MMP-2 were lower in the WB-1100mg/kg administration group than that in the control group (P<0.05), but no difference for pro-MMP-9 expression was observed between the drug administration group and the control group.Conclusions:1. Two peptides M204C4 and M205C4 were obtained after screening the phage display library.2. In vitro, M204C4 and M205C4 inhibited the activity of MMP-2 enzyme significantly, meanwhile inhibited MMP-2 mediated pancreatic cancer cell invasion.3. The mimetic compound WB-1 not only inhibited MMP-2 activity and cancer cell proliferation in vitro, but also inhibited tumor growth and metastasis and decreased the serum levels of VEGF, pro- and active MMP-2 in vivo.

【中文名称】适于我国不同地区的防治碘缺乏病技术方案的研究报告
【英文名称】Research on prevention and control of iodine deficiency disorders for different areas in China
【研究起始时间】2009-09
【研究终止时间】2011-01
【中文关键词】不同地区 防治 碘缺乏病 技术方案
【英文关键词】different areas prevention and cure iodine deficiency disorders technology programe
【中文摘要】目的：提出适于我国不同地区的防治碘缺乏病的技术方案。方法：综合上述各研究报告的结果和结论，进行科学地分析，最终提出适于我国不同地区的碘缺乏病技术方案。结论：今后我国的防治策略应为科学补碘，加碘盐浓度应为10-15mg/kg，允许波动范围为食用盐碘含量±30%。南方城市、北方农村地区的碘盐浓度可选择10 mg/kg；中部城市、北方城市、南方农村地区，可选择15 mg/kg的碘盐浓度；为防止居民碘营养水平偏低，中部农村的缺碘地区可选择15 mg/kg的碘盐浓度。碘盐覆盖率≥95%的地区，仅采用浓度为10-15mg/kg的碘盐进行碘营养补充；碘盐覆盖率＜95%且＞80%的地区，采用浓度为20-30mg/kg的碘盐进行补碘；碘盐覆盖率≤80%，且在历史上曾为地克病病区的地区或者查证有新发地克病的地区除采用20-30mg/kg的碘盐进行碘营养补充以外，还应对孕妇、哺乳妇女采用碘油进行应急补碘，补碘制剂为口服碘化油胶丸。补碘剂量和剂次为每人每年口服碘油丸2次，间隔6个月，每次服用200mg。
【英文摘要】Objective: Putting forward the technical solutions that is siutable for different regions of China. Method:Synthesize and scientific analysis the above findings and conclusions,ultimately,raise the suitable technical solutions preventing iodine deficiency disorders in different regions of China.Conclusion: In the future,the strategies should be scientific about preventing iodine deficiency disorders in China.The concentration of iodized salt should be 10-15mg/kg, allowing fluctuations in the range of iodine content of salt ± 30%. Southern cities, northern rural areas can choose iodized salt concentration 10 mg / kg; the central city, northern cities, southern rural areas, choose 15 mg / kg of the salt concentration; In order to preventing residents of low iodine nutrition, rural central iodine-deficient areas can choose 15 mg / kg of salt concentration.The excess Iodized salt supplement concentration of 10-15mg/kg was adapted to the region where the rate of Iodized salt coverage ≥95%;Iodized salt coverage <95% and> 80% of the country, with the concentration of 20-30mg/kg Iodized salt for iodine; In the area where Iodized salt coverage ≤80% used to be called the area of endemic cretinism and the area where was found the new case , pregnancy and lactating women not only use the Iodized salt supplement concentration of 20-30mg/kg, but also use oral iodized oil for emergency iodine supplyment.Oral iodine oil pill was taken 200mg every time,and 2 times per year,six months interval.

【中文名称】肿瘤生长相关的多糖结构和构象分析及其技术
【英文名称】Study on the structure and conformation of anti-cancer polysaccharides and the technique
【研究起始时间】2006-12

【研究终止时间】2008-12
【中文关键词】肿瘤，多糖结构，构象分析，技术
【英文关键词】cancer，polysaccharide structure, conformation, technique
【中文摘要】本项目按原计划的内容顺利完成，并取得优秀成果。建立了6种研究多糖结构和链构象新方法和新技术，并运用这些新方法和新技术研究了有抗肿瘤活性的多糖结构与构象及其相关功能机制。系列成果已在本领域国际专业期刊发表28篇，已申请或获得授权的发明专利共计9项（其中获授权专利3项，申请专利6项）。
【英文摘要】 Six new methods and techniques have been set up to study on the structure and conformation of polysaccharide. Polysaccharides with anti-cancer bioactivities have been studied with these new methods and techniques. Results have been published in 28 papers in the international authorized journal and 9 patents have been applied or granted.

【中文名称】国家高技术研究发展计划(863计划)课题2008年度工作总结
【英文名称】no
【研究起始时间】2008-01
【研究终止时间】2008-12
【中文关键词】先导化合物,构效关系,蛋白酪氨酸磷酸酯酶1B,细胞分裂周期 25(CDC25)磷酸酶，人源促肝细胞再生磷酸酯酶-3（PRL-3）
【英文关键词】no
【中文摘要】本课题在上一年度的基础上，按照课题合同中规定的本年度课题执行计划实施,顺利完成了课题合同中所拟定的内容并取得了一定进展：首先，分析总结了上一年度所合成的PTPs靶向集中化合物库及活性筛选数据，完成Hit和先导化合物的构效关系分析及选择性分析；获取到了针对PTP1B,CDC25B，PRL-3为靶点的化学结构－生物活性信息；其次，针对这些靶点分别进行了靶向集中化合物库的设计、虚拟筛选及类药性分析，从中选择出其中评价较好类型的合成砌块（building block），并进行了靶向集中化合物库及单一化合物的合成。最后，经活性筛选，结构优化及构-效关系研究，分别在这三个靶点上找到可进一步深入研究的先导化合物。在获得抑制PTP1B活性化合物的基础上，选取活性较好的化合物进行了细胞水平CHO/IR测试，发现化合物LZ179，LZ180分别在一定的程度上可增强胰岛素信号通路中关键点胰岛素受体以及下游AKT的磷酸化水平，这表明通过对PTP1B的活性抑制可逆转其对下游底物的去磷酸化能力，从而提高细胞对胰岛素的敏感性。进而我们分别考察了该两个化合物口服治疗对BKS糖尿病db/db小鼠的治疗作用。从初步的
【英文摘要】no

【中文名称】肠出血性大肠杆菌 O157：H7人源化治疗性抗体的研制
【英文名称】Study on the humanized engineering antibody of EHEC O157:H7
【研究起始时间】2006-12
【研究终止时间】2008-12
【中文关键词】肠出血性大肠杆菌 O157：H7；人源化治疗性抗体
【英文关键词】EHEC O157:H7；
humanized engineering antibody
【中文摘要】肠出血性大肠杆菌(EHEC) O157：H7于1975年被首次分离，因其能产生致死性志贺毒素（shiga toxin, Stx），引发溶血性尿毒综合症(Hemolytic uremic syndrom，HUS)等严重并发症，致死率达5～10%，被确认为严重的人兽共患致病菌。其感染已经成为全球公共卫生问题。同时，EHEC O157：H7培养容易、感染力强、传播途径多样，使其极有可能作为未来军事斗争的细菌武器和生物恐怖战剂。美国疾病控制中心（CDC）已将EHEC O157：H7列为B类生物恐怖病原体严加防范。我国曾多次爆发、散发O157：H7感染，当前暴发性流行趋势日益严重。我国已将EHEC列为21世纪可能对国人卫生健康有重大影响的12种病原微生物之一。临床研究证实：使用抗生素可促使O157：H7菌体破裂，“爆发性”释放Stx毒素，使患者死亡的危险性增加。因此，2002年国家卫生部规定：“EHEC O157：H7病人和疑似病人禁止使用抗生素，疫区内的其他一般腹泻病人应慎用抗生素”。目前国内外尚无治疗人O157：H7感染的特效药物。因此，加强对O157：H7感染的防治研究，研制高效、特异
【英文摘要】Shiga toxins (stx) are produced by enterohemorrhagic Escherichia coli (EHEC). Infections with EHEC can lead to a variety of gastrointestinal and systemic complications, such as bloody and non-bloody diarrhea, hemorrhagic colitis, and hemolytic-uremic syndrome (HUS). However, an epidemiological study indicated that treatment of EHEC O157:H7 infection cannot involve antibiotics because they can sometime increase the incidence of HUS due to the pathogen. Stxs have been divided into 2 subtypes, stx1 and stx2. Stx2 is usually more strongly associated with clinical disease than stx1 when consider from the standpoint of both epidemiological and experimental studies. Furthermore, the two types of toxins are AB5 holotoxins that are comprised of a single

enzymatically active A subunit (32 kDa) that non-covalently associates with multiple B subunits (7.6 kDa). The A subunit that acts as an N-glycosidase removes an adenosine residue from the 28S rRNA of the 60S ribosome, inhibits protein synthesis, and this in turn leads to cell death. The B subunit is responsible for binding to target cells via its glycolipid receptor, the globotriaosyl ceramide (Gb3) or Gb4 cellular receptor. The crystal structure of stx2 shows the A subunit to consist of the A1 portion (28 kDa) covalently associated with the A2 portion (4 kDa) through a disulfide bond. The A2 peptide forms an α-helix and traverses the pore of the B-pentamer. The tyrosine residue (A77) of the A1 portion forms the catalytic site. Despite decades of research, we still lack an effective prevention and therapy for EHEC infections, and novel therapeutic strategies have yet to be found. Thus, it is important to investigate the A subunit, especially of the toxic active fragment, i.e. the A1 subunit of the shiga toxin. The humoral immune response evoked by Stx2A1 can more effectively prevent EHEC O157:H7 infections, with the antibody raised to Stx2A1 having a better specificity against the toxin. However, the use of rodent antibodies in a therapeutic setting has the disadvantage that repeated administrations of such monoclonal antibodies often result in a human anti-mouse (HAMA) immune response. So producing human antibodies had become an emergency problem. An alternative approach to these humanization techniques is the use of epitope guided selection (EGS) in recently years. Firstly, the Fd or Lc gene of a murine anti-Stx2a1 antibody was paired with a repertoire of human light chain or heavy chain, and displayed on the filamentous phage forming a hybrid phage antibody library. The selected human light chain or heavy chain were in turn paired with a repertoire of human Lc or Fd fragments forming a human phage antibody library, then human Fab antibodies that binds to an epitope of the original rodent antibody are isolated. In the study, we constructed a murine Fab phage antibody library against the toxic fragment (stx2a1) of Shiga Toxin II from EHEC O157:H7 and adopted EGS for humanization murine Fab phage antibody library, it would lay a solid foundation for its further application in the therapy of infection with shiga-like toxin from EHEC O157:H7.

【中文名称】国家高技术研究发展计划（863计划）课题自验收报告
【英文名称】no
【研究起始时间】2006-12
【研究终止时间】2008-12
【中文关键词】集群式高通量筛选,蛋白酪氨酸磷酸酶,靶向集中化合物库,构效关系,蛋白酪氨酸磷酸酯酶1B ,人源促肝细胞再生磷酸酯酶-3（PRL-3）,白细胞共同抗原相关蛋白(LAR),蛋白酪氨酸磷酸酯酶SHP-1,SHP-2,细胞分裂周期磷酸酶cdc25B
【英文关键词】no
【中文摘要】课题研究期间，通过基因质粒构建，酶的表达纯化，活性测定方法的确认研究，针对已建立的31个分子水平蛋白酪氨酸磷酸酶（Protein Tyrosine Phosphatases，PTPs）高通量筛选模型，集中肿瘤、糖尿病、感染性疾病等重大疾病的有限目标，选择其中有代表性的PTP家族成员PTP1B, PRL-3，SHP1, SHP2，Cdc 25 及LAR，优化和完善了高通量筛选的条件及技术，制定了高通量筛选的质量控制标准。并应用上述6个PTPs模型对 48000 个化合物进行集群式高通量筛选（初筛的化合物浓度为2 μg/mL），发现了一批具有活性的化合物，经复筛验证了其活性。这一工作的完成为本课题的开展奠定了良好的基础。与此同时，通过文献检索和数据库搜寻，收集近50个PTPs和小分子抑制剂复合物的3D结构进行分析。由此发现，尽管其催化域结构比较相似，但其结合位点处仍有一定程度的不同。在此基础上，通过结构联配建立了32个结合位点的模型，并形成数据库，作为以后进行Docking分析的基础。在本课题研究过程中，发展靶向集中化合物库以及高效化学合成技术研究，针对PTPs，构建了14个化合物
【英文摘要】no

【中文名称】自体口腔粘膜上皮细胞、骨髓间充质干细胞与猪小肠粘膜下层复合修复食管颈段缺损的实验研究
【英文名称】Grafts of porcine small intestinal submucosa with cultured autologous oral mucosal epithelial cells and bone mesenchymal stem cells for esophageal repair in a canine model
【研究起始时间】2007-02
【研究终止时间】2009-03
【中文关键词】组织工程；骨髓间充质干细胞；小肠粘膜下层；肌肉再生
【英文关键词】extracellular matrix; tissue engineering; autologous oral mucosal epithelial cell; esophagus; small intestinal submucosa
【中文摘要】第一部分自体口腔粘膜上皮细胞与猪小肠粘膜下层复合移植修复犬颈段食管缺损背景：单纯猪小肠粘膜下层（SIS）材料已成功用于犬颈段食管的重建，然而，它不能及时的完全上皮化。因此，复合种子细胞对重建食管是必要的。目的：探讨自体口腔粘膜上皮细胞(OMECs)与猪小肠粘膜下层材料复合重建犬颈段食管的可行性和有效性。方法：12支比格犬随机分为2组。切取6支比格犬的颊粘膜分别在体外进行口腔粘膜上皮细胞培养并连续传代，选第二代口腔粘膜上皮细胞（总数达1×107）接种于单层猪小肠粘膜下层上并共培养1周。将犬颈段食管切除5cm长1/2周径造成不完全

食管缺损模型，用单纯SIS或复合自体口腔粘膜上皮细胞的SIS原位重建食管缺损。术后行钡餐、组织学、免疫组织化学评估手术效果。结果：术后4周，单纯SIS组只有部分上皮化伴有明显炎症，而复合细胞的SIS组的组织学显示再生食管完全再上皮化，而且几乎没有明显炎症。术后8周，鳞状上皮细胞完全覆盖两组移植处，但复合细胞的SIS组显示有明显的肌肉细胞的再生。结论：复合口腔粘膜上皮细胞的SIS移植重建食管的缺损，促进再生组织再上皮化和肌细胞的再生。因此复合

【英文摘要】Part oneGrafts of porcine small intestinal submucosa with cultured autologous oral mucosal epithelial cells for esophageal repair in a canine modelBackground: The acellular porcine small intestinal submucosa (SIS) has been successfully used for esophagoplasty; however, it does not lead to a complete re-epithelialization in a canine model. A cellular component may be required for better reconstruction. Objective: To investigate the feasibility and effectiveness of the combination of SIS with autologous oral mucosal epithelial cells (OMECs) for esophageal reconstruction in a canine model. Methods: Twelve male beagle dogs were divided into two groups. The OMECs harvested from beagle dogs were cultured and propagated, and the 3rd passage cells (1×107) were seeded on a single-layer SIS for 1 week. Male eagle dogs were subjected to surgical resection to produce cervical esophageal defects (5 cm in length, 180 ° in range). SIS with or without OMECs was implanted into the esophageal defects. Barium esophagram, immunohistochemistry, and histology were performed to evaluate the therapeutic effectiveness.Results: The barium esophagrams showed that there was no evidence of leakage, stricture or diverticulum formation 2 weeks after the operation. Four weeks after surgery, the histological examination showed a complete re-epithelialization and almost no inflammation in the SIS with OMECs group. But in the SIS alone group, only a partial epithelialization was observed along with inflammation. Eight weeks after surgery, the squamous epithelium was found to cover the entire graft surface in both groups; however, the muscular regeneration was more prominent in the SIS with OMECs group.Conclusions: The graft of SIS combined with autologous OMECs promotes re-epithelialization and muscular regeneration. It is a feasible and effective alternative method for esophageal repair. Part TWOGrafts of porcine small intestinal submucosa with cultured autologous bone mesenchymal stem cells for esophageal repair in a canine modelBackground: The extracellular matrix (ECM) materials have been used successfully in esophagus, but the muscle regeneration is not ideal. Stem cells are undifferentiated cells with the capability of self-renewal and the potential for multilineage differentiation. We focused on bone mesenchymal stem cells (BMSCs) as a source of muscle regeneration.Objective: To compare BMSCs with esophageal myoblast by growth capability. immunohistochemistry in vitro, and to assess the effect of muscle regeneration using BMSC seeding onto the ECM scaffold for esophageal defects in a canine dog model in vivo.Methods: Eight beagle dogs were chosen for the study .Bone marrow was taken by direct needle aspiration from the dogs for the study in vitro ,then the autologous MSC s derived from the bone marrow (1×107 cells) were seeded onto the small intestine submucosa (SIS) .The cervical esophagus was resected approximately 5 cm length and 50% circumference. The defect was repaired with SIS seeded with cells in 4 animals or SIS without cells in 4 .The dogs were sacrificed at 4 and12 weeks after surgery. Samples of the excised normal esophagus were collected for myoblast culture in vitro .The cultured BMSCs and myoblast were compared by cell proliferation and immunohistochemical analysis. Results: The BMSCs showed spindle-shaped in vitro similar to the myoblast, and they were similar cell growth during 7 days culture and expressed α-smooth muscle actin by immunohistochemical staining and Western blotting.At 4 weeks after surgery, the cell-matrix implants smooth muscle island by immunostaining, the control group was negative for α-smooth muscle actin. At 12 weeks, the BMSCs-seeded group showed bundles of smooth muscle regeneration and connection to the adjacent normal skeletal muscle. But in the SIS alone group, there were only a few muscular islands regeneration.Conclusion: Autologous BMSCs may serve for a source of muscle tissue and induce muscle regeneration, and represent a promising tissue-engineered approach for the repair of esophagus.

【中文名称】脱细胞处理对SIS细胞残留及生长因子和胶原蛋白含量影响实验研究

【英文名称】THE EFFECT OF DECELLULARIZATION ON RESIDUE OF CELLS AND CONCENTRATION OF GROWTH FACTORS AND COLLAGEN PROTEINS OF SMALL INTESTINAL SUBMUCOSA

【研究起始时间】2007-02

【研究终止时间】2009-04

【中文关键词】小肠粘膜下层 生长因子 DAP12 胶原蛋白

【英文关键词】small intestinal submucosa growth factor DAP12 collagen protein residual cell

【中文摘要】目的 探讨利用机械-酶消化法制备小肠粘膜下层（small intestinal submucosa, SIS）的脱细胞效果，研究其对SIS结构及生长因子和胶原含量的影响，为优化其制备工艺提供实验基础。 方法 取屠宰后4 h内新鲜猪空肠，用钝性器械刮除浆膜层、黏膜层及肌层，用氯仿/甲醇（1:1, v/v）脱脂，0.25%胰酶消化,0.5%十二烷基磺酸钠(SDS)去垢剂处理，冷冻干燥制备SIS，分别留取样品（为SISa、 SISb、SISc、SISd、SISe和新鲜猪小肠为对照组F（n=4）），通过组织学染色、扫描电镜观察评价制备方法对材料的脱细胞效果及结构变化，采用Nest-PCR技术测定样品猪免疫基因DAP12含量，对制备方法的脱细胞效果进行定量评价。ELISA法检测样品VEGF、bFGF、TGF-β和TNF-α的含量，研究制备方法对生长因

子的影响，碱水解法测定样本胶原蛋白含量。结果 HE及V.G染色均显示SISa和SISb有明显细胞残留，SISc、SISd和SISe未见蓝染细胞核，含大量胶原纤维。V.G染色显示各样品具有黄染的肌纤维。扫描电镜观察显示在SISa和SISb有细

【英文摘要】Small intestinal submucosa (SIS) possesses special biological characteristics and is comprehensively researched for tissue repairing at varied tissues and organs. This study investigated the effects of acellularization on the remain of porcine cell and content of growth factors within SIS. SIS are produced by mult-step method which including treatment with formaldehyde/chloroform, trypsin, sodium dodecylsulphate(SDS), freeze-drying and sterilization by irradiation. Flesh small intestine of pig in a slaughter house with four hours were chosed to prepare SIS. At first, the muscular layer,placenta percreta and mucous layer of small intestine were removed by physical method;then degreasing by chloroform : methanol(1:1,v/v), trypsinization by 0.25%trypsin ,denudation with SDS and freeze drying were carried out.To keep samples separately in the preparation process(named with SISa、SISb、SISc、SISd、SISe, and fresh pig intestine as comparison, n=4). The efficacy of decellularization was evaluated by by histology and the NEST-PCR technique using porcine immunoreceptor DAP12 gene. The contents of vascular endothelial cell growth factor(VEGF), basic fibroblast growth factor(bFGF), transforming growth factor-β(TGF-β), tumor necrosis factor-α(TNF-α) within SIS are quantitatively assessed by ELISA. The content of collogen was tested by hydrolytic method. The results indicated that the growth factors are retained in SIS. The histological analysis showed much residual cells in SISa and SISb,and massive red gollagen fibrers and no blue-stain cytoblsat in SISc、SISd and SISe. There are more cells adhereing to collagen fibers in SISa and SISb,but only collagen fibers in SISc,SISd and SISe.Nest-PCR test revealed the content of DAP12 in the F、SISa、SISb、SISc、SISd and SISe respectively was (183.50±120.13), (18.01±9.53), (11.87±2.35), (0.59±0.27), (0.29±0.05) and (0.19±0.04)(copy×106). The statistical analysis results indicated that the copys of DAP12 in F was significant higher than SISa、SISb、SISc、SISd、SISe(P＜0.05), the copys of DAP12 in SISa and SISb were higher than SISc、SISd and SISe(P＜0.05),and the copys of DAP12 within SISc was more compared with that within SISd or SISe (P＜0.05),and copys of DAP12 within SISd was significantly more compared with SISe(P＜0.05). The content of growth factors within SISa were (75.43±25.30) ng/mg(VEGF), (6.03±3.84) pg/mg(bFGF), (11.38±3.62) pg/mg(TGF-β),and (9.36±4.70) pg/mg(TNF-α)；The content of growth factors within SISb were (39.03±9.38) ng/mg(VEGF), (4.11±1.02) pg/mg(bFGF), (6.53±1.89) pg/mg(TGF-β), and (6.52±4.02) pg/mg (TNF-α)；The content of growth factors within SISc were (37.73±22.60) ng/mg(VEGF), (4.10±1.16) pg/mg(bFGF), (4.96±1.35) pg/mg(TGF-β), and (4.60±1.70) pg/mg(TNF-α)；The content of growth factors within SISd were (21.90±6.47) ng/mg (VEGF), (3.92±1.28) pg/mg(bFGF), (4.68±0.91) pg/mg (TGF-β), and (5.12±1.32) pg/mg (TNF-α)；The content of growth factors within SISe were (27.45±6.09) ng/mg(VEGF), (3.32±1.79) pg/mg(bFGF), (4.80±1.66) pg/mg(TGF-β), and (5.77±2.50) pg/mg(TNF-α)。The contents of all the kinds of growth factors within SISa were remarkbale higher than SISb、SISc、SISd andSISe(P＜0.05).Degrease with formaldehyde/chloroform dramatically reduced the content of above growth factors in SIS, but advanced treatment could not sigificantlly reduced the content of growth factor. The contents of collagen protein were（10.76±4.42）(SISa)，（15.01±5.09）(SISb)，（36.05±8.88）(SISc)，（36.75±13.14）(SISd) and（30.45±4.58）(SISe)ug/mg. The statistical analysis results indicated that the content of collagen protein wihin SISa or SISb were significantly lower than that within SISc, SISd, and SISe (p＜0.05).Conclusion: The porcine cell within SIS could be clean out by physical-chemical method. No remain cells were observed in SIS prepared by mult-step in histology test. The physical-chemical method could signiffinitly decreased the porcine DNA content of SIS. The content of growth factors within the SIS samples gradually decreased, but parts of them are reserved,and content of collagen protein have significantly increased after physical-chemical method. The decellularization process by physical treatment combined with chemical treatment could remove the cell within SIS. SIS prepred by this method preserve the growth factors partly. The morphology of SIS was not influenced intensely by this method.

【中文名称】雪旺细胞纯化培养及体外复合小肠黏膜下层的实验研究

【英文名称】EXPERIMENTAL STUDY ON CULTIVATION AND PURIFICATION OF SCHWANN CELLS AND ITS COMPOSITION WITH SIS

【研究起始时间】2007-02

【研究终止时间】2009-04

【中文关键词】雪旺细胞 纯化 小肠黏膜下层 神经生长因子 组织工程 相容性

【英文关键词】SCs Purification SIS NGF Tissue engineering Biocompatibility

【中文摘要】现阶段，短距离的周围神经缺损，临床上主要采用头尾相接缝合技术；对于较大的缺损，最常用的方法是自体神经移植，但是它存在着明显的缺点，如可供移植的神经数量和长度有限，造成供区的功能障碍，大小难以匹配和可能造成错向再生等。近年来，利用组织工程技术研制一种可替代自体神经移植的人工神经是研究的热点。

SCs（Schwann cells，SCs）是周围神经系统的主要胶质细胞，能形成有髓神经纤维和无髓神经纤维的内膜，具有多种生理功能，特别是在神经再生过程中起重要作用，是周围神经组织工程的核心。小肠黏膜下层（small intestinal submucosa，SIS）作为一种天然的生物材料，因有其特有的生物学特性，接近于天然结缔组织复杂的成分结构，不含细胞和血管，植

入体内不会引起免疫排斥反应。目前SIS已作为组织工程的支架材料广泛应用于下尿路、膀胱、血管、肌腱、韧带、神经、骨、半月板、腹壁、硬脑膜、筋膜等多种组织缺损修复的实验研究。神经生长因子（Nerve growth factor，NGF）具有神经元营养和促突起生长双重生物学功能的一种神经细胞生长调节因子，它对中枢及周围神经元的发育、

【英文摘要】Objective: To obtain highly purified and large amount of SCs by improved passage culture, and to investigate the biocompatibility of SIS and SC, and upgrade biological feature of SIS.Methods: (1) Sciatic nerves were isolated from three-day-old SD rats and digested with Collagenase II and Trypsin. Schwann cells were purified with 20-min difference adhesion once and G418 selection two days. Then the fibrolast was further removed by gradually reduce fetal bovine serum. Cells were detached from the flask with low concentration enzyme.(2) SIS was obtained by firstly removing the tunica mucosa, serosa and tunica muscularis through mechanical erasion. Cells escaping and sterilization was further done through chemical method. Finally SIS was preserved by freeze drying and sterilization. Light microscope and scanning electron microscope examination showed the residual cells on prepared SIS were almostly removed.(3) The prepared SIS and Schwann cells were co-cultured in vitro and biocompatibility was studied. The SCs suspension was seeded on the SIS, then adhension, proliferation and differentiation of SCs was investigated,by light microscope and scanning electron microscope examination and SCs secretion activity of neurotrophic factors was also evaluated at different times by Elisa kit.(4) Cultured rat SCs were seeded on SIS couple days and then SCs were moved from SIS by freeze thawing. The material was frozen drying at last. SIS without SCs was grinded and its content of NGF was tested by Elisa kit.Results：(1) The viability was 96%±0.5% and the purity of cells was more than 98%.(2) Light microscope and scanning electron microscope examination showed the residual cells on prepared SIS were almostly removed, and the stereochemical structure and thermal stability of collagen fibers were nearly not destroyed. SIS possessed three-dimensional structure suitable for cell growth and could be used as scaffold in peripheral nerve tissue engineering.(3) It showed that SCs adhered and proliferated well on the surface of SIS by contrast phase microscope, histological section and SEM, growing on the edge of the material or of SIS and reaching confluens on the surface of surface of SIS after 5~7d. SCs divided and proliferated in three-dimensional fashion, demonstrating long olivary, triangular or long fusiform shape with obvious prominence. Furthermore, the SCs connected end-to-end with each other or aligned in clusters and the protein granules secreted on cellular surface were also showed. TEM showed SCs grew well on SIS. Furthermore, ELISA measurement revealed that, cultured in combination with SIS, SCs secreted NGF prosperously without obvious difference with the control group, the secretory volume increasing with the prolonged time.(4) The concentration of NGF released in vitro from SIS which were cultured SCs for 3，5，7，10，13，15 days, were 64.12±10.84, 192.30±21.34, 282.00±27.54, 414.29±20.87, 404.43±19.21 and 390.17±26.72pg/cm2 respectively, while the concentration of NGF in simple SIS was 4.92±2.06)pg/cm2. Conclusion: 1 This method has advantages of convenience, little time consuming and high cell purity. 2 SIS possessed three-dimensional structure suitable for cell growth and could be used as scaffold in peripheral nerve tissue engineering.3SIS had good biocompatibility with SCs, providing the basis for further study in vivo to fabricate the artificial nerve conduit utilizing SIS compound of SCs.4The modified SIS which has NGF secreted by SCs are optimal tissue-engineered bioartificial nerve graft.

【中文名称】上皮细胞条件培养液对骨髓间充质干细胞增殖和分化的影响

【英文名称】EFFECTS OF EPITHELIAL CELLS CONDITIONED MEDIUM ON PROLIFERATION AND DIFFERENTIATION OF BONE MARROW MESENCHYMAL STEM CELLS

【研究起始时间】2007-02

【研究终止时间】2009-06

【中文关键词】骨髓间充质干细胞 上皮细胞 诱导 分化 犬

【英文关键词】BMSCs Epithelial cell Induction Differentiation Canine

【中文摘要】目的：探讨ECCM体外诱导犬BMSCs向上皮细胞分化的可行性。方法：成年健康雄性比格犬1只，体重10 kg。于犬髂后上棘采用骨髓穿刺法取骨髓5 mL，分离培养骨髓间充质干细胞（bone marrow mesenchymal stem cells, BMSCs）。取犬口腔黏膜，剪除黏膜下组织，剪成约4mm×4 mm大小，制备上皮细胞条件培养液（epithelial cell conditioned medium，ECCM）。取第2代BMSCs以2×10 4个/孔细胞密度接种，实验组于ECCM中培养，对照组于低糖DMEM完全培养基中培养。观察两组细胞形态特征，MTT法绘制生长曲线，诱导培养21 d免疫组织化学染色鉴定上皮细胞特异性标志物——细胞角蛋白19（cytokeratin19，CK-19）和细胞角蛋白AE1/AE3，透射电镜观察细胞超微结构。结果：倒置相差显微镜下见两组细胞均呈长梭形，均匀分布生长，折光性较强，增殖迅速。两组细胞生长曲线均呈“S”形，实验组生长曲线较对照组右移，提示ECCM对细胞增殖有抑制作用

【英文摘要】ObjectiveTo investigate the feasibility of inducing canine BMSCs to differentiate into epithelial cells in vitro with ECCM. Methods Five mL BMSCs were obtained from iliac spine of a healthy adult male canine with body weight 10-15kg, and then isolated and cultured. The oral mucosa was harvested and cut into 4 mm×4 mm after the submucous tissue was eliminated; the epithelial cells conditioned medium was prepared. BMSCs of the 2nd passage were cultured and divided into two groups, cultured in ECCM as

experimental group and in L-DMEM as control group.The cell morphological characteristics were observed and the cell growth curves of two groups were drawn by the continual cell counting. The cells were identified by immunohistochemical staining through detecting cytokeratin 19 (CK-19) and anti-cytokeratin AE1/AE3 on the 21st day of induction. The ultra-structure characteristics were observed under transmission electron microscope. Results The cells of two groups showed long-fusiform in shape and distributed uniformly under inverted phase contrast microscope. The cell growth curves of two groups presented S type. The cell growth curve of the experimental group was right shifted, showing cell proliferation inhibition in ECCM. The result of immunohistochemical staining for CK19 and anti-cytokeratin AE1/AE3 was positive in the experimental group, confirming the epithelial phenotype of the cells; while the result was negative in the control group. The cells were characterized by tight junction under transmission electron microscope. ConclusionThe canine ECCM can induce allogenic BMSCs to differentiate into epithelial cells in vitro.

【中文名称】铜对血管内皮细胞增殖与分化的影响
【英文名称】THE EFFECT OF COPPER ON THE PROLIFERATION AND DIFFERENTIATION OF VASCULAR ENDOTHELIAL CELLS
【研究起始时间】2007-02
【研究终止时间】2009-04
【中文关键词】铜；血管内皮细胞；细胞增殖；基因表达
【英文关键词】Copper; Vascular endothelial cell; Proliferation; Gene expression
【中文摘要】目的：评价不同浓度的铜离子对血管内皮细胞增殖的影响，并检测血管内皮细胞在铜的作用下eNOS和Tie-1基因的表达变化，了解铜对血管内皮细胞分化的影响。方法：在体外培养人脐静脉血管内皮细胞（HUVEC）。将体外培养的HUVEC分成A、B、C三组，基础培养基为MCDB131。A组，添加5μM CuSO4；B组，添加25μM CuSO4；C组，为不添加CuSO4的对照组。MTT法检测细胞增殖，绘制三组细胞的生长曲线，比较实验组和对照组之间增殖能力的差异。用荧光定量RT-PCR法检测A、B、C三组血管内皮细胞的eNOS和Tie-1基因表达。流式细胞术检测三组细胞的凋亡率。结果：生长曲线显示：前3天为指数增长期，从第4天开始进入平台期。A组平台期显著高于C组；而B组指数增长期后其平台期呈下降趋势。A组细胞从第3天开始增殖能力强于C组（P＜0.05）；B组细胞在48小时以内增殖能力强于C组（P＜0.05），但从第4天开始B组细胞的增殖能力下降，低于C组（P＜0.05）。荧光定量RT-PCR结果显示：和C组相比，A组的eNOS和Tie-1的表达均上调（P＜0.05），表达量分别是7.294±
【英文摘要】Objective: To evaluate the effect of copper ions in different concentration on vascular endothelial cells` proliferation, to detect the expression of eNOS and Tie-1 in the vascular endothelial cells under the effect of copper and understand the effect of copper on the differentiation of vascular endothelial cells.Methods: Human umbilical vein endothelial cells (HUVEC) were cultured in vitro. Cells were divided into A, B and C groups. The basal culture medium was MCDB131. Group A, added 5 μM CuSO4; group B, added 25 μM CuSO4; group C, was the control group which did not add CuSO4. The cell growth curves of three different groups were made by using MTT and their proliferation ability was compared. The expression of eNOS and Tie-1 of three different groups were detected by real time RT-PCR. The apoptosis rates of three different groups were detected by using flow cytometry. Results: The growth curves revealed that the exponential growth time was the first three days, plateau growth time begun at fourth day. The plateau growth of group A was higher than that of group C significantly, and the plateau growth of group B was decreasing. The proliferation of group A was stronger than group C since the third day (P＜0.05); Within the 48h, the proliferation of group B was stronger than group C (P＜0.05), however it decreased and was weaker than the group C since the fourth day (P＜0.05). The results of real time RT-PCR revealed that the expression of eNOS and Tie-1was up-regulated (P＜0.05), they were 7.294±1.488 and 1.481±0.137 in the group A. The expression of eNOS was down-regulated (P＜0.05) and the expression of Tie-1 showed no significant difference (P＞0.05), they were 0.149±0.044 and 1.131±0.191 in group B. All of those data were the results of comparing with group C. The result of flow cytometry revealed: the apoptosis rates of all groups were very low at 48h, and the differences of the three groups were very small.Conclusion: 5 μM copper could promote the proliferation of vascular endothelial cell, and 25 μM copper could promote it within 48h. But the proliferation of cells decreased after the fourth day under the effect of 25 μM. At the same time, 5 μM copper could up-regulate the eNOS and Tie-1 in the HUVEC, however 25 μM copper did not have this ability. To sum up, 5 μM copper could promote the proliferation and differentiation of vascular endothelial cell effectively, and it has very good prospects for clinical application.

【中文名称】软骨脱细胞基质海绵和SIS海绵修复关节软骨缺损的实验研究
【英文名称】EXPERIMENTAL RESEARCH OF REPAIRING ARTICULAR CARTILAGE DEFECT BY A NOVEL ACELLULAR CARTILAGE MARTRIX SPONGE AND SIS SPONGE IN RABBITS

【研究起始时间】2007-02
【研究终止时间】2009-04
【中文关键词】软骨修复 脱细胞基质 海绵 小肠粘膜下基质 支架材料 组织工程 改性 天然衍生生物材料 冷冻干燥
【英文关键词】Cartilage repair Acellular cartilage matrix Sponge Small intestinal submucosa Scaffold Tissue engineering Modification Native biomaterial Freeze-drying
【中文摘要】无血管分布的软骨组织细胞增生活力极低，由外伤或风湿等导致的软骨缺损自我修复能力差。因此，软骨病变常导致进行性的软骨退变进而最终导致骨关节炎。微骨折，软骨钻孔等软骨缺损的治疗无法重建天然的软骨甚至可能造成进一步损伤。随着研究的深入，目前骨软骨移植，组织工程等以组织为基础的软骨修复理论已经引出很多新的治疗技术。尽管通过移植组织工程制造的软骨样组织进行修复获得了部分成功，不过结果却并不满意。在大的软骨缺损，关节表面常常不是由透明软骨修复。修复的不完全导致不能形成完整的软骨表面，随着时间发展演变成进行性退变。产生这样的结果的原因尚不清楚，一些研究表明是因为软骨细胞从支架和缺损处的流失所致。另外一些结果提示支架尚不足以模拟软骨细胞外基质环境以维持软骨细胞的表型和诱导间充质干细胞分化成软骨细胞。所有这些研究表明可降解的多孔支架材料在产生足够细胞以保持软骨再生的组织工程中扮演重要角色，因此有必要制备新型的有利于间充质干细胞分化成具有软骨表型的细胞以构建三维软骨组织。目的 探讨分别利用猪耳软骨脱细胞基质及小肠粘膜下基质（Small intestinal submucosa, SIS）制备海绵

【英文摘要】Objective: The object of this research is to fabricate novel acellular matrix sponge scaffold derived separately from swine auricular cartilage and small intestinal submucosa, investigate their physico-chemical properties and biocompatibility, evaluate their applicability for cartilage tissue engineering by comparing performance of two scaffolds in repairing articular cartilage defect model. Methods: Fresh swine auricular cartilage was freeze-dried and freeze-ground into microparticle, sieved particles that diameter less than 90 μm and then was treated sequentially with TNE, pepsin and hypotonic solution for decellularization. The decellularized matrix in concentration of 2% was dissolved in 1.5% HAc and then lyophilized for molding and cross-linked by UV radiation. SIS was dissolved directly in 1.5% HAc and then lyophilized for molding and cross-linked by UV radiation.then, SIS sponge(SISS) was obtained. Histological, immunohistological, SEM, porosity assays were used to characterize the two sponge scaffolds, the in vitro cytotoxicity of ACMS ’s lixivium was detected by MTT assay. The histocompatibility was evaluated by local effects after implantation in SD rats. Two scaffolds were implanted separately into articular cartilage defect in rabbits. The effect of ACMS and SISS on the repairing of articular cartilage defects were investigated in at 4,8,12 and 24 weeks, all results compared with the blank control group. According to the International Cartilage Repair Society Histological Scoring (ICRS), the effect of cartilage repair was assessed at 24 weeks postoperatively. Results: Histological analysis suggested that the acellular cartilage matrix sponge scaffold was constructed by cartilage matrix without any cells or cell fragments left; Masson staining indicated that material retained the collagen of cartilaginous matrix. SEM scanning of ACMS showed that scaffold had a porous spongy-like structure, and the pores were interconnected. The aperture size ranged from 90.66 μm ± 21.26 μm .The porosity assay showed that the average porsity was 90.10%±2.42%, water absorption ratio is 2029% ± 253%. SEM scanning of SISS showed that scaffold had a porous honeycomb-like structure, and the pores were interconnected. The aperture size ranged from 61.43 μm±13.36 μm. The porosity assay showed that the average porsity was 86.25%+3.40%, water absorption ratio is 4191%±195%. The MTT assay revealed that scaffold had good cellular compatibility without cytotoxicity. Subcutaneous implantation demonstrated the tissue growth in scaffold, angiogenesis, low inflammatory reaction, and scaffolds can degrade in some rate. The obvious degradation of scaffolds was observered at the 4th week. The scaffolds degraded completely, hyperplasia of fibrous tissue reached its peak at the 8th week. From then, cartilage cells from defect and MSCs from bone marrow migrate to defect and proliferate/differentiate into chondrocytes, however because scaffolds degraded too fast, the supply of chondrocytes was insufficient, the repair of defect is incomplete. The result of histological score of the specimens at 24 weeks showed that a total of 6 aspects including formation of chondrocytes and integration with the surrounding cartilages were superior in the experimental group to those in the control group, and there were significant differences between the two groups ($P < 0.05$). Conclusions: The acellular cartilage matrix sponge reserved most of extracellular matrix after thoroughly decellularization, has appropriate aperture size and porosity, non-cytotoxicity and good histocompatibility, may be used as a novel scaffold or cell-carrier for cartilage tissue engineering. The articular cartilage defect repaired by biomaterial scaffold derived from acellular cartilage matrix and SIS can form fibrous connective tissue containing chondrocytes, but the repair is incomplete.

【中文名称】上皮细胞与SIS复合培养及犬口腔黏膜上皮细胞构建组织工程食管的体内植入实验研究
【英文名称】Epithelial Cells Co-cultured with SIS and Grafts of Porcine SIS with Cultured Autologous Oral Mucosal Epithelial Cells for Esophageal Repair in a Canine Model
【研究起始时间】2007-02

【研究终止时间】2009-04
【中文关键词】食管黏膜上皮细胞 口腔黏膜上皮细胞 猪小肠黏膜下层 复合培养 生物学特性 组织工程
【英文关键词】Esophageal mucosa epithelial cells；Oral mucosal epithelial cells； Small intestinal submucosa；Coculture；Biological characteristics；Tissue engineering.
【中文摘要】各种食管病变多数需行病变切除并实施食管重建术。运用组织工程技术构建有活性的人工食管，为食管缺损的修复提供一种新的方法，其基本技术包括种子细胞培养、支架材料研制、细胞与支架材料的相互作用及工程食管组织的构建等。小肠黏膜下层（small intestinal submucosa，SIS）是一种具有引导/诱导组织再生功能的膜材料，含有多种生长因子，有良好的组织相容性。上皮细胞是构建组织工程食管必需的种子细胞，如何在体外培养扩增食管或口腔黏膜上皮细胞？上皮细胞与SIS的生物相容性如何？以口腔黏膜上皮细胞与SIS复合培养构建的组织工程食管是否能有效地修复食管缺损是本研究要解决的关键问题。本研究采用上皮细胞无血清培养基（defined keratinocyte serum free medium，DKSFM）为基础培养基添加6%胎牛血清（fetal bovine serum，FBS），采用酶消化法培养犬食管黏膜上皮细胞（esophageal mucosa epithelial cells，EMECs），探索原代及体外连续培养的方法。通过观察EMECs在SIS上的生长、增殖情况，评价SIS的生物相容
【英文摘要】A variety of conditions can lead to damage or lose of the esophagus， needing to eventual repair or reconstruction of the organ. The use of tissue engineering technology to build artificial esophagus has been proposed as a new strategy for esophageal reconstruction，following the principles of cell transplantation，materials science，and engineering to develop biological substitutes that restore or maintain the normal esophagus. Small intestinal submucosa (SIS) is a guided tissue regeneration and good histocompatibility membrane materials，containing many growth factors. Epithelial cells in esophageal tissue engineering are necessary. How to cultivate in vitro amplification of esophageal or oral mucosal epithelial cells? How is the biocompatibility of epithelial cells co-cultured with SIS? Whether esophageal defect can be effectively repaired oral epithelial cells cultured with SIS? In this study，we cultivated canine esophageal mucosa epithelial cells（EMECs）in DKSFM containing 6% FBS and EMECs co-cultured with SIS to explore an effective method to culture EMECs of canine in vitro，and to observe the biological characteristics of EMECs growing on SIS. At the same time，this study was undertaken to evaluate the feasibility and effectiveness of the combination of autologous oral mucosal epithelial cells (OMECs) and SIS for the esophageal repair in a dog model. The results of this study show that the EMECs and OMECs grew fast in DKSFM containing 6% FBS without fibroblast contamination. The cells could pass generations. After EMECs and OMECs co-cultured with SIS，the cells adhered and began to spread on SIS. EMECs and OMECs can be used esophageal tissue engineering. SIS can be used as scaffold material. The experimental of animals results show that 5 cm in length esophageal defect of animals could be effectively repaired by the tissue engineered esophagus.The esophageal lumen surface at the site of the patch graft in the SIS with OMECs group had new blood vessels and skeletal muscle bundles，and were smoother than that of the SIS group. It provides the experimental basis for further research and clinical applications.

【中文名称】神经生长因子与小肠粘膜下层基质复合材料（NGF-SISM）的初步研究
【英文名称】The preliminary study of nerve growth factor/small intestinal submucosa matrix compositive materials (NGF-SISM)
【研究起始时间】2008-02
【研究终止时间】2010-05
【中文关键词】神经营养因子 小肠粘膜下层 人真皮成纤维细胞 人脐静脉内皮细胞
缓释
【英文关键词】nerve growth factor; small intestinal submucosa; human dermal fibroblasts; human umbilical vein endothelial cells; controlled release
【中文摘要】目的 探讨神经生长因子（nerve growth factor, NGF）促进创面愈合的作用机理，制备NGF与小肠粘膜下层基质（small intestinal submucosa matrix, SISM）的复合材料（NGF-SISM），研究其NGF体外释放和细胞相容性，为其应用于临床糖尿病溃疡提供理论基础和实验依据。方法 （1）体外分离培养人真皮成纤维细胞（human dermal fibroblasts, HDFs），取第 3 代细胞进行实验。分别加入 0、25、50、100、 200、 400 ng/ml NGF，培养 48 h 采用 MTT 法检测细胞增殖；加入 0、 50、100、200 ng/ml NGF，培养 48 h 后采用实时荧光定量 PCR 测定细胞 Col Ⅰ、Col Ⅲ mRNA 表达水平；建立体外细胞划痕创伤模型，加入 0、 50、 100、 200 ng/ml NGF，培养 24 h 观察细胞迁移。（2）取生长良好的人脐静脉内皮细胞（human umbilical vein endothelial cells, HUVECs）进行实验，分别加入 0
【英文摘要】Objective To investigate the effects of Nerve growth factor (nerve growth factor, NGF) on human dermal fibroblasts (human dermal fibroblasts, HDFs) and human umbilical vein endothelial cells (human umbilical vein endothelial cells, HUVECs), prepare the NGF- small intestinal submucosa matrix (small intestinal submucosa matrix, SISM) compositive material (NGF-SISM), and evaluate the release of NGF and cell compatibility in vitro. Methods (1)The 3rd generation of HDFs were incubated with various concentrations (0,25,50,100,200,400ng/ml) of NGF, cells proliferation was measured with methyl thiazolyl tetrazolium (MTT) assay;

Real-time fluorescence quantitative polymerase chain reaction (FQ-PCR) were used to measure collagen synthesis on mRNA level; The in vitro cell scratch wound model was set up to observe the effect of NGF （0,50,100,200ng/ml） on the migration of HDFs.(2) The HUVECs were incubated with various concentrations (0,6.25,12.5,25,50,100, 200ng/ml) of NGF, cells proliferation was measured with methyl thiazolyl tetrazolium (MTT) assay; The in vitro cell scratch wound model was set up to observe the effect of NGF （0,25,50,100ng/ml） on the migration of HUVECs; Treated with NGF at 0, 10, 25, 50,100ng/ml, Real-time fluorescence quantitative polymerase chain reaction (FQ-PCR) were used to measure VEGF and Ang-2/Tie-2 synthesis on mRNA level.（3） NGF-SISM was prepared by embedding NGF into SIS gel. NGF release was quantified using ELISA; HDFs or HUVECs were seeded on NGF-SISM within 9 days or 7 days respectively, cells proliferation was measured with MTT assay; The growth of HDFs or HUVECs were observed by scanning electron microscope and HE staining.Results (1) Absorbent value of HDFs for different concentrations of NGF (0~400ng/ml) was 0.132±0.013, 0.123±0.010, 0.132±0.012, 0.134±0.016, 0.138±0.015, 0.126±0.007 respectively (p>0.05), showing that NGF did not influence the proliferation of HDFs; The expression fold of collage type I under NGF (50~00ng/ml) were 0.962±0.218, 1.094±0.206 and 0.976±0.268 respectively, the expression fold of collage type III were 1.017±0.113, 0.900±0.154 and 0.984±0.165 respectively, Compared with control group, there were not significantly different (p>0.05); The distance of HDFs ' migration at various concentrations of NGF (0~200ng/ml) was 416.96±52 μm, 645.36±65.2 μm, 530.64±28.64 μm and 489.52±77.6 μm respectively, indicating that NGF could significantly induced migration of HDFs at 50ng/ml and 100ng/ml. 50ng/ml was presented higher response.(2)Absorbent value of HUVECs for different concentrations of NGF (0~200ng/ml) and NGF antibodies was 0.233±0.020, 0.285±0.024, 0.284±0.013, 0.274±0.015, 0.297±0.013, 0.281±0.026, 0.277±0.012 and 0.208±0.011 respectively (p<0.05), showing that NGF induced the proliferation of HUVECs; The addition of NGF (25, 50 and 100ng/ml) significantly decrease the distance between the sides of wound line as compared with control (207.5±15.4 μm, 235.0±14.5 μm, 228.3±11.9 μm vs. 98.3±22.9 μm respectively, P<0.01). And in the range form 25ng/ml to 50ng/ml, the effect of NGF was does-dependent. The levels of mRNA for VEGF and Ang-2 were stimulated significantly by NGF (10ng/ml, 25ng/ml, 50ng/ml, and 100ng/ml). And the highest response was seen at 100ng/ml (about 2-fold and 1.7-fold respectively). Similarly, the level of mRNA for Tie-2 was up regulated with the treatment of NGF in comparison to the controls, and reached a maximal level at 50ng/ml(about 2.4-fold). On the contrary, treatment with antibody of NGF completely abrogated NGF-induced mRNA expression.(3) The SISM have the pore diameter of 50~200 μm and an interconnective porous structure. There was an initial burst of NGF (approximately 52.3±3.9%) for about 12 h. After 12 h, the release was almost constant. Release process was prolonged over 13 days; 87.4±4.5% of total NGF was released. The Absorbent value of HDFs and HUVECs between control group and NGF-SISIM group were significantly different. Scanning electron microscope and HE stain results showed that HDFs and HUVECs attach to NGF-SIS sponge within 2 hours, and show the typical morphology after 4h.Conclusion(1) The possible promoting healing ulcer mechanisms of Nerve growth factor were: NGF significantly induced migration in an in vitro model of wounded fibroblasts; NGF significantly induced proliferation, migration and mRNA level of VEGF, Ang-2/Tie-2 of HUVECs. And the effective concentration of NGF was: 50-100ng/ml.(2) NGF can constantly release form NGF-SISS. NGF-SISS has well cell compatibility with HDFs and HUVECs, and induced cell proliferation.

【中文名称】人胎盘间充质干细胞在低氧无血清下的生物学特性
【英文名称】Characterization of placental derived mesenchymal stem cells in hypoxia and serum deprivation
【研究起始时间】2008-02
【研究终止时间】2010-07
【中文关键词】组织工程；胎盘；间充质干细胞；低氧；无血清；种子细胞；
【英文关键词】Tissue Engineering; Placenta; Mesenchymal Stem Cells; Hypoxia; Serum Deprivation; Seed Cells;
【中文摘要】间充质干细胞(MSCs，Mesenchymal Stem Cells)是组织工程研究中重要的组成部分，在多种组织的修复与再生中发挥着巨大的作用。MSCs是一类具有多向分化潜能的干细胞，可以分化为成骨、脂肪、软骨、神经、内皮、心肌等终末分化细胞[1,2]。MSCs最先从骨髓中分离得到[3]，随后在人脂肪组织、外周血、肌肉、结缔组织等也先后分离出了MSCs[4-7]。目前MSCs是临床研究中最普遍的细胞来源，在组织工程研究、创伤修复和肿瘤治疗等应用广泛。但是，MSCs在骨髓、外周血等组织中的含量是非常低的，同时有研究表明随着人体年龄的增长MSCs的含量变得更低，细胞的增殖分化能力也大大的降低[1,8]。因此，国内外学者们开始研究更幼稚的组织如胚胎、胎盘组织是否含有MSCs。此外，正常机体组织平均O2浓度一般在3%左右[2]，一些病理组织例如心肌缺血、脑卒中以及受损组织等则是一个缺血低氧的环境。因此在干细胞治疗中，干细胞都必需先克服缺血低氧的生理微环境来实现增殖、分化和促进组织再生。为了更充分地研究人胎盘基蜕膜来源的MSCs作为缺血相关组织工程产品种子细胞的可行性，本研究将围绕PDB-MSC
【英文摘要】Objectives In the present study, we will characterize MSCs residing in the human placental decidua basalis, termed as placental decidua basalis (PDB)-MSCs, for their surface phenotypes as well as multipotent differentiation potency in vitro; Imitate an ischemic environment in vitro via hypoxia and serum deprivation, and determine the characterization of PDB-MSCs in hypoxia and

serum deprivation for their further utility in ischemic related tissue engineering as seed cells.Methods1. Combination of enzymatic digestion and density gradient centrifugation was used to isolate the MSCs from the human term placental decidua basalis. FACS and chemical induced reagents were carried to evaluate the cell surface antigens and multipotent differentiation potency respectively.2. Two components of ischemia were simulated by hypoxia and serum deprivation of the complete medium in vitro, and PDB-MSCs from the 4th passage were used in the following assays: proliferation, CFUs, apoptosis and attachment rate.3. The metabolic activity (glucose utilization and lactate production) of PDB-MSCs in hypoxia and serum deprivation were determined by biochemical methods; their phenotypes in H/SD were also analyzed by FACS; finically, the VEGF, HGF, bFGF and BMP-2 secretion of PDB-MSCs in H/SD and N/SD were also measured by commercial available ELISA kits.Results1. A fibroblast-like cell population was isolated from the human placental decidua basalis, their phenotypic characterization was similar to BM-MSCs, besides, they were also positive for SSEA-4, TRA-1-60, and TRA-1-81 which are expressed in embryonic stem cells (ESCs); PDB-MSCs also differentiated into osteogenic, adipogenic and chondrogenic cells in vitro.2. PDB-MSCs kept the phenotypes stably and survived under hypoxia and serum deprivation in 96h; PDB-MSCs grow tardily and almost fail to form a colony unit in serum deprivation, but they metabolize moderately in hypoxia and serum deprivation.3. Hypoxia obviously enhances the proliferation, colony forming potential, metabolic activity of PDB-MSCs in complete medium, but suppresses the secretion of bFGF and BMP-2 of PDB-MSCs in serum deprivation.ConclusionsA clonogenic cell population of PDB-MSCs was isolated from the human placental decidua basalis, which can be resistance to hypoxia and serum deprivation in 96h. PDB-MSCs appear to be promising seed cells for ischemia relevant tissue engineering.

【中文名称】内皮型一氧化氮合酶在铜促进血管内皮细胞增殖中的作用
【英文名称】Copper stimulates proliferation of human umbilical vein endothelial cells in a endothelial nitric oxide synthase-dependent pathway
【研究起始时间】2008-02
【研究终止时间】2010-05
【中文关键词】铜，细胞增殖，VEGF，eNOS
【英文关键词】Copper, Cell proliferation, VEGF, eNOS
【中文摘要】背景：在早期的铜与血管生成关系的研究中发现，微摩尔级的CuSO4能诱导兔眼球内血管发生，而在兔的食物中去掉铜能抑制其血管的形成。提示铜可能在血管化中起重要作用。此后不断有研究发现铜对血管的发生有促进作用，但是铜促进血管发生的作用机制直到最近才开始研究。在小鼠模型的体内研究发现，在饮食中补充、添加铜离子可以逆转由于持续压力负荷引起的心肌肥大，且这一过程由血管内皮生长因子（Vascular endothelial growth factor，VEGF）介导，通过促进血管新生来实现的。目的：铜对内皮细胞增殖的作用可能是血管新生的关键环节。本研究以人脐静脉内皮细胞（Human umbilical vein endothelial cells，HUVECs）作为模型，探讨铜对血管内皮细胞的作用及其分子机制。方法：以0、5、10、25、50、100、25、500、1000μM等不同浓度的CuSO4加入HUVECs的培养体系，通过MTT法检测不同浓度的铜对血管内皮细胞增殖的影响，确定了CuSO4浓度在5~100μM时会对HUVEC的增殖活性有促进作用。通过三种不同的方法，噻唑蓝（Colori
【英文摘要】Background: Copper (Cu) involvement in blood vessel growth was first indicated in a study, in which micromolar amount of CuSO4 was used to induce intraocular vascularization in rabbits. In the later study , people found that feeding rabbits diets deficient in Cu suppressed blood vessel formation, indicating an essential role of Cu in the vascularization. After that, more studies have found copper has the ability of promoting angiogenesis, but the mechanism has not been explored until recently. Studies in vivo have shown that dietary Cu supplementation reverse pressure overload-induced cardiac hypertrophy in a mouse model, which is vascular endothelial growth factor (VEGF)-dependent and correlates with enhanced angiogenesis.Objective: Because of the ability of stimulating endothelial cell proliferation , copper would play a crucial role in the process of angiogenesis. In this study, we use human umbilical vein endothelial cells (HUVECs) as a model of copper on vascular endothelial cells and its molecular mechanism.Methods: The HUVECs in cultures were treated with different concentrations of Cu sulfate (0, 5, 10, 25, 50, 100, 250, 500 or 1000 μM). The effects of different concentrations of copper on the proliferation of HUVEC were determined By MTT assay. We found that Cu stimulated cell proliferation within the concentration range from 5 to 100 μM. The HUVECs in cultures were treated with Cu sulfate only or both Cu and Cu chelator tetraethylenepentamine(TEPA). We evaluated the ability of cell proliferation by three different method. MTT assay evaluates the cell metabolism, 3H-Thymidine (3H-TdR) incorporation assay evaluates the amount of DNA synthesis and cell count evaluates the total cell number. Cell proliferation and Cu effect on cell cycle were determined by flow cytometry (FCM). In addition, the effect of Cu on VEGF and endothelial nitric oxide synthase (eNOS) mRNA levels was determined by real time RT-PCR, and anti-VEGF antibody and siRNA targeting eNOS were applied to determine the role of VEGF or eNOS in Cu effect on cell proliferation.Result: We found that Cu stimulated cell proliferation within the concentration range from 5 to 100 μM, and when the

concentration was above 100 μ M that shows a toxic effect of the cell. The TEPA-inhibited HUVECs cell proliferation can be reversed by Cu supplementation. Cu did not increase the level of VEGF mRNA, and TEPA inhibited VEGF mRNA expression. Furthermore, neutralizing VEGF by anti-VEGF antibody did not suppress Cu-stimulation of cell proliferation. Cu significantly increased eNOS mRNA, and siRNA targeting eNOS completely blocked Cu reversal of TEPA inhibition of cell proliferation.Conclusion: The data demonstrate that Cu stimulation of HUVEC cell proliferation is eNOS-dependent.

【中文名称】微量元素与高血压的关系及其降压机制的初步研究
【英文名称】Impact of Trace Element Supplementation on Hypertension and the Mechanism of Its Effect on Blood Pressure
【研究起始时间】2008-02
【研究终止时间】2010-05
【中文关键词】微量元素；铜；高血压；降压机制；VEGF；HIF-1
【英文关键词】Trace elements; Copper; Hypertension; Mechanism of depressurization; VEGF; HIF-1
【中文摘要】第一部分 铜锌补充对自发性高血压大鼠血压的影响目的：通过动物实验找出微量元素铜锌补充对SHR大鼠的主要影响方面，为以后体外实验指明方向。方法：在饲养的实验组SHR、WKY大鼠饮水中添加生理剂量的硫酸铜、硫酸锌，对照组SHR、WKY大鼠饲喂去离子水。实验过程中每4周用智能无创血压仪监测血压。在实验0周、4周、8周、12周、16周时间点，用超声心动仪监测各组大鼠的心功能指标。监测指标包括LVEDD、LVESD、%FS、LVEDV、LVESV、SV、EF、LVPWd、LVPWs和心指数。饲养16周以后，抽血处死大鼠，用国际临床化学协会（International Federation of Clinical Chemistry，IFCC）推荐方法检测大鼠血液中微量元素及血清学指标等。取材大鼠心脏、肺脏、肝脏、肾脏以及血管等组织样本，称量脏器、体重，计算脏器体重比，用原子吸收光谱法检测大鼠心脏中微量元素含量。结果：血压监测发现，实验进行的12周和16周时SHR铜锌补充组的血压比对照组明显下降，用统计学分析（Student t-test）具有显著差异。超声心动图显示，WKY大鼠铜锌补
【英文摘要】Aims: Through the animal experiment to find the main impact of SHR after copper and zinc supplementation.Methods: The experimental group SHR and WKY rats were fed with physiological dose of copper sulfate and zinc sulfate in drinking water along with drinking deionized water controls. The rat blood pressure was detected at 12 weeks and 16 weeks time-point. Every four weeks during the experiment, rat heart function was detected by echocardiography, including LVEDD, LVESD, %FS, LVEDV, LVESV, SV, EF, LVPWd, LVPWs, and cardiac index. After fed for 16 weeks, rats are sacrificed by directly draw blood from heart. The blood samples were detected by serological testing using IFCC methods. The heart, lung, liver, kidney, and aortic vessel were resected and their weight, organ/body weight ratio, and trace element content were detected. Results: The blood pressure monitoring showed that copper/zinc supplementation significantly decreased blood pressure of SHR compare to the control at 12 week time-point and 16 week time-point. The statistical analysis (Student t-test) showed significant difference. Echocardiography results showed that there was no obviously change of LVESD, and LVEDD in WKY rats compared with the control (P>0.05, Student t-test). At 8 weeks time-point, SHR copper/zinc supplement group increased these LVESD compared to its control (P<0.05). At 8 weeks and 12 weeks time-point, %FS of SHR copper/zinc supplement group was shorter than the control (P<0.05). The differences of LVEDV, LVESV and SV between SHR copper/zinc supplement group and control group had no statistical significance since the fourth week (P>0.05). At 8 weeks and 12 weeks time point, SHR copper/zinc supplement group LVPWs was decreased obviously compared to control (P<0.05). LVPWd decreased obviousely at 4 weeks and 8 weeks time-point (P<0.05). Heart index of copper zinc supplement WKY and SHR rats. Rats were sacrificed after 16 weeks of observation for serum physiological and biochemical indexes test， including liver function, kidney function, fasting blood glucose, early indicator of myocardial necrosis, blood lipid and blood electrolytes. The results of hepatic function showed that alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (TB), total protein (TP), albumin (ALB), globulin (GLB), albumin/globulin (A/G) were not significantly changed (P>0.05). Detection of renal function found that blood urea (BU), creatinine (Cr) also did not change significantly (P>0.05). Fasting blood sugar has not changed. MB isoenzyme of creatine kinase (CK-MB), creatine phosphate isoenzyme (CK) test results showed that after adding copper and zinc, WKY rat CK-MB, CK were significantly lower (P<0.05, Student t-test), CK-MB, CK of SHR rats did not increase significantly. Serum lipids, total cholesterol, low density lipoprotein, high density lipoprotein were deteced, the results showed that after adding copper and zinc, WKY rats and SHR rats serum total cholesterol, low density lipoprotein levels did not change significantly. WKY rats high-density lipoprotein decreased significantly compared with the control group (P<0.05). Electrolyte analysis showed that, after adding copper and zinc, WKY rats and SHR rats serum elements content, such as potassium (K+), sodium (Na+), chlorine (Cl-), total calcium (Ca), total magnesium (Mg), calcium (Ca2+), magnesium (Mg2+), iron (Fe2+), zinc (Zn2+), compared with the control group did not change significantly. SHR copper/zinc supplementation group increased serum Copper was not obviously (P>0.05), but copper/zinc ratio was significantly higher (P<0.05). Organ/body weight ratio calculation showed that after adding copper and zinc, SHR rats' heart/body weight ratio compared with the control group decreased (P<0.05), lung/body weight ratio decreased even more (P<0.01), kidney/body weight ratio

was not significant changed. It is noteworthy that after the copper and zinc supplement, WKY rats lung/body weight ratio was significantly increased (P<0.01). After the addition of copper and zinc, SHR rats liver/body weight ratio decreased compared with the control group, but was not obvious (P>0.05). Trace elements by AAS detection of copper and zinc content of rat heart found that copper, zinc content did not change significantly, and no significant changes in copper and zinc ratio (P>0.05).Conclusion: The copper and zinc added to the SHR rats without apparent side effects, the physiological function of the SHR rats have shown some improvement. Adding trace elements copper and zinc by drinking water, can significantly reduce blood pressure in spontaneously hypertensive rats.

【中文名称】糖尿病胰岛移植免疫耐受的基础问题研究
【英文名称】Basic research of islet transplantation immune tolerance targeting to diabetes mellitus
【研究起始时间】2009-05
【研究终止时间】2011-05
【中文关键词】胰岛移植；排斥反应；免疫耐受
【英文关键词】islet transplantation;rejection;immune tolerance
【中文摘要】胰岛移植是很有前途的治疗I型糖尿病的新方法，但该方法所面临的主要问题是移植术后的排斥反应和长期使用免疫抑制剂的毒副作用。本课题以小鼠动物模型为基础，应用蛋白芯片技术分析移植前后血清蛋白谱的改变，定量检测血清中所筛选出的生物标志分子的水平，找到早期排斥反应的生物标志分子并探索其改变与排斥反应发生的关系，并阐明诱导移植物耐受形成的机制并解决早期排斥反应的检测问题。研究认为EGF与胰岛移植物损伤程度有直接关系，EGF可以作为一个指示排斥反应发生发展的生物标志分子。
【英文摘要】Islet transplantation is an ideal method to cure type I diabetes mellitus， but it is limited by the rejection and the application of immune inhibitor. On the basis of mouse model, we analysis the cytokines profile in mouse serums before and after transplantation using the cytokine array and quantified the biomarker. We find EGF is a good biomarker to predict the degree of rejection.

【中文名称】细胞色素C氧化酶在肥大心肌细胞逆转过程中的作用及其与血管内皮生长因子的关系
【英文名称】Cytochrome c Oxidase Is Essential for Copper-induced Regression of Cardiomyocyte Hypertrophy
【研究起始时间】2008-02
【研究终止时间】2010-05
【中文关键词】铜；细胞色素C氧化酶；血管内皮生长因子；心肌细胞；细胞大小；肥大
【英文关键词】 Copper, Cytochrome c oxidase, Vascular endothelial growth factor, Cardiomyocytes, Cell size, Hypertrophy
【中文摘要】背景：体内研究发现，饲料中添加生理剂量的铜可逆转由主动脉升支缩窄术诱导的小鼠心肌肥大。体外实验证明，心肌肥大的逆转与肥大心肌细胞的逆转相关。培养基中铜的添加可逆转因去氧肾上腺素诱导的原代心肌细胞肥大改变，这一过程依赖于血管内皮生长因子的表达。此外，血管内皮生长因子也可逆转由去氧肾上腺素诱导的肥大的原代心肌细胞。目的：研究细胞色素C氧化酶在铜及血管内皮生长因子逆转肥大心肌细胞过程中所发挥的作用。方法：（1）用新出生三天内的乳鼠进行心肌原代培养，向原代心肌细胞培养基中加入终浓度为l00μM的去氧肾上腺素，培养48小时引起心肌细胞肥大。在去氧肾上腺素依然存在的情况下，向肥大心肌细胞培养基中加入终浓度为5μM的硫酸铜或20ng/ml血管内皮生长因子，使肥大的心肌细胞发生逆转。通过细胞大小、细胞内总蛋白含量、心肌细胞肥大相关基因表达、细胞数、细胞凋亡等指标的检测进行评价。（2）通过siRNA技术，沉默细胞色素C氧化酶亚基Ⅰ导致细胞色素C氧化酶失活，观察细胞色素C氧化酶在铜及血管内皮生长因子逆转肥大心肌细胞过程中的作用，并通过细胞大小、细胞内总蛋白含量、心肌细胞肥大相关基因表达、细胞数、细
【英文摘要】Background: In vivo study, the results show that dietary copper supplementation can reverse heart hypertrophy which is induced by pressure overload in a mouse model. The studies show that both copper (Cu) and vascular endothelialgrowth factor (VEGF) reduce the size of hypertrophic cardiomyocytes in vitro, and Cu regression of cardiac hypertrophy is VEGF dependent. Cytochrome c oxidase (COX) plays a critical role in mitochondrial function and its activity is regulated by Cu status. Aims: Because mitochondrial integrity is essential for VEGF-mediated cellular function, the present study is undertaken to test the hypothesis that COX is a determinant factor in Cu- and VEGF- induced regression of cardiomyocyte hypertrophy.Methods: (1) Primary cultures of neonatal rat cardiomyocytes were treated with phenylepherine (PE) at a final concentration of l00 μM in cultures for 48 h to induce cell hypertrophy. The hypertrophic cardiomyocytes were treated with Cu sulfate or VEGF at a final concentration of 5 μM and 20ng/ml respectively in cultures for 24 h with a concomitant presence of PE. The results were determined by cell size, total protein content, cell number, expression of cardiomyocyte hypertrophy related gene and cell apoptosis. (2) Gene silence was applied to study

the effect of COX activity change on the regression of cardiomyocyte hypertrophy. COX activity was significantly inhibited by using siRNA targeting COX-I, then the role of COX in the progress of Cu or VEGF-induced regression of hypertrophic cardiomyocytes was detected. The results were determined by cell size, total protein content, cell number, expression of cardiomyocyte hypertrophy related gene and cell apoptosis. (3) The influence of COX in the progress of Cu or VEGF induced regression of cardiomyocyte hypertrophy was determined by COX activity assay.Results: (1) Cu or VEGF restored the hypertrophic cardiomyocyte which was induced by PE. The results were determined by cell size, total protein content, cell number, expression of cardiomyocyte hypertrophy related gene and cell apoptosis. (2) Gene silencing using siRNA targeting COX- I significantly inhibited COX activity and blocked the Cu- and VEGF-induced regression of cell hypertrophy. The results were determined by cell size, total protein content, cell number, expression of cardiomyocyte hypertrophy related gene and cell apoptosis. (3) PE treatment decreased COX activity in hypertrophic cardiomyocytes and Cu addition restored the activity along with regression of cell hypertrophy. VEGF alone also restored COX activity; but under the condition of COX inhibition by gene silencing, VEGF induced regression of cell hypertrophy was suppressed. The results indicate a new study direction in mechanisms on the process of hypertrophic cardiomyocyte reversion. VEGF may influence the expression of Cu-binding protein and leads to the redistribution of Cu in cardiomyocyte.Conclusion: This study demonstrates that both Cu and VEGF can restore COX activity that is depressed in hypertrophic cardiomyocytes and COX plays a determinant role in both Cu- and VEGF- induced regression of cardiomyocyte hypertrophy.

【中文名称】基于DnaE内含肽的定量检测GPCRs内吞方法的建立
【英文名称】Development of a Novel Assay Based on DnaE Intein for Quantitative Analysis of GPCRs Internalization
【研究起始时间】2007-09
【研究终止时间】2010-01
【中文关键词】G 蛋白偶联受体；定量内吞；功能筛选；DnaE 内含肽；荧光素酶
【英文关键词】G-protein-coupled receptors; quantitative analysis of internalization; functional assay; DnaE intein; Luciferase
【中文摘要】G 蛋白偶联受体（G-protein-coupled receptors, GPCRs）家族参与了机体内多种生理过程的调节，是治疗多种人类疾病的主要药物靶点。检测非G 蛋白亚基依赖的G 蛋白偶联受体的内吞可用于研究受体激动剂的活性。本论文首先从蓝细菌克隆到新的DnaE 内含肽并鉴定其自我剪接功能；此后我们建立了一种新型的定量分析GPCRs 内吞的方法，该方法基于Npu-DnaE 内含肽介导的蛋白剪接而重组断裂Renilla 荧光素酶活性和被配体活化的受体与β-arrestins2 之间的相互作用。试验检测了4 个功能差异（即偶联不同亚型G 蛋白）的G 蛋白偶联受体：昆虫脂动激素受体（AKHR）、人源烟酸受体（HM74a）、人源大麻受体2（CB2）、人源组胺受体1（H1）的内吞作用，结果所得的已知激动剂或拮抗剂引起相应受体内吞的EC50 或IC50 值与文献一致，充分证明了该方法的可行性与灵敏性。其方便快速、灵敏定量的特性可进一步用于细胞水平上G 蛋白偶联受体的功能筛选，为高通量药物筛选领域注入新的力量。
【英文摘要】G-protein-coupled receptors (GPCRs) are involved in a wide range of physiologicalprocesses and diseases, and represents significant and attractive targets for drugdiscovery. GPCR internalization provides a G-protein-subtype-independent method todetermine agonist-stimulated activation of receptors. Firstly a new split DnaE inteingene was cloned from the Cyanobacteria and characterized. Then we have developeda novel assay for quantitative analysis of GPCR internalization based onreconstitution of split fragments of Renilla Luciferase (RLuc) by proteintrans-splicing with Npu-DnaE intein and the interaction between agonist-activatedGPCR and β-arrestins2. This assay system has been further validated with fourfunctionally divergent GPCRs: the insect adipokinetic hormone receptor (AKHR), thehuman nicotinic acid receptor (HM74a), the human cannabinoid receptor 2 (CB2) andthe human Histamine 1 receptor（H1）. The EC50 data obtained for known agonists andantagonist are in close agreement with the results of previous reports, indicating thatthis assay system has sufficient sensitivity for quantization of GPCR internalization.This rapid and quantitative assay could therefore be used as a universal and functionalcell-base assay for GPCR high-throughput screening for drug discovery.

【中文名称】基于报告基因检测系统的G蛋白偶联受体第二信使cAMP、Ca2+检测方法的建立
【英文名称】Development of Novel Assays for Detection of GPCR Mediated Second Messenger-cAMP and Ca2+
【研究起始时间】2008-09
【研究终止时间】2011-03
【中文关键词】G蛋白偶联受体； 报告基因检测系统； cAMP、Ca2+信号通路；
【英文关键词】G-protein-coupled receptors； reporter-gene assay system； cAMP and Ca2+ signal pathways；
【中文摘要】G蛋白偶联受体(G-protein-coupled receptors, GPCRs)家族参与了机体内多种生理过程的调节,是治疗多种人类疾病的主要药物靶点。检测G蛋白偶联受体活化后第二信使cAMP和Ca2+信号可用于研究受体激动剂活性、信号通路

及受体功能研究,并应用于G蛋白偶联受体药物筛选和研发。本论文构建了新型的双反应元件、双报告基因检测系统CRE-rLuc/NFAT-fLuc,可同时检测胞内cAMP和Ca2+信号变化。试验检测了6个功能差异(即偶联不同亚型G蛋白)的G蛋白偶联受体：昆虫脂动激素受体(AKHR)、人源大麻受体1、2(CB1、CB2)、人源组胺受体1、3(H1R、H3R)、人源烟酸受体(HM74a)、人源胰高血糖素样肽1(GLP-1),结果所得的已知激动剂引起相应受体cAMP和Ca2+的EC50与文献一致,且cAMP和Ca2+信号特征与经典胞内cAMP和钙流检测法测得的结果一致,充分证明了该方法的可行性与灵敏性。应用该检测系统,初步检测了各类抑制剂对受体cAMP和Ca2+信号通路的影响,及共表达不同受体的信号整合效果。该检测系统方便快速、灵敏定量的特性可进一步用于细胞水

【英文摘要】G-protein-coupled receptors (GPCRs) are involved in a wide range of physiological processes and diseases, and represents significant and attractive targets for drug discovery. GPCRs interact with heterotrimeric G proteins to regulate a range of second messenger pathways to enable communication from the cell surface to the nucleus. Ca2+ and cAMP are important second messengers that regulate multiple cellular processes. Based on cAMP response element (CRE) and nuclear factor of activated T-cells (NFAT), we have developed a novel assay system with dual-reporter gene to detect both cellular cAMP and Ca2+ signals, providing a G-protein subtype-independent method to determine agonist-stimulated activation of receptors. This assay system has been further validated with six functionally divergent GPCRs:the insect adipokinetic hormone receptor (AKHR), the human cannabinoid receptor 1 and 2 (CB1 and CB2), the human Histamine receptor 1 and 3 (H1R and H3R), the human nicotinic acid receptor (HM74a) and the human Glucagon-like peptide 1 (GLP-1). The EC50 data obtained for known agonists are in close agreement with the results of previous reports. Our data derived from this assay were found to be comparable to the results obtained with the classical cAMP and Ca2+ assay methods, indicating that this assay system has sufficient sensitivity for detection of GPCR-mediated second messenger signal. In the current study, we used this assay system to analyze the crosstalk between cAMP and Ca2+signal pathways, and also crosstalk between different GPCRs. This cell-based assay has been demonstrated to be easily manipulated, and to be cost-effective, with no requirements for sophisticated instruments and expensive reagents as a primary assay for GPCR. Therefore, this rapid and quantitative assay could be used as a universal and cell-based function assay for GPCR high-throughput screening for drug discovery.

【中文名称】家蚕脂动激素受体信号转导机制研究
【英文名称】The Mechanism of Signal Transduction of Adipokinetic Hormone Receptor in Bombyx Mori
【研究起始时间】2007-09
【研究终止时间】2010-06
【中文关键词】 信号转导； 激素受体； 家蚕； 内吞作用； 信号通路； 受体表达； 细胞分泌； 介导的； 脂类； 抑制剂； 信号途径； 内质网； 糖类代谢；
【英文关键词】hormone；adipokinetic； receptor； Arrestin；siRNA；cAMP；ERK；
【中文摘要】脂动激素受体(AKHR)是一类典型的G蛋白偶联受体,介导了昆虫体内的脂类及糖类代谢调控,AKHR的功能缺失会导致昆虫体内脂肪的积累及血淋巴糖浓度的升高,因此认为昆虫AKHR/脂动激素(AKH)系统是一个很好的研究人类脂类、糖类代谢紊乱的模型。之前的研究表明,AKH可以结合脂肪体上的受体,经Gs蛋白激活腺苷酸环化酶,导致胞内cAMP浓度的增加；另一方面激活磷脂酶C,进而诱导胞内Ca2＋水平的升高。但是有关信号转导的具体机制我们仍不清楚。为了弄清AKHR的信号转导机制,我们从家蚕脂肪体中克隆得到了家蚕AKHR,并且在HEK293(人胚肾293)细胞上检测了受体的功能。我们的结果表明,AKHR受到配体刺激后,会导致胞内Ca2+和cAMP水平的提高,随后丝裂原活化蛋白激酶(MAPK)信号通路被激活,并且在高浓度AKH刺激下,AKHR会从细胞膜上内吞到细胞质中。我们通过cAMP、MAPK及内吞(internalization)的检测,功能性证明了AKH2和AKH3也是AKHR的配体,其中AKH2(EC50=11.7±1.6 nM)与AKH1(EC50=6.4±1.9 nM)活性相当,但是AKH3

【英文摘要】Insects, the largest group of animals on earth, play very important roles in their ecosystems through plant pollination, nutrient recycling, and maintenance of plant community composition and structure. In addition, they provide us with many useful materials, such as honey, silk, and varnish. The importance of insects as biomedical models is evident by the fact that many discoveries in digestion, muscle contraction, and important metabolic and developmental pathways in insects are applicable to vertebrate systems.Adipokinetic hormones (AKHs) produced by the insect corpora cardiaca are among the most extensively characterized peptide hormones with almost 40 family members from most of the major insect orders. AKH is normally 8-10 amino acids long with a pyroglutamate at the N-terminus and an amidated C-terminus. In addition to the essential role of mobilization of metabolites during energy-expensive activities such as flight and locomotion, AKH is involved in the control of carbohydrate homeostasis in the haemolymph of Drosophila and Bombyx larvae. As shown in Table1, in Bombyx, a nonapeptide identical with Manduca AKH (AKH1) has been chemically identified, and recently another two cDNAs encoding the prepro-Bombyx AKH2 and AKH3 have been annotated and identified by combining homology search with cDNA cloning.The receptor of AKH was first identified as a typical G protein-coupled receptor from the fruitfly Drosophila melanogaster and the silkworm Bombyx mori in 2002, and then from the

cockroach Periplaneta americana and African malaria mosquito Anopheles gambiae. Previous biochemical characterization with isolated fat body suggested that AKH binds to its receptor and activates adenylyl cyclase via the Gs protein, which results in an increase of intracellular cAMP levels. In addition, AKH activates phospholipase C (PLC) to induce the release of Ca2+ from intracellular Ca2+ stores. However, the mechanistic details of AKHR signaling remain to be further elucidated.In this present study, we cloned the AKHR from the fat body of the silkworm Bombyx mori and further functionally characterized it and its peptide ligands in HEK293 cells. We conclude that after activation of AKHR, in addition to cAMP accumulation and Ca2+ release from Ca2+ stores, the mitogen-activated protein kinase (MAPK) pathway is subsequently activated and AKHRs are rapidly internalized from the plasma membrane upon agonist stimulation. AKH1 and AKH2 activated AKHR with similar affinity, but AKH3 exhibits almost much less activity on AKHR. These findings strongly implying that it is more likely that a second intrinsic AKHR exists as a high affinity receptor for AKH3 in Bombyx.Mitogen-activated protein kinase (MAPK) pathways regulate diverse processes ranging from proliferation and differentiation to apoptosis. Although it is well established that GPCRs play important roles in the regulation of intermediary metabolism, they have only recently been recognized as important mediators of cellular growth and differentiation via the MAPK pathway. To know the mechanistic details of AKH-mediated ERK1/2 activation, Using HEK293 cells stably or transiently expressing AKHR, we demonstrated that activation of AKHR elicited transient phosphorylation of ERK 1/2. Our investigation indicated that AKHR-mediated activation of ERK1/2 was significantly inhibited by H-89 (Protein kinase A inhibitor), Go6983, and GF109203X (Protein kinase C inhibitors), but not by U73122 (PLC inhibitor) or FIPI (PLD inhibitor). Moreover, AKHR-induced ERK1/2 phosphorylation was blocked by the calcium chelators EGTA and BAPTA-AM. Furthermore, ERK1/2 activation in transiently AKHR expressing HEK293 cells was found to be sensitive to pretreatment of pertussis toxin, whereas AKHR-mediated ERK1/2 activation was insensitive to siRNA-induced knockdown of p-arrestin and to pretreatment of inhibitors of EGFR, Src and PI3K. Based on our data, we propose that activated AKHR signals to ERK 1/2 primarily via PKA-and extracellular calcium-involved PKC- dependent pathways. Our current study provides the first in-depth study defining the mechanisms of AKH-mediated ERK activation through the Bombyx AKHR. Internalization is an important pattern to regulate the activity of GPCR, which are against-activated receptors from the surface into the intracellular membrane compartments of the cell. A large volume of data has accumulated regarding the mechanisms regulating the endocytosis of a wide variety of different GPCRs. Therefore, to identify the internalization details of GPCR is important to reveal its mechanism of signaling. We established a stable HEK293 cell line expressing AKHR-EGFP. Upon activation of AKHR-EGFP with ligand, the receptor was rapidly and dramatically redistributed in the cytoplasm with distinct perinuclear accumulation. From the results of siRNA, we can deduce GRK2, GRK5, and arrestin3 are involved in the internalization process of AKHR……

【中文名称】大麻素受体与G蛋白相偶联的分子机制及其信号转导途径研究
【英文名称】Investigation on the Molecular Mechanisms for the Regulation of Cannabinoid Receptor-G-protein Coupling and Their Signal Transduction Pathways
【研究起始时间】2007-09
【研究终止时间】2010-06
【中文关键词】大麻素； CB1受体； CB2受体； G蛋白； 刺激型G蛋白； 抑制型G蛋白； 环腺苷酸； 嵌合体； 突变体； 内吞； 促分裂原活化蛋白激酶； 钙离子；
【英文关键词】 Cannabinoid； CB1； CB2； G-protein； G_s； G_i； cAMP； chimera； mutant； internalization； MAPK； Ca2+；
【中文摘要】大麻是(Cannabis)一种古老的药用植物,它的最早使用记录可追溯到五千多年前。最新的研究发现,大麻素通过结合并激活特殊细胞表面的两类大麻素受体CBl和CB2发挥作用。CB1受体是中枢神经系统中最丰富的G蛋白偶联受体之主要参与精神和行为方面的调节。相比之下,CB2受体主要表达在周边免疫组织,参与机体的免疫应答。因此,深入研究大麻素受体的结构和功能关系及其信号转导途径,可以进一步阐明相关疾病发生的分子机制,为开发更有效的创新性治疗药物提供更好的理论基础和更广阔的思路。7跨膜受体与G蛋白的选择性偶联主要受两者的接触面调控,涉及到受体的多个部位和G蛋白的各亚基。然而,迄今为止决定受体与不同G蛋白偶联的高保真结构决定因子仍不被我们所知。CBl受体主要通过偶联Gi反向调节胞内cAMP,然而多个研究发现CB1受体可在某些特殊条件下通过偶联Gs介导胞内cAMP的产生。在本研究中,我们证明CB1受体可同时偶联到Gs提高胞内cAMP的水平和Gi介导ERK1/2和Ca2+信号的活化。相比之下,CB2受体选择性偶联到G；介导胞内cAMP水平的抑制。通过CB1/2嵌合体策略的运用,我们发现CB1受体的胞内第
【英文摘要】 Cannabis is an ancient medicinal plant, its first use of records can be traced back 5000 years ago. The latest study found that cannabinoids work through binding and activation of two types of cannabinoid receptors CB1 and CB2 in specific cell surface. CB1 receptors are among the most abundant G protein-coupled receptors in the central nervous system where they mediate the majority of the psychotropic and behavioral effects of cannabis. In comparison, CB2 receptors are expressed in peripheral immune tissues suggesting a role in immune response. Therefore, further investigation of cannabinoid receptors structure and function relationship and

their signal transduction pathways could further clarify the molecular mechanisms of related diseases, provide a better theoretical basis and broader thought to develop more effective and innovative therapeutic medicine.7TM receptor coupling selectivity to G-proteins is controlled by a large contact area that involves several portions of the receptor and each subunit of the G protein. However, fidelity structure determinants discriminate between different G-proteins are not well understood. The CB1 receptor is primarily known to be functionally coupled to the Gi-mediated pathway, through which it negatively regulates cyclic AMP production. However, several lines of evidence suggest that CB1 receptors can also stimulate the formation of cAMP through coupling to Gs. In the present study, we demonstrate that the CB1 receptor is capable of dually coupling to Gs-mediated cAMP accumulation and Gi-induced activation of ERK1/2 and Ca2+mobilization. In comparison, the cannabinoid CB2 receptor selectively couples to Gi and mediates an inhibitory effect on cAMP production. Through the analysis of CB1/CB2 chimeric receptors, the second intracellular loop (ICL2) of the CB1 receptor was primarily responsible for mediating selective coupling to Gs and Gi, whereas the C-terminal region of the receptor plays an important role in defining the effectiveness of G protein activation. Furthermore, the results obtained from mutagenesis indicate that mutation of Leu-222 in ICL2 to either Ala or Pro resulted in a switch in G protein coupling from Gs to Gi. Moreover, mutants with replacement of Leu-222 with either Ile or Val led to. balanced coupling of the receptor with Gs and Gi. We also noted that the three positive charged amino acids (His-219,Arg-220 and Arg-226) presented at the ICL2 are associated with selective coupling to Gs and essential for CB1 keeping in constraint state. Data from theoretical modeling of the GPCR-Ga complex reveal that different mutations of Leu-222 could lead to distinct local conformation, which constitutes the molecular basis of selective coupling of CB1 receptor to different G-proteins. Taken together, these results first demonstrate that L222, within a highly conserved DRY(X)6L motif in CB1 receptor, plays a critical role in mediating selective coupling to Gs and Gi, two contrary proteins with opposing effects in regulation of cAMP, and this mechanism likely plays an important role in mediating the specificity of other members of the GPCR family. Our studies provide new insight into the mechanisms governing the coupling of the CB1 receptor to G proteins and cannabinoid-induced tolerance and biphasic effects.In contrast to CB1, the CB2 only couple to Gi and inhibit adenylyl cyclase activity. In an attempt to convert the CB2 into a Gs-linked adenylate cyclase activating receptor we proceeded to make global domain replacement of the intracellular face of the CB2 with the corresponding regions of the CB1. The ICL2 exchange resulted in impaired cAMP inhibition and had significantly basal cAMP accumulation in the absence of agonist. Furthermore, results from multi-domains chimeras indicate replacement both of ICL2 and Cter resulted in a chimera capable of induce intracellular cAMP upon agonist treatment, and this effect was synergistically enhanced in the presence of forskolin. Moreover, we also mutated the pro-139 in CB2 receptor corresponding to L222 in CB1 receptor into alanine and leucine, and found that the P139L abrogated the Gi coupling while the P139A could still couple to Gi but with moderate impairment in inhibition of cAMP accumulation. Taken together, these results demonstrated that the ICL2 can alter the binding affinities of G proteins to which a receptor is coupled, but interaction among multi-loops is thoroughly involved in fully determining G-protein selectivity. Moreover, these results also initially suggested that the residue located at DRY(X)6L motif serves as a key site responsible for selective coupling to Gi in class A GPCRs. Desensitization and receptor trafficking tightly control the temporal and spatial regulation of GPCR signaling. We examined agonist-induced internalization and sorting mechanisms using cannabinoid CB2 receptors fused to green fluorescent protein (EGFP)……

【中文名称】在聚丙烯酰胺凝胶上，快速、灵敏的蛋白质双重染色技术
【英文名称】无
【研究起始时间】2006-12
【研究终止时间】2010-12
【中文关键词】聚丙烯酰胺凝胶，电泳，双重染色
【英文关键词】无
【中文摘要】本研究开发的快速、灵敏的蛋白质双重染色技术，灵敏度达0.05-0.1 ng/band，为目前最灵敏的蛋白质银染法。操作步骤灵活可控，1小时可完成离子对染料染色过程，灵敏度为2-8 ng/band，如有需要可在此基础上进一步进行银染，使灵敏度提高100倍。染色后的蛋白质经质谱鉴定显示本检测技术不影响蛋白质的后续研究，质谱兼容性良好。在开发蛋白质双重染色技术的同时，本本研究还开发了高灵敏度的蛋白质荧光检测技术、高通量的蛋白质负染检测技术和DNA染料、银染检测技术等。
【英文摘要】无

【中文名称】烟酸受体GPR109A信号转导和内吞分子机制研究
【英文名称】Characterization of Agonist-Mediated Signaling and Internalization of Human Nicotinic Acid Receptor GPR109A

【研究起始时间】2006-09
【研究终止时间】2011-05
【中文关键词】烟酸；人烟酸受体；内吞；失敏；自身活；促分裂原活化蛋白激；钙离子
【英文关键词】Nicotinic acid; GPR109A; Internalization; Desensitization; Consititutive activation; MAPK; Ca2+
【中文摘要】烟酸作为一种降脂药物已经在临床上广泛使用了50多年，烟酸不仅能够有效降低LDL-C的同时，还能提高HDL-C的水平，而烟酸受体GPR109A的发现为治疗高血脂和心血管系统疾病提供了一个很好的分子靶标，GPR109A受体信号转导机制的研究和小分子激动剂药物的研发因而受到广泛的重视。然而GPR109A受体内吞和其介导的信号转导的详细机制还不清楚。研究表明GPR109A受体的内吞主要由GRK2和arrestin3调节，而Gβγ起到了招募GRK2到细胞膜上的作用。蔗糖预处理或siRNA干扰网格蛋白的表达，GPR109A受体的内吞均受到显著抑制，说明其内吞是网格蛋白小泡依赖性的。进一步研究表明，当配体去除后，GPR109A能迅速回到细胞膜上，而且内含体的酸化对这一过程并不是必需的。百日咳毒素预处理不仅能抑制烟酸对forskolin引起的胞内cAMP 含量升高的抑制，还能抑制烟酸介导的胞内钙流以及GPR109A受体的内吞。通过缺失和定点突变，我们发现GPR109A羧基端在调控受体从内质网转运到细胞膜上，以及受体内吞、失敏及其自身活化方面扮演非常重要的角色。△295-314突变体完全不能定位
【英文摘要】Nicotinic acid (niacin) has been widely used as a favourable lipid-lowering drug for 50 years, and the orphan G protein-coupled receptor GPR109A has been identified to be a receptor for niacin with the ability to lower levels of total plasma cholesterol, free fatty acids and triglycerides and to strongly raise high-density lipoprotein cholesterol (HDL-C). Therefore, GPR109A has been validated as a good target for treatment of lipid disorders and atherosclerosis. However, the underlying molecular mechanisms that regulate signalling and internalization of GPR109A remain largely unknown. Our research indicated that the internalization of GPR109A was mainly regulated by GRK2 and arrestin3, and Gβγ subunits recruited GRK2 to the membrane. GPR109A internalization was significantly blocked by pretreated with hypertonic sucrose or transfected with clathrin specific SiRNA, indicating that GPR109A internalize via the clathrin-coated pit pathway. Further investigation demonstrated that internalized GPR109A was recycled to the cell surface after the removal of agonist, and recycling of the internalized receptors was not blocked by treatment with acidotropic agents, NH4Cl and monensin. Pertussis toxin pretreatment not only inhibited forskolin-induced cAMP accumulation and intracellular Ca2+ mobilisation, but it also significantly attenuated agonist-promoted GPR109A internalization. By generating a number of mutatants with deletion or site-directed mutagenesis, we identified different domains at the C-terminal tail responsible for receptor export from the endoplasmic reticulum (ER), internalization and desensitization, and receptor consititutive activation. Deletion of the 295-314 amino acids completely abolished surface expression of the receptor. This mutant receptors were retained in the ER and failed to response to agonost in signaling. The △315-328 mutant was functional in inducing the agonist-mediated signaling as the wild type (WT) receptor, but this mutant exhibited dificiency in agonist-induced internalization and desensitization. By progressively site-directed mutation we found the serine and threonine cluster STS (326-328) plays a key role in receptor internalization and arrestin3 association. These data indicate that the STS cluster is the phosphorylation sites after agonist treated. The △329-343 mutant underwent rapid agonist-induced internalization in the absence of agonists, showing constitutive activity in signaling and internalization.Almost all GPCRs signal through the mitogen-activated protein kinase (MAPK) cascades, which are traditionally associated with growth factor receptor signaling and are involved in the control of cell proliferation and growth, mobility, differentiation and apoptosis. Using CHO-K1 cells stably expressing GPR109A, and A431 cells, which is a human epidermoid cell line with high levels of endogenous expression of functional GPR109A receptors, we found that activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2) by niacin was rapid, peaking within 2-5 min, and was significantly blocked by pertussis toxin. Furthermore, time course experiments with different kinase inhibitors demonstrated that GPR109A induced ERK1/2 activation via the MMP/EGFR transactivation pathway with a maximum response at 2-5 min, distinct from the PKC pathway-mediated ERK1/2 phosphorylation that occurs at early time points (≤2 min) in response to niacin. Overexpression of Gβγ subunits scavengers βARK1-CT and α-transducin led to a significant reduction of ERK1/2 phosphorylation, suggesting a critical role for βγ-subunits in GPR109A-activated ERK1/2 phosphorylation. Using arrestin-2/3 specific siRNA and an internalization-deficient GPR109A mutant, we found that arrestin-2 and arrestin-3 were not involved in GPR109A-mediated ERK1/2 activation.Through this study, we clarified the detailed mechanism of internalization of human nicotinic receptor GPR109A, and identified the role of its carboxyl terminus on receptor localization, endocytosis, desensitization, arrestin3 association and consititutive activation, as well as the regulation of ERK1/2 phosphorylation. On this basis, we hope to through follow-up experiments to further elucidate the detailed mechanism of lowering blood lipids and causing skin flushing induced by GPR109A. And our researh provide a theoretical basis for development of more efficient but without causing skin flushing drugs.

【中文名称】水稻灌浆基因GIF1的图位克隆、功能和分子驯化研究
【英文名称】Map-based clone, function and domestication of GIF1
【研究起始时间】2004-01
【研究终止时间】2009-12
【中文关键词】水稻，GIF1基因，灌浆，产量，水稻驯化，复制扩增，功能分化，仓储病害，抗病性，发芽势。
【英文关键词】rice, GIF1 gene，grain-filling, yield, rice domestication, gene duplication, sub-functionalization, neo-functionalization, rice resistance, germination ratio
【中文摘要】1.水稻产量性状是数量性状，由一系列的基因控制，许多这些性状和水稻的驯化相关。水稻灌浆直接决定水稻的产量，而许多优良品种存在灌浆不足、瘪粒多的问题，因此灌浆性状是高产育种的潜力所在。但由于水稻灌浆的复杂性与研究的困难，对于水稻灌浆的研究一直很难获得突破，是目前育种中的一个瓶颈问题。为了解水稻籽粒灌浆的遗传调控，通过筛选突变体库，得到一个影响水稻灌浆和千粒重的突变体（gif1）。该突变体的灌浆在3到15天时明显受到抑制，并导致淀粉粒发育不规则，支链淀粉和直链淀粉含量发生明显变化。遗传分析发现，gif1突变体的表型是由一个隐性基因控制。通过图位克隆的方法把gif1位点定位在四号染色体的长臂端的32-Kb的基因组片断内。测序发现，在一个预测的细胞壁蔗糖转化酶基因的外显子上有一个脱氧核糖核酸缺失，导致该基因功能性缺失（knockout）。互补试验表明，野生型的GIF1基因能够使突变体的表型回复到野生型。同时通过生物化学的方法证明GIF1蛋白有蔗糖转化酶活性，并且定位在细胞壁。利用原位杂交和GIF1启动子驱动GUS的转基因植株分析表明，GIF1基因主要表达在组织生长旺盛的、需要能量供应的库
【英文摘要】Rice grain yield consists of several key components, including grain number and grain weight, which is controlled by a number of QTLs derived from natural allelic variations. Grain-filling is an important trait greatly contributing to grain weight mostly regulated by many genes and associated with the crop domestication syndrome. We have screened for mutants with grain-filling defect in our mutant population (O. sativa japonica Zhonghua11). One mutant, grain incomplete filling 1 (gif1), showed much slower grain-filling than wild-type rice during early filling stage with 3-15 days after pollination (DAP). The mutant accumulated less sugar and starch contents, and also showed markedly more grain chalkiness as a result of abnormally developed and loosely packed starch granules. Through map-based cloning with a mapping population, we located the GIF1 gene to a 32-kb region on chromosome 4. We find that the GIF1 gene, which encodes a predicted cell wall invertase required for carbon partitioning during grain-filling, has 1-bp deletion in the coding region that leads to a premature protein. We confirmed that GIF1 functions as a key regulator of grain-filling by functional complementation test. We also determined its activity as cell well invertase by biochemical assay and the subcellular localization of the GIF1-GFP fusion protein. The GIF1 gene is expressed mainly in the ovular vascular and lateral stylar vascular traces of filling grains, and elongating internodes and roots where large amount of sugars and energy is needed. Interestingly, the cultivated rice GIF1 gene shows a restricted expression pattern during grain-filling compared to the wild rice allele, probably a result of accumulated mutations in the gene's regulatory sequence through domestication. The nucleotide diversity of the GIF1 loci in cultivated and wild rice indicates that GIF1 was most likely subjected to domestication selection. The wild rice GIF1 allele is semi-dominant with a broader expression pattern particularly in the pericarp and endosperm compared to the cultivated rice allele. Fine mapping with introgression lines (ILs) revealed that the wild rice GIF1 is responsible for grain weight reduction. While the introgression lines carrying the cultivated japonica and indica alleles produced same-weight grains, indicating that cultivated GIF1 alleles have achieved the same function in grain-filling. Ectopic expression of the cultivated GIF1 gene with the 35S or rice Waxy promoter resulted in smaller grains, whereas overexpression of GIF1 driven by its native promoter increased grain production. These findings, together with the domestication signature, strongly suggest that GIF1 is a potential domestication gene and that such a domestication-selected gene can be used for further crop improvement.The genetic and molecular basis of morphological evolution is poorly understood in evolutionary biology. How gene duplication and divergence contribute to genetic novelty and morphological adaptation has been interesting to biologists. We showed that functional sub-functionalization evolution of duplication genes contributed to genetic novelty and morphological difference in genus Oryza. Phylogenetic analyses showed that GIF1 and OsCIN1 are orthologous genes derived from a duplication occurring about 44 million years ago. After duplication, GIF1 and OsCIN1 underwent sub-functionalization by both divergent expression pattern and cell wall invertase enzyme activity. The transgenic plants ectopically expressing the GIF1 and OsCIN1 genes showed different phenotypes in morphology and grain-filling, indicating that GIF1 and OsCIN1 were neo-functionalized in Oryza sativa. Moreover, we have shown that the cis-regulatory region of GIF1 was selected, most likely resulting in different expression patterns in Oryza sativa and O. rufipogon during rice domestication at a recent time. On other evolutionary trajectory, the orthologous GIF1 was either lost or degenerated in the Non-AA genomes , BB, CC, BBCC and CCDD wild rice relatives. Our results suggest that gene duplication is a necessary contributor to evolution, and gene sub- or neo-functionalization is required for morphological evolution.It has been suggested that sugar metabolism is an important factor of plant defense responses, particularly in enhancing the cell wall fortification. The mutant gif1 was susceptive to postharvest pathogenic fungi, and the transgenic plants ectopically expressing the GIF1 showed

enhanced resistance to bacterial blight (Xoo) and fungal blast (M. grisea). Microarry data and RT-PCR results showed that cell wall synthesis genes were greatly regulated in the gif1 mutant. Together, the genetical results indicate that sucrose homeostasis is actively involved in plant disease resistance.

【中文名称】自发脑出血模型建立及EIT检测的实验报告
【英文名称】the report of the establishment of experimental spontaneous intracerebral hemorrhage animal model and the testing of EIT monitoring
【研究起始时间】2010-02
【研究终止时间】2010-08
【中文关键词】自发性脑出血动物模型；EIT；实时监测
【英文关键词】experimental spontaneous intracerebral hemorrhage model；EIT；real-time monitoring
【中文摘要】本实验报告为总试验计划的初始部分。本报告记录了实验模型的建立和EIT检测对脑出血监测的可行性。
【英文摘要】This study reports the initial part of the total trial. This report documents the establishment of experimental animal model and the feasibility of EIT on monitoring the spontaneous intracerebral hemorrhage.

【中文名称】SD大鼠肌肉注射Ad-HBx/IL-12急性毒性试验
【英文名称】The acute toxicity test of SD rats with a single intramuscular injection Ad-HBx/IL-12
【研究起始时间】2008-10
【研究终止时间】2008-11
【中文关键词】腺病毒，HBx，急性毒性
【英文关键词】Adenovirus, HBx, acute toxicity
【中文摘要】Ad-HBx/IL-12是由四川大学生物治疗国家重点实验室提供的蛋白重组腺病毒，拟用于肝癌的治疗。临床拟用途径为肌肉注射。国家成都中药安全性评价中心按照新药申报的相关要求对四川大学生物治疗国家重点实验室提供的Ad-HBx/IL-12进行了SD大鼠单次肌肉注射急性毒性试验，观察给药后可能引起毒性反应，初步推测Ad-HBx/IL-12安全范围及毒性靶器官或靶组织，为重复给药毒性试验可能的靶器官和毒性反应等指标的设计提供参考。本试验中，供试品Ad-HBx/IL-12共设3个剂量组：分别为3.6×109 、1.8×1010、9.0×1010VP/kg，另设一溶剂对照组（病毒保存液），每组大鼠10只，雌雄各半，共40只。各组大鼠均按1ml/kg的比例单次肌肉注射给予相应浓度的供试品或溶剂。给药后每天观察动物外观体征、行为活动、腺体分泌、呼吸、粪便性状、生殖器、死亡等情况及其他毒性反应，并于给药后第1、3、7天从眼眶采血进行血液学、血液生化学检查，第14天观察结束时所有存活动物麻醉后（60mg/kg戊巴比妥钠，腹腔注射）腹主动脉采血安乐死进行检查，并进行系统尸解，全面观察动物的外观和内脏情
【英文摘要】无

【中文名称】食蟹猴肌肉注射Ad-HBx/IL-12急性毒性试验
【英文名称】The acute toxicity test of Cynomolgus monkeys with a single intramuscular injection Ad-HBx/IL-12
【研究起始时间】2008-10
【研究终止时间】2009-03
【中文关键词】腺病毒，HBx，急性毒性
【英文关键词】Adenovirus, HBx, acute toxicity
【中文摘要】Ad-HBx/IL-12是由四川大学生物治疗国家重点实验室提供的蛋白重组腺病毒，拟用于肝癌的治疗。临床拟用途径为肌肉注射。国家成都中药安全性评价中心按照新药申报的相关要求对四川大学生物治疗国家重点实验室提供的Ad-HBx/IL-12进行了食蟹猴单次肌肉注射急性毒性试验，观察给药后可能引起毒性反应，初步推测Ad-HBx/IL-12安全范围及毒性靶器官或靶组织，为重复给药毒性试验可能的靶器官和毒性反应等指标的设计提供参考。试验设Ad-HBx/IL-12 2.56×1010vp/kg 1个剂量组，另设一溶剂（病毒保存液）对照组，每组食蟹猴4只，雌雄各半。给药组及对照组食蟹猴均按1mL/kg的比例单次肌肉注射给予相应浓度的供试品或溶剂。给药后每天观察动物外观体征、行为活动、腺体分泌、呼吸、粪便性状、生殖器、死亡等情况及其他毒性反应，并于给药后第1、7、14天进行体温、血液学、血液生化学、心电图、尿液等检查，第14天观察结束时所有存活动物麻醉后（30mg/kg戊巴比妥钠，静脉注射）股动脉放血实施安乐死，并进行系统尸解，全面观察动物的外观和内脏情况。对发现异常的脏器组织进行病理组织学检查。
【英文摘要】无

【中文名称】SD 大鼠注射给予Ad-HBx/IL-12 3 个月长期毒性实验
【英文名称】The chronic toxicity test of SD rats with intramuscular injection Ad-HBx/IL-12
【研究起始时间】2009-08
【研究终止时间】2011-03
【中文关键词】腺病毒，HBx，长期毒性
【英文关键词】Adenovirus, HBx, chronic toxicity
【中文摘要】成都华西海圻医药科技有限公司（国家成都中药安全性评价中心）按《药品注册管理办法》对新药申报的相关要求，对Ad-HBx/IL-12进行SD大鼠肌肉注射给药3个月长期毒性试验，观察该药物可能引起毒性反应的性质、程度、时效关系及可逆性，推测毒性靶器官或靶组织，为临床研究提供参考信息。本试验将130只大鼠按体重随机分成5个组，分别为Ad-HBx/IL-12 0.5、2.5、12.5×109 VP/kg剂量组，空载腺病毒组及溶剂对照组（病毒保存液），每组26只，雌雄各半。各组均按2 mL/kg的体积肌肉注射给予相应浓度的供试品、空载腺病毒或对照品，每周给药一次，连续给药3个月，停药恢复性观察33天。给药期及恢复期每天观察动物一般状况；每周进行体重和摄食量测定；于给药后2、4周，2、3个月及恢复期结束时检测抗体；于给药结束和恢复期结束，每组分别取16、10只SD大鼠（雌雄各半）采血进行血液学、血生化、细胞因子、细胞分型、补体及免疫复合物检测，并施以安乐死后进行系统尸检以及相应组织或器官的病理组织学等检查；于给药结束检测血浆、注射部位肌肉腺病毒滴度及X蛋白水平。主要结果如下：一般状况
【英文摘要】无

【中文名称】食蟹猴肌肉注射给予Ad-HBx/IL-12 3 个月长期毒性实验
【英文名称】The chronic toxicity test of Cynomolgus monkeys with intramuscular injection Ad-HBx/IL-12
【研究起始时间】2009-09
【研究终止时间】2011-05
【中文关键词】腺病毒，HBx，长期毒性
【英文关键词】Adenovirus, HBx, chronic toxicity
【中文摘要】摘 要乙肝病毒X蛋白是具有多功能的一种蛋白。委托方提供资料显示，该蛋白通过诱导特异性细胞毒T细胞（CTL）杀伤肿瘤细胞，达到治疗肝癌的目的。根据委托方提供的资料，Ad-HBx/IL-12小鼠有效剂量约为5×108 VP/kg。临床拟用剂量为5×107~5×108 VP/kg。按照《药品注册管理办法》对新药申报相关要求，参照国家食品药品监督管理局药审中心《治疗用生物制品非临床安全性技术审评一般原则》（2007年1月），对Ad-HBx/IL-12进行食蟹猴3个月肌肉注射给药长期毒性试验，观察该药物可能引起毒性反应的性质、程度、量效和时效关系及可逆性，推测毒性靶器官或靶组织，寻找NOAEL，提示临床试验中需重点监测的安全性指标。本试验设5个组，分别为溶剂对照组（病毒保存液），空载腺病毒对照组及Ad-HBx/IL-12 0.05、0.5、5×1010 VP/kg剂量组，每组6只食蟹猴，雌雄各半。各组猴均按0.5 mL/kg的体积肌肉注射相应浓度的供试品或对照品，每周给药一次，连续给药3个月，停药恢复性观察约8周。给药期及恢复期每天观察动物一般状态至少1次，每周测定体重、摄
【英文摘要】无

【中文名称】雅连濒危保护研究
【英文名称】Studies on endangered of Coptis deltoidea C. Y. Cheng et Hsiao
【研究起始时间】2007-09
【研究终止时间】2011-12
【中文关键词】雅连；濒危保护
【英文关键词】Coptis deltoidea C. Y. Cheng et Hsiao；endangered
【中文摘要】（1）完善雅连的种质资源圃的建设。（2）开展雅连的保护生物学研究，提出相应的保护措施，制定雅连濒危保护和可持续利用策略与途径。
【英文摘要】(1) improve the germplasm nursery with elegant construction. (2) to carry out the protection of biological research with elegant, propose appropriate protection measures, Coptis deltoidea endangered the development of elegant and sustainable use of strategies and approaches.

【中文名称】味连规范化种植研究
【英文名称】Studies on GAP for Coptis chinensis Franch.
【研究起始时间】2007-09

【研究终止时间】2011-12
【中文关键词】味连；GAP
【英文关键词】Coptis chinensis Franch.;GAP
【中文摘要】开展在种植适宜区的味连规范化种植研究，以《中药材规范化种植（养殖）技术指南》为指导，提高味连规范化种植技术含量，形成味连规范化种植标准操作规程（SOP），建立味连规范化种植基地。
【英文摘要】Appropriate to carry out the planting area Coptis chinensis Franch. standardized planting study to "traditional Chinese medicine standardized planting (breeding) Technical Guide" for guidance, Coptis chinensis Franch. standardized cultivation techniques to improve Coptis chinensis Franch.technology content, the formation of Coptis chinensis Franch. standardized plant standard operating procedures (SOP), the establishment of Coptis chinensis Franch. standardized planting base.

【中文名称】基于本草知识的酒蒸黄连“止消渴”作用的系统研究
【英文名称】The systemic study of JiuZhengHuangLian in diabetes based onthe Literature of Materia Medica
【研究起始时间】2007-09
【研究终止时间】2011-08
【中文关键词】酒蒸黄连；消渴；2型糖尿病；本草；系统研究
【英文关键词】JiuZhengHuangLian; Xiao-Ke; Type 2 Diabetes; Materia Medica; systemic study
【中文摘要】糖尿病已成为严重危害人类健康的重大疾病，积极防治尤为关键。黄连酒蒸炮制“止消渴”，历代本草多有记载，临床疗效确切。本课题在前期研究的基础上，基于古代本草知识，从临床有效性出发，系统围绕黄连酒蒸炮制前后的药效差异及其作用机制、降低”苦寒”毒副作用、入血成分变化、药效物质基础以及相关酒蒸炮制机理，多方面、多层次、多学科交叉结合开展酒蒸黄连“止消渴”的系统研究，从“入血成分变化——药效发挥——药效物质基础——体内物质变化——相关药效及炮制机理”，全方位阐述中药黄连酒蒸炮制机理和“止消渴”疗效的专属性，以期指导中医药糖尿病特色专科的临床用药。酒蒸黄连“止消渴”的疗效专属性、药效物质基础及其作用机制、炮制机理已较为明确。酒蒸黄连对2型糖尿病及其并发症的发生，具有良好的防治作用。酒蒸黄连“止消渴”，本草记载历史悠久，炮制特色鲜明，增效减毒作用明确。为此，我们建议，在中医药治疗“消渴证”的临床组方配伍用药或新药开发研究中，较生品黄连更适宜于选用酒蒸黄连，使用时应考虑临床用药剂量的个体化。这也体现了中医“随症炮制”的临床用药特色，值得更进一步的研究、关注。
【英文摘要】JiuZhengHuangLian (Rhizoma Coptidis steamed with rice wine, JZHL) was widely used in Traditional Chinese Medicine clinic as “Stop Xiao-Ke” (anti-diabetic) according to literatures of material medica and clincical potential application. The present dissertation were carried on aroud the pharmacodynamic variability, mechanisms, toxicity of bitter and cold, migrating to blood ingredients changes, material basis for efficacy, and related processing mechanism between pre and post steaming with rice wine. Subsequently, the following parameters were omnidirectionally elucidated including the processing mechanism of steaming with rice wine and the specificity of anti-diabetic effect of Rhizoma Coptidis (Huang-Lian), and then provide the guideline of clinical prescription in the treatment of diabetes using traditional Chinese medicine.Firstly, the pharmacodynamics of JZHL significantly improved glycolipid metabolic disturbance and insulin resistance as well as protected pancreatic beta cell both in diabetic animal models and 3T3-L1 lipocytes, compared with Rhizoma Coptidis (HL). In addition, the toxicity of bitter and cold of Rhizoma Coptidis and its alkaloids is remarkable attenuated by steaming with rice wine, which is more suitable for clinical diabetic patients. Furthermore, results confirm that the protected of JZHL against diabetic maybe involve in ameliorating glycolipid metabolic disturbance, attenuating in fl ammatory responses and oxidative stress, and reducing the impacts of metabolic stress, pro-inflammatory factors and oxidative stress products on insulin signaling transduction pathway. JZHL also improved insulin resistance and protected the structure and function pancreatic beta cell in the prevention and treatment of diabetes and diabetic complications.Secondly, material bases of pharmacodynamic: the anti-diabetic effects of JZHL were synergistic effects of multi-component and multi-target of JZHL depended on diabetic animal models, insulin resistance lipocytes model in vitro, and combined with analysis of constituents migrating to blood, the biological effects of related monomer ingredients, and effective fractions to demonstrate that.Finally, processing mechanism of JZHL were investigated at several levels, including characters and histological change of medicinal mater- ials, changes of constituents migrating to blood and pharmacokinetics of effective components. The results indicated that the processing mechanism of JZHL may be related to the changes of crystal form, structure and polarity of effective components, resulting in increases of decocting rate and solubility of effective components and enhancement of the absorbance and distribution of effective components in gastrointestinal tract, attenua- teing toxicity as well as enhancing the bioavailability and therapeutic specificity.In summary, the present research clarify that the therapeutic specificity of JZHL protected against diabetes and diabetic complications, pharmacodynamic material bases, pharmacodynamic mechanism and processing mechanism of JZHL. Moreover, it is very clear that the effect of “Stop Xiao-Ke” and processing mechanism of JZHL in literatures of materia medica, which had been cited in the traditional Chinese herbal literatures.

Hence, we propose that JZHL is more suitable than HL in several aspects, including the clinical prescription of traditional Chinese medicine, research and development of new anti-diabetic medicines, etc. Furthermore, the individual dosage should be certainly considered in the clinical application, which also incarnates the characteristic of processing according to symptoms in traditional Chinese medicine. Further research need to investigate the detailed mechanism.

【中文名称】焦虑障碍患者和正常被试者的影像数据分析
【英文名称】
【研究起始时间】2008-12
【研究终止时间】2010-12
【中文关键词】焦虑障碍；功能磁共振成像；数据分析
【英文关键词】
【中文摘要】实验目的：通过分析焦虑障碍患者和正常被试的功能磁共振图像，进而发现焦虑障碍患者的特征性脑结构、血流以及功能异常，确定该病各种临床特征与脑影像学表征模型的相关性。实验方法：应用各种单模态图像数据处理技术以及其整合后的多模技术。实验结果：发现了不同亚型的焦虑障碍患者存在不同的特征性的结构、血流及功能的异常改变。结论：焦虑障碍患者具有特征性的结构、血流及功能的异常改变。
【英文摘要】

【中文名称】绵羊椎体骨质疏松性生物力学模型的建立及评价
【英文名称】Establishment and evaluation of biomechanical model similar to lumbar vertebrae osteoporosis in sheep
【研究起始时间】2008-04
【研究终止时间】2010-05
【中文关键词】骨质疏松；椎体脱矿化模型；动物模型；骨密度；生物力学
【英文关键词】osteoporosis;invitro demineralized vertebra model;animal model;bone mineral density ; biomechanics
【中文摘要】自1959年Boucher首次采用长螺钉经椎板、椎弓根达椎体固定腰骶关节取得良好的临床效果以来,椎弓根螺钉内固定技术取得了迅速的发展，并被广泛的应用于脊柱外科的常见临床疾病。目前，椎弓根螺钉内固定技术已经成为脊柱外科领域最常用的脊柱后路内固定方法。研究发现:椎弓根螺钉的稳定性取决于骨质螺钉界面的把持力。然而，椎弓根螺钉内固定技术在临床的应用中发现，随着患者骨质疏松程度的加重，椎弓根螺钉松动率显著增高。为解决这一问题，目前临床上常用的方法包括：改进椎弓根螺钉设计；应用的钉道固化技术。然而，针对各种新型螺钉以及钉道固化技术的临床前实验研究，由于获取骨质疏松标本比较困难，大多限于在正常骨质的动物或健康的成人椎体上进行研究，较少应用骨质疏松或严重骨质疏松的动物或人椎体。因此，建立用于骨质疏松生物力学研究的模型是进行各种新型螺钉以及钉道固化技术的临床前实验研究的基础。目前用于骨质疏松情况下生物力学研究的动物模型，最常选用的动物为成年绵羊(山羊)，其建模的方法主要有：去势法，激素诱导，低钙饮食三种方法，它们存在的缺点：1、建模周期长且费用高，至少需要6个月饲育，延长了实验的研究周期；2、建模过
【英文摘要】Objective：1).To place sheep lumbar vertebrae into a beher-glass filled withhydrochloric acid and infuse hydrochloric acid by infusion pump into it as an in-vitro method to establish a biomechanical model similar to osteoporosis in sheep lumbar vertebrae.2). For the first time to comprehensively evaluate osteoporotic and biomechanical model from multiple levels ,which are two-dimensional and three-dimensional, macro and micro, qualitative and quantitative.and to analyze the related factors about the mechanical properties of this model.and analysis of the mechanical properties of the model of reasons for the decline.Material and Methods: 1) Designing a cylindrical perfusion connector with side hole as a bridge connecting the vertebrae and the infusion pump. 2): Forty-eight fresh lumbar vertebrae from 3±0.5years sheep, were randomly assigned to four groups by completely randomized design: Group A (no decalcification, the control group), Group B (decalcified with Hcl for 2 hours), Group C (decalcified with Hcl for 4 hours), Group D (decalcified with Hcl for 6 hours). 12 verterbraes of each group. 3): For the first time to comprehensively evaluate osteoporotic and biomechanical model from multiple levels ,which are two-dimensional and three-dimensional, macro and micro, qualitative and quantitative， and are in detail X ray, spiral CT, MicroCT, pathology; BMD; biomechanical testing（the axial pullout strength, maximum compressive strength）and bone histomorphometry analysisResult: 1): model assessment: ① After decalcification, vertebrae ’s BMD in A, B, C, D groups respectively decreased by 0,19%, 28% 38%;②we can observed fromX-ray, CT that with the extend of decalcification vertebrae ’s density image gradually became darker and vertebrae ’s cortical and cancellous bone became thinner and the space of cancellous bone became wider.③the results of three-dimensional reconstruction by Micro-CT show that with the prolong of decalcification time trabecular bone harvested from pedicle and central vertebrae in group B,C,D respectively became wider than that in group A,and its connection density gradually broke off,and the thickness of cortical bone havested from pedicle and

anterior vertebrae in group B,C,D is respectively obvious thinner than that in group. Accompanied by a decline in bone mineral density Tb.th,Tb.N,BV/TV and Cor.th of pedicle and central vertebrae in group B,C,D were significantly lower than those in group A,while Tb.sp was higher (P< 0.05) compared with group A. BS/BV of pedicle in each group has no significant difference,but BS/BV of vertebrae in each group gradually increased with the extendence of decalcification time.④Histopathological examination revealed that the trabecular bones from pedicle became thinner, their number decreased and the space between them widened, and the antrum of bone marrow enlarged in group B,C and D compared with group A. ⑤Biomechanical tests show means of Fmax , ε ult and its energy absorption of group B, C and D were significantly lower than those of group A(P < 0. 05) . while these values in each group are continuously falling With the extendence of decalcification time.2)Correlation analysis:After decalcification, the mechanical properties of vertebral body(Fmax and σ ult) have closely related to BMD and decalcification time, and also have significant relationship with space parameters of bone structure (tb.th, tb.N, tb.sp, BV / TV, BS / BV, Cor . th) , which is similar to mechanical changes in human vertebral osteoporosis.Conclusion：The method of acid decalcification may be useful for producing a quick, effective, and controllable biomechanical model similar to osteoporosis, it can provide reference data for biomechanical study in vivo model of osteoporosis.

【中文名称】骨质疏松条件下膨胀式椎弓根螺钉与骨水泥强化 螺钉的稳定性和钉道界面的比较研究

【英文名称】Comparative study of expansive pedicle screw and polymethylmethacrylate-augmented pedicle screw in osteoporosis: biomechanical and interfacial evaluations

【研究起始时间】2011-12

【研究终止时间】2010-05

【中文关键词】骨质疏松；膨胀式椎弓根螺钉；聚甲基丙烯酸甲酯；最大轴向拔出力；能量吸收值；显微CT；钉道界面

【英文关键词】Osteoporosis; Expansive pedicle screw; Polymethylmethacrylate; The maximum pullout strength; Energy absorbed to failure; Micro-CT; Interface

【中文摘要】椎弓根螺钉技术已经成为脊柱外科最常用的内固定技术。随着我国人口老龄化的日益加剧，越来越多的骨质疏松(osteoporosis, OP)患者因脊柱疾病需要进行内固定手术。然而，OP严重影响钉骨界面的结合强度，使螺钉的把持力下降，常常导致螺钉松动、退出。因此，如何有效的提高OP条件下椎弓根螺钉的稳定性、防止螺钉松动已经成为脊柱外科亟待解决的难题。本课题组在前期设计出膨胀式椎弓根螺钉(expansive pedicle screw, EPS)，研究表明EPS可以显著提高螺钉的稳定性，也可以有效的降低因增加螺钉的直径和长度带来的风险。有趣的是，通过文献回顾我们发现：尽管骨水泥(polymethylmethacrylate, PMMA)存在热损伤、渗漏和神经压迫等风险，但凭借其良好的机械强度和强化效果，PMMA仍然被广泛的用于OP条件下螺钉的强化处理。然而，在提高螺钉稳定性和优化钉道界面方面， EPS与传统的PMMA强化螺钉(polymethylmethacrylate-augmented pedicle screw, PMMA-PS)谁更具有优势呢？目前国内外还没有这方面的研究。

【英文摘要】Objective: To compare stability and interface of EPS and PMMA-PS through experiments in samples in vitro and in animal in vivo, and to provide sufficient theretical basis for wide application of EPS in clinic.Methods: 1) Experiments in vitro. OP biomechanical tests blocks, OP cadaveric lumbar vertebrae, sheep lumbar vertebrae in vitro were all randomly divided into three groups. A pilot hole was prepared using the same method in samples in each group. The conventional pedicle screw (CPS) was inserted directly into the pilot hole in CPS group. In PMMA-PS group, the pilot hole was filled with PMMA followed by insertion of CPS. In EPS group, EPS was inserted directly into the pilot hole and the component elements were assembled to EPS. Twenty four hours after insertion of pedicle screw, X-ray and CT examination and axial pullout tests were performed to all OP biomechanical tests blocks and OP cadaveric lumbar vertebrae, and axial pullout tests, cyclic bending resistance tests, micro-CT analysis and histological observation were performed to all sheep lumbar vertebrae in vitro.2) Experiments in vivo. After successful establishment of OP sheep, sheep lumbar vertebrae (L1-L6) were randomly divided into CPS, PMMA-PS and EPS groups and treated with the same methods in experiment in sheep lumbar vertebrae in vitro. Four sheep were selected randomly and killed at two study periods of 3 months and 6 months after operation respectively and axial pullout tests, micro-CT analysis and histological observation were performed.Results: 1) Experiments in vitro. No malpositioned screw and cement leakage were detected and all EPSs were obviously expanding in X-ray and CT examination. ① In OP biomechanical tests block, the maximum pullout strength (Fmax) and energy absorbed to failure (E) in PMMA-PS and EPS groups were all significantly higher than those in CPS group, but Fmax and E in EPS group were all significantly lower than those in PMMA-PS group. ② In OP cadaveric lumbar vertebrae, Fmax and EAV in PMMA-PS and EPS groups were all significantly higher than those in CPS group, but there were no significant differences in both Fmax and EAV between EPS and PMMA-PS groups.③ In sheep lumbar vertebrae in vitro, both axial stability and vertical stability of screws in PMMA-PS and EPS groups were significantly enhanced compared with those in CPS group, but there were no significances on both axial stability and vertical screw stability between EPS and PMMA-PS groups. Bone trabeculae wrapped up the screw directly forming a “ screw-bone ”

interface in CPS group. PMMA was found surrounding the screw totally and existing between screw and bone and in cavitas medullaris surrounded screw, which hampered the direct contact between bone and screw and formed a “ screw-PMMA-bone ” interface in PMMA-PS group. 2) Experiments in vivo. ① At 3-month and 6-month, Fmax and E in PMMA-PS and EPS groups were significantly higher than those in CPS group; however, there was no significant difference in both Fmax and E between EPS and PMMA-PS groups at two study periods. No significant differences were found in both Fmax and E in CPS and PMMA-PS groups between 3-month and 6-month, but Fmax and E in EPS group at 6-month were significantly higher than those at 3-month. ② At 3-month and 6-month, bone trabeculae wrapped up the screw directly forming a “ screw-bone ” interface in CPS group. In PMMA-PS group, PMMA was found surrounding the screw totally and existing between screw and bone and in cavitas medullaris surrounded screw, which hampered the direct contact between bone and screw and formed a “ screw-PMMA-bone ” interface. Newly formed bone wrapped up the expanding part of EPS and grew into the interspace between two fins from 3 months to 6 months, which significantly improved the bone condition and formed a better “ screw-bone ” interface.Conclusions: 1) EPS can significantly increase screw stability and obtain the similar fixation strength of traditional PMMA-augmented pedicle screw. 2) EPS can form a significant better interface and bone condition around screw compared with traditional PMMA-augmented pedicle screw, which significantly improve long term stability of screw in vivo. 3) EPS can effectively avoid complications caused by using of PMMA such as thermal injury, leakage and neurologic compression and so on. As an effective, safe and easy method, EPS has great potentiality on wide application in clinic.

【中文名称】RNA干扰药物的临床前研究
【英文名称】preclinical study of RNA interference drug
【研究起始时间】2007-06
【研究终止时间】2010-11
【中文关键词】RNA干扰，质粒DNA，阳离子脂质体，抗肿瘤，临床前研究，
【英文关键词】RNA interfernence,plasmid DNA,cationic liposome,anti-cancer,preclinicial study
【中文摘要】本成果针对人的FAK、PLK1、EGFR、VEGF、Aurora kinase等在肿瘤中高表达、与肿瘤治疗、预后等相关的基因为靶点开展RNA干扰治疗肿瘤的药物研发。将针对单个基因的siRNA序列或两个基因的siRNA构建到同一质粒DNA表达载体中，并与DOTAP-Chol阳离子脂质体包裹，形成复合物，通过尾静脉给药的方式对多种人的肿瘤裸鼠移植瘤进行治疗，通过不同给药剂量的疗效观察，发现每只小鼠尾静脉注射2-5 μg RNA干扰质粒DNA具有明显的抑瘤效果，治疗组小鼠肿瘤明显缩小，开发前景很好，目前该研究成果已经建立了质粒DNA和阳离子脂质体的中试生产技术平台，并建立了两种复合物冻干的生产工艺，该成果具有很强的创新性，国内外未见报导，共申请了3项发明专利，其中2项已经获得了授权，开发前景很好。
【英文摘要】Distinct subsets of cancers harbor specific oncogenes that are crucial for maintaining the malignant phenotype, which is important in cancer therapy and prognosis. We adopted RNA interference technology to downregulate these oncogenes including FAK、PLK1、EGFR、VEGF and Aurora kinase, thereby developing novel therapeutic drugs for tumor. In our strategy, we constructed a plasmid-based shRNA expression system targeting one oncogene or two oncogenes simultaneously. To increase intravenous DNA delivery in vivo, we used DOTAP:Chol liposomes to form complexes with the plasmid, which was intravenous administrated and resulted in enhanced antitumor effects in many xenografts of nude mice. Among the various dose, the choice of 2-5 μg RNA interference plasmid through intravenous administration showed significant antitumor effects and promising prospect. We have built the GMP platform of DOTAP:Chol liposomes and plasmid, as well as the technology of freeze drying. Our achievements bring new ideas in the field of cancer research for the first time, and we have also applied 3 patent rights (2 approved). Our accomplishments raise hope for application of RNA interference in clinical use of cancer.

【中文名称】非复制型腺病毒抗肿瘤作用的临床试验研究
【英文名称】Clinical trial of the non-replicative adenovirus EDS01 in the treatment of neck and head cancer
【研究起始时间】2007-03
【研究终止时间】2010-12
【中文关键词】重组腺病毒，内皮抑素，基因治疗，临床试验
【英文关键词】recombinant adenovirus,, endostatin, gene therapy, clinical trial
【中文摘要】本研究主要开展非复制型腺病毒EDS01的I期临床试验，该试验为开放、单中心、剂量递增的I期临床试验。该试验的主要目的为观察头颈部肿瘤患者瘤内注射EDS01的耐受性和安全性，探索最大耐受剂量（MTD）和剂量限制性毒性（DLT），为Ⅱ期临床试验的用药剂量及方案提供依据。本次研究一共入组25例头颈部恶性肿瘤或其他恶性肿瘤伴头颈部转移灶的患者。临床单次给药组经过3个剂量（1.0×1011 VP，5.0×1011 VP，1.0×1012 VP）的爬升，未出现剂

量限制性毒性和严重不良事件。完成单次给药后，另入组6例患者给以高剂量药物（1.0×1012 VP），一周2次，连续两周的多次给药。本I期临床单药剂量递增试验表明：肿瘤病人对该药的耐受良好，未出现剂量限制性毒性（DLT）和最大耐受剂量（MTD）。主要不良反应为发热和局部注射部位疼痛，并有流感样症状发生。重组人内皮抑素腺病毒注射液（EDS01）1.0×1011 VP～1.0×1012 VP的多剂量给药，每周两次，连续两周瘤内注射方法治疗，同样安全、可耐受，但药物不良反应增加。单次或多次给药后均见到目标病灶初步疗效反应，多次给药的有效缓解率达16
【英文摘要】无

【中文名称】人类神经管缺陷发病机理研究
【英文名称】
【研究起始时间】2008-09
【研究终止时间】2012-07
【中文关键词】内胚层发育蛋白，microRNA，神经管缺陷，多梳蛋白
【英文关键词】embryonic ectoderm development, microRNA, neural tube defects, polycomb proteins
【中文摘要】目的：找到与人类神经管发育缺陷相关的基因，并对其调控网络进行研究方法：首先从研究对象不同部位组织中提取总蛋白，利用western blot技术对ploycomb家族蛋白不同组分进行表达量的检测。利用荧光素酶报告系统对参与此蛋白调控的microRNA进行研究。利用免疫组化、免疫荧光等方法对组织中H3K27甲基化情况进行检测。结果：研究发现EED在胎盘和NTD胎儿神经组织中均存在差异表达。H3K27甲基化情况也存在显著差异。结论：EED表达量改变导致的组蛋白甲基化改变是神经管缺陷发病的原因之一。
【英文摘要】

【中文名称】中国地区汉族人群神经管畸形的遗传相关性研究
【英文名称】
【研究起始时间】2009-09
【研究终止时间】2012-07
【中文关键词】神经管畸形，多态性位点，microRNA，单体型
【英文关键词】recurrent pregnancy loss, polymorphism, microRNA, haplotype
【中文摘要】目的：找到与中国地区汉族人群神经管畸形相关的基因及多态性位点，并对其功能进行初步研究。方法：首先从研究对象全血中提取基因组DNA，通过PCR测序的方法对感兴趣的microRNA编码基因进行扩增并得到目的基因序列。利用haploview和SHEsis软件对测序结果进行统计学分析，得到有意义的SNP位点。将含有此SNP位点的不同基因型的microRNA前体编码基因克隆到pCR3.1真核表达载体中，在体外水平研究此SNP位点对microRNA表达量的影响。结果：研究发现microRNA-125a编码基因中存在两SNP位点与神经管畸形有关。细胞水平研究显示此两SNP位点可降低microRNA-125a的表达量。进一步研究表明此两SNP位点影响了microRNA-125a与核蛋白的相互作用。结论：microRNA-125a 编码基因中两SNP位点影响了microRNA前体与核蛋白的相互作用，从而改变了microRNA-125a的表达量，进一步导致了神经管畸形。
【英文摘要】

【中文名称】邻苯二甲酸酯对早期胚胎毒性机制的研究
【英文名称】
【研究起始时间】2010-10
【研究终止时间】2011-12
【中文关键词】邻苯二甲酸酯，早期胚胎，发育阻滞，毒性
【英文关键词】PAEs, preimplantation embryo, development block, toxicity
【中文摘要】目的：研究邻苯二甲酸脂对早期胚胎发育的影响，并进一步探讨其对胚胎发育影响的机理。方法：通过向胚胎培养液中添加不同浓度PAEs，研究其对胚胎受精率、囊胚率的影响；通过Tunel染色，研究PAEs暴露对胚胎细胞凋亡的影响；通过免疫荧光染色的方法，研究引起胚胎细胞凋亡的通路以及干细胞因子的定位；通过real-time PCR，研究PAEs暴露对胚胎基因组启动相关基因表达的影响；进一步通过添加过氧化物酶研究是否可以恢复胚胎的发育能力。结果：研究发现10-3mol/L的MEHP会使胚胎发生2细胞阻滞，MEHP暴露还会引起胚胎细胞活性氧水平升高，细胞色素C释放，SOX2转位方式发生改变，发生2细胞阻滞的胚胎基因表达水平与2细胞阶段胚胎相似。结论：MEHP通过氧化应激抑制了胚胎基因组的转录启动，诱发早期胚胎发生发育停滞。

【英文摘要】

【中文名称】PcG家族蛋白在胚胎发育中的表达调控
【英文名称】
【研究起始时间】2009-10
【研究终止时间】2011-08
【中文关键词】EED,SUZ12,BMI-1,EZH2,胚胎发育，神经发育
【英文关键词】EED,SUZ12,BMI-1,EZH2,embryonic development，neurodevelopment
【中文摘要】PcG家族蛋白是一种控制基因表达的转录调节蛋白，虽然PcG家族蛋白在神经系统中的表达已经清楚了，但是在早期胚胎神经发育中的表达模式还不清楚。在本研究中，我们分析了在小鼠和人的早期胚胎发育中，PRC1(BMI-1)和PRC2 (EED, SUZ12, and EZH2)的表达模式。在小鼠中，随着胚胎的发育，EED的表达上调，SUZ12和EZH2反而下调，BMI-1变化不大。所以在小鼠的早期胚胎神经发育中，PRC2起了重要的作用，而PRC1作用不是很明显。但是在人中，随着胚胎的发育，BMI-1表达上调，EED,SUZ12和EZH2的变化不是很大。所以在人的早起胚胎神经发育中，PRC1起了重要的作用。
【英文摘要】

【中文名称】microRNA在砷致胚胎发育毒性中的作用机制研究
【英文名称】
【研究起始时间】2008-10
【研究终止时间】2011-07
【中文关键词】microRNA，砷，胚胎发育毒性，作用机制
【英文关键词】microRNA，Arsenic，embryonic development toxicity，mechanism
【中文摘要】近年来，对miRNA在毒理学分子机制中的调控与生物学作用的研究受到人们重视且发展迅速，越来越多的证据表明非编码小RNA，特别是miRNA在环境污染物所致毒理学效应中发挥着重要作用，但是，目前关于miRNAs在环境物质砷暴露所致早期胚胎发育异常中的具体作用机制目前还不明确。该论文首次从miRNA的角度研究环境污染物砷暴露所致胚胎发育毒性和畸形的分子机制。论文以鸡胚为动物模型，通过高通量的miRNA芯片和mRNA芯片方法筛选到大量的砷暴露所致差异表达的基因，运用生物信息学分析构建了差异miRNA与差异基因功能间的相互作用网络，筛选出调控网络中起关键作用的mRNA和miRNA。进而，利用人的脐静脉血管内皮细胞系验证了调控网络中筛选到的关键miRNA 181b和miRNA9与下游靶基因NRP1的调控关系，同时验证了无机砷通过miRNA调控NRP1基因而干扰血管生成的分子机制。该课题研究不仅在基因水平上获得了胚胎暴露在低剂量无机砷环境下的microRNA 毒理基因组和动态基因表达图谱，为环境中无机砷的风险评价提供了新的理论依据和预测评价指标，还从miRNA角度进一步解释了低浓度砷对血管生成促进作
【英文摘要】

【中文名称】氧化应激和DNA 甲基化在同型半胱氨酸诱导神经管畸形中的作用机制探讨
【英文名称】
【研究起始时间】2008-10
【研究终止时间】2010-08
【中文关键词】同型半胱氨酸，神经管畸形，氧化应激，甲基化
【英文关键词】Homocysteine, Neural tube defects, Oxidative stress, Methylation
【中文摘要】背景：同型半胱氨酸（homocysteine，HCY），是一种含硫氨基酸，是一碳代谢的中间产物。神经管畸形(Neural Tube Defects NTDs)是指胚胎发育早期，由于遗传因素和环境因素的影响，致神经管的发生和分化紊乱而出现的人类出生缺陷中最常见和最严重的一组畸形。近年来的研究表明:体内HCY 升高与NTDs 关系密切，但HCY致NTDs 的分子机制尚不完全清楚。目的：研究HCY 导致NTDs 的新的致病机制，并针对致病机制提出保护措施，为神经管畸形的治疗和预防提供基础。方法：以鸡胚为动物模型，研究HCY 对鸡胚神经管发育的影响及可能的分子机制。通过石蜡切片和H-E 染色分析HCY 对鸡胚神经管的影响；检测HCY 对活性氧（ROS）、丙二醛（MDA）、总谷胱甘肽（GSSG）、超氧化物岐化酶（SOD）、谷胱甘肽过氧化物酶（GPX）等氧化应激相关指标的影响；高效液相色谱（HPLC）、全胚免疫荧光、western blot 检测HCY 对DNA 甲基转移能力的影响；Taqman real timePCR 检测HCY 处理后miR-124 的变化；免疫组化分析SCP1.、P

【英文摘要】

【中文名称】利用miRNA控制白菜类蔬菜作物病毒病
【英文名称】无
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】芜菁花叶病毒，黄瓜花叶病毒，人工miRNA，大白菜
【英文关键词】无
【中文摘要】在大白菜上建立能够抗芜菁花叶病毒TuMV和黄瓜花叶病毒CMV的人工miRNA表达系统，抑制或减轻病毒病的症状，为农作物抗病毒病育种提供先进的生物技术和抗病种质资源。
【英文摘要】无

【中文名称】抑郁症和精神分裂症的疾病特征与多模态神经影像学诊断
【英文名称】
【研究起始时间】2008-12
【研究终止时间】2010-12
【中文关键词】抑郁症，精神分裂症，多模态神经影像
【英文关键词】
【中文摘要】针对抑郁症以及精神分裂症，具体运用结构性、功能性、代谢性的磁共振影像技术，结合临床特征鉴定了一系列疾病相关的重要影像学指标；尝试了对多模态影像信息进行整合；试验了基于影像数据建立疾病的诊断模型；开展了抑郁症相关的影像遗传学研究。
【英文摘要】

【中文名称】缺失bp26基因的重组马耳他布鲁氏菌活疫苗M5-90-26在黑龙江省的生产性试验
【英文名称】null
【研究起始时间】2011-05
【研究终止时间】2011-11
【中文关键词】布氏杆菌,bp26基因,重组M5-90-26,生产性试验
【英文关键词】null
【中文摘要】本研究以bp26基因作为重组靶位点,以M5-90为亲本,利用bp26基因作为同源臂,将卡那霉素抗性基因(Kanr)整合到细菌基因组中,通过筛选以双交叉重组方式整合的阳性菌株,经PCR 和序列测定证明bp26基因缺失并被卡钠霉素基因替换,命名为M5-90-26。马耳他布鲁氏菌M5-90-26为 bp26基因缺失株与常规弱毒疫苗相比,具有相同或相似的免疫效果,满足了对安全新型疫苗的迫切需求。M5-90-26可以利用血清学区分M5-90-26免疫与野生型布氏杆菌感染,对布氏杆菌病防制、监测及净化具有重要的意义。实验表明,缺失株M5-90-26和亲本株M5-90经皮下接种后不经天然孔粘膜排菌。缺失株M5-90-26在羊体内停留时间、复制水平、不发生水平传播及诱导布鲁氏菌特异性抗体反应等方面与亲本株M5-90相同。证明缺失株M5-90-26和M5-90具有相同的安全特性和免疫原性。布鲁氏菌缺失株M5-90-26是一个有潜力的疫苗候选株,为下一步实验提供了试验依据。在黑龙江省哈尔滨市进行了环境释放试验的结果表明,此重组疫苗没有能力释放到周围环境中去并感染非标靶动物,因此对环境是安全的。
【英文摘要】无

【中文名称】重组融合蛋白rTMP-GH的药效学，毒理学及其体内分布代谢研究
【英文名称】Recombination fusion protein rTMP-GH of pharmacodynamics, toxicology and metabolic distributed in the body
【研究起始时间】2009-01
【研究终止时间】2011-12
【中文关键词】重组融合蛋白，rTMP-GH，药效学，毒理学，代谢及分布
【英文关键词】Recombination fusion protein, rTMP-GH, pharmacodynamics, toxicology,metabolism ,distribution
【中文摘要】重组融合蛋白rTMP-GH的药效学实验研究，明确了该产品具有显著升血小板作用，探索并制订出其最佳用药方案，并证实该药物对放射损伤和化学药物所致的小鼠血小板减少症具有突出疗效。分析了重组融合蛋白rTMP-GH在动物体内的分布与代谢特点。开展了融合蛋白rTMP-GH的急、长毒等安全性评价实验研究。

【英文摘要】无

【中文名称】rTMP-GH融合蛋白的构建，表达纯化及制备工艺
【英文名称】 Expression and Purification of rTMP-GH and studies of its preparation technology
【研究起始时间】2008-08
【研究终止时间】2010-09
【中文关键词】构建，表达，纯化，rTMP-GH
【英文关键词】Building, expression, purification, rTMP-GH
【中文摘要】构建了高效表达rTMP-GH融合蛋白的工程菌株，建立了三级种子库，并对发酵表达和纯化的工艺路线进行了摸索。完成了rTMP-GH融合蛋白生物制品的配方优化和稳定性研究，实现了其中试工艺优化和生产放大。对重组融合蛋白rTMP-GH的质量标准和检定方法进行了系列研究，建立了该产品的质量标准和检测方法（草案），完成了三批中试产品的制造与检测。
【英文摘要】无

【中文名称】“瘀热”病机的分子生物学基础研究
【英文名称】"stasis heat"pathogenesis molecular biology basic research
【研究起始时间】2007-10
【研究终止时间】2010-10
【中文关键词】瘀热，分子生物学，大鼠
【英文关键词】stasis heat, molecular biology, rats
【中文摘要】本实验包括临床实验、动物实验、体外实验三方面。通过临床实验初步探讨了出血性中风急性期瘀热阻窍证的分子本质，通过临床实验及动物、细胞实验评价了凉血通瘀方作用，反证瘀热阻窍证的本质。
【英文摘要】The experiment includes three aspects: clinical experiment, animal experiments, in vitro experiments. We preliminary discussed the molecular nature of hemorrhagic stroke in acute stage through clinical experiment, while evaluated the effect of Liangxue Tongyu Formula, in order to demonstrate the stasis heat blocking brain syndrome through clinical, animal and cell experiment.

【中文名称】名老中医诊治优势病种诊疗方案临床应用推广研究
【英文名称】Extension research of coronary heart disease diagnosis and treatment scheme use regulating the spleen and protecting the heart method of Deng Tietao
【研究起始时间】2007-09
【研究终止时间】2010-12
【中文关键词】名老中医；诊疗方案；推广；
【英文关键词】experienced chinese Medcine doctors ；Diagnosis and treatment scheme；Promotion；
【中文摘要】课题组采用了前瞻队列研究的方法，在推广应用中评价老中医方案。各子课题联合了多家单位，使老中医方案在基层单位得到了推广培训及应用。共投入236名研究人员，联合54家单位，纳入了3815例病例进行观察，制订了16位名老中医诊治优势病种诊疗方案，结集出版专著《名老中医治疗优势病种诊疗方案选》。
【英文摘要】In this study,Research group used prospectie cohort study to extend coronary heart disease diagnosis and treatment scheme of sixteen experienced chinese Medcine doctors in fifty-fourhospitals.and two hundred and thirty-six researchers,Included 3815 patients.made the diagnosis and treatment scheme of diseases for advantage disease of sixteen experienced chinese Medcine doctors, Published the book "the diagnosis and treatment scheme of diseases for advantage disease selections of experienced chinese Medcine doctors". .

【中文名称】纳米血管替代物及胆道支架的研发实验报告
【英文名称】Development report of nano vascular graft and biliary stent
【研究起始时间】2008-01
【研究终止时间】2010-12
【中文关键词】纳米； 血管替代物； 胆道支架
【英文关键词】nano; vascular graft;biliary stent
【中文摘要】本课题针对纳米血管替代物、纳米胆道支架两种具有重要经济价值的医疗器械，经过近三年的攻关研究，在静电纺丝血管替代物的制备，血管表面基因、抗菌涂层材料的修饰，仿生血管内膜微结构的构建，银系抗菌亲水胆

道支架的研发，对血管替代物和胆道支架质量检验，动物实验，产业化制作工艺和流程确定以及产品标准制定等方面取得了一批重要成果，按期、保质地完成了攻关目标，达到或超过合同规定的主要技术指标。

【英文摘要】The development of nano-vascular graft, nano-biliary stents has important economic value, after nearly three years of research ,great advance has been made in vascular graft prepared with electrostatic spinning, gene, anti-bacterial coating material modification in the surface of vascular graft, development of intima bionic microstructure, the hydrophilic silver antimicrobial research of biliary stents, quality testing of vascular graft and biliary stent, animal testing, presentation of industrial processes and procedures. All research tasks have been finished on time, and the results meet or exceed the main technical specifications stipulated in the contract.

【中文名称】基于古代文献的针灸适宜病症研究

【英文名称】Study on disease menu of acupuncture and moxibustion therapy in China based on the Ancient Literature

【研究起始时间】2006-10

【研究终止时间】2010-09

【中文关键词】针灸; 适宜病症; 古代文献

【英文关键词】Acupuncture;Diseases of treatment on acupuncture ; Graded Evidence-Based Diseases-Spectrum of Acupuncture-Moxibustion ; ancient literature

【中文摘要】目的: 获得中国古代针灸病谱, 为针灸适宜病症的确立提供参考。方法: 通过对73部代表性中医典籍，应用传统文献研究方法对提取的病症数据进行整理、分析、归类，建立基于古代文献的针灸适宜病症的疾病谱系。结果:获得古代文献针灸适宜病症条目11万余条，按照人体不同部位分类为主，参考临床各科不同系统分类，共分为6类470种病症。结论: 古代文献研究结果表明，古代针灸适宜病症的基本特点与现代研究的结果高度相同。

【英文摘要】Abstract: Objective To acquire the list of diseases treatment on acupuncture based on the ancient literature. Methods Apply the traditional way that extraction of disease data collation, analysis, classification in 73 representation classical ancient literature, Establish the system of disease menu of acupuncture and moxibustion therapy based on the ancient literature. Results A total of 110 000 obtained information ,according to the classification of the human body parts and clinical subjects , are divided into 470 diseases of six categories. Conclusion: Basic features of ancient diseases menu treatment on acupuncture and results of modern research the same height

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【中文名称】慢性盆腔炎中医四联疗法的优化及诊疗规范研究——慢性盆腔炎中医综合疗法的优化研究统计分析报告

【英文名称】Chronic pelvic inflammatory disease with quadruple therapy in Chinese medicine diagnosis and treatment standard of optimization

【研究起始时间】2007-09

【研究终止时间】2011-12

【中文关键词】慢性盆腔炎 中医综合治疗方案 疗效评价 安全性评价 生存质量评价 成本-效果分析

【英文关键词】chronic pelvic inflammatory disease TCM integrated scheme therapeutic evaluation safety evaluation evaluation of quality of life cost-effectiveness analysis

【中文摘要】为优化、筛选出针对慢性盆腔炎疗效确切、可供推广的中医综合治疗方案, 本课题组在科技支撑项目支持下采取前瞻性、随机、开放、平行对照、多中心临床试验研究方法，评价者盲法评价，得出与单一治疗方案比较，中医综合治疗方案组具有疗效显著，可明显改善患者症状、体征，且可明显提高患者生存质量及安全性高、复发率低、成本相对低廉的优势。最终形成结论为中医综合治疗方案疗效确切，安全性高，适宜临床推广应用。

【英文摘要】For optimization, screening for chronic pelvic inflammatory disease curative effect is accurate, for the promotion of Chinese medicine comprehensive treatment scheme, this task group in support of science and technology project support by prospective randomized, open, parallel controlled, multicenter clinical research methods, raters blind evaluation, drawn with a single treatment scheme comparison, traditional Chinese Medicine comprehensive treatment program group has remarkable curative effect, can significantly improve symptoms, signs, and can obviously improve the quality of life of patients and high safety, low recurrence rate, low relative cost advantage. Eventually forming conclusions for traditional Chinese medicine integrated scheme of exact curative effect, high safety, suitable for clinical application.

【中文名称】基于临床文献数据独立评价中医临床效应的方法研究

【英文名称】none

【研究起始时间】2009-04

【研究终止时间】2011-04
【中文关键词】临床文献数据；独立评价；中医临床效应；方法研究
【英文关键词】clinical literature data; individual evaluation;clinical efficiency of TCM; methodology
【中文摘要】本研究主要在评价方法的构建和解决关键技术问题两方面进行了基于临床文献数据独立评价中医临床效应的方法研究。
【英文摘要】none

【中文名称】系统科学视角下的肝炎肝硬化临床疗效评价方法研究
【英文名称】none
【研究起始时间】2009-04
【研究终止时间】2011-04
【中文关键词】系统科学；肝炎肝硬化；临床疗效评价；方法研究
【英文关键词】complexity systemic science; post-hepatitis B cirrhosis; clinical evaluation
【中文摘要】以乙型肝炎（乙肝）后肝硬化为研究切入点，基于中医药理论，按照循证医学原理、采集中医临床表征信息和临床生物信息，并建立相关信息科学量表，应用系统生物学和复杂科学的相关理论和方法，以及临床疗效评价的群体分析方法和个体疗效预测等方法，通过多学科合作方式，开展乙肝后肝硬化中医个体化诊疗规范化方案制定的关键技术研究，以及中医个体化诊疗效应和安全性评价的共性规律分析技术研究的研究，建立符合中医药特色和疗效优势的、乙肝后肝硬化临床疗效评价和安全性评价的方法和标准。
【英文摘要】none

【中文名称】川白芷硫熏前后质量控制
【英文名称】Quality control and discrimination of Angelica dahurica var. formosana
【研究起始时间】2008-07
【研究终止时间】2009-12
【中文关键词】川白芷，硫熏前后，质量控制
【英文关键词】Angelica dahurica var. formosana.; RRLC
【中文摘要】目的：采用高分离度快速液相色谱（RRLC）研究并建立川白芷药材的指纹图谱。方法：采用Agilent zorbax SB-C18 (4.6×100 mm，1.8 μm)色谱柱；以甲醇-水为流动相梯度洗脱，流速1.0 mL·min-1，检测波长310 nm；采用主成分分析、系统聚类分析及相似度评价等方法对川白芷熏硫前后进行质量控制和模式识别。结果：该方法可使川白芷中各成分得到较好的分离，并根据检测结果确定了23个共有指纹峰。川白芷熏硫前后样品的指纹图谱存在较大差异。结论：建立了川白芷熏硫前后的RRLC指纹图谱，并结合化学计量学方法对川白芷熏硫前后样品进行准确、可靠的识别和验证，可为川白芷内在质量控制提供参考。
【英文摘要】OBJECTIVE To establish RRLC fingerprints of Angelica dahurica var. Formosana. METHODS The analysis was carried out on a Agilent zorbax SB-C18 (4.6×100 mm, 1.8 μm) column eluted with the mobile phases of methanol (A) – water (B) in gradient elution. The flow rate was 1.0 mL·min-1, and the UV detector was monitored at 310 nm. Principal component analysis and hierarchical cluster analysis were applied to study RRLC finger printing and chemical pattern reorganization. RESLUTS The chemical constituents of Angelica dahurica var. Formosana. were optimally separated, among which 23 fingerprint peaks in common were confirmed. There was an apparent difference in fingerprint between drying and Dryness after sulfurring. CONCLUSION The developed RRLC fingerprint, combined with chemometrics, can accurately identify and validate Angelica dahurica var. Formosana by drying and Dryness after sulfurring. The research provide theoretical basis for the process mechanism anf quanlity assess Angelica dahurica var. Formosana by drying and Dryness after sulfurring.

【中文名称】川白芷中6种主要香豆素成分含量
【英文名称】To determine the contents of six major coumarins and establish the chemical fingerprint of Angelica dahurica
【研究起始时间】2008-08
【研究终止时间】2009-12
【中文关键词】川白芷，香豆素，含量
【英文关键词】six major coumarins, Angelica dahurica
【中文摘要】采用RRLC-UV法，建立了川白芷中6种主要香豆素成分含量的测定方法，并建立了不同产地川白芷的RRLC-UV指纹图谱，对比分析了不同产地川白芷中6种主要香豆素类成分（水合氧化前胡素、佛手柑内酯、氧化前胡素、

欧前胡素、Cnidilin和异欧前胡素）含量，所建立的RRLC含量方法在测定浓度范围内与色谱峰面积线性关系良好（R≥0.9998），方法的回收率在99.42%~101.44%，RSD≤2.4%。

【英文摘要】To determine the contents of six major coumarins and establish the chemical fingerprint of Angelica dahurica from different producing areas by RRLC-UV. The contents of six major coumarins and the chromatographic fingerprints of the different samples have been analyzed and investigated by RRLC-UV.

【中文名称】近红外光谱技术测定黄连中6种生物碱含量的新方法

【英文名称】A New Method for Analysis Six Alkaloids in Coptis chinensis Franch. by Near Infrared Diffuse Reflectance Spectroscopy

【研究起始时间】2008-04

【研究终止时间】2009-06

【中文关键词】黄连，生物碱，近红外

【英文关键词】Near infrared diffuse reflectance spectroscopy; C. chinensis Franch.; alkaloids; MPLS

【中文摘要】目的 应用近红外光谱技术对黄连中药根碱、非洲防己碱、表小檗碱、黄连碱、巴马汀和小檗碱含量进行快速无损测定。方法 选择在1308-2393nm范围内的近红外光谱，比较了光谱不同预处理方法对校正结果的影响，并比较了主成分分析法（PCR）、偏最小二乘法（PLS）、改进偏最小二乘法（MPLS）建模的效果，并对模型进行内部和外部验证。结果 采用SNV and Detrend散射处理技术，2.4.4.1数学处理方法及改进偏最小二乘法回归建立的定标方程模型的准确性最好。6种生物碱成分定标模型的校正决定系数（R2）为0.8047～0.9674，校正标准误差（SEC）为0.0312～0.2471。对预测集样品进行外部验证，预测值与真值的相关系数（Rv2）为0.744～0.929，预测标准误差（SEP）为0.043～0.346。结论 建立了利用近红外光谱法直接测定黄连中6种生物碱含量的新方法。该方法快速简便，准确可靠，适合于黄连中主要生物碱类成分的快速测定分析。

【英文摘要】Objective To establish a method for rapid determination of gatrorrhizine, columbamine, epiberberine, coptisine, palmatine and berberine in Coptis chinensis Franch. by near infrared diffuse reflectance spectroscopy. Methods The range of 1308-2393nm of near infrared spectra (NIRS) was selected. Different spectra pretreatment methods and mathematics methods such as PCR,PLS and MPLS were compared and the calibrations of the alkaloids content were performed. Results The results showed that SNV+Detrend, 2,4,4,1 pretreatment and MPLS can be best factors for the model. The average determination coefficient of validation (R2) and the square error of cross(SEC) of the models of six alkaloids were respectively 0.8047～0.9674 and 0.0312～0.2471. For the models based on prediction samples, the determination coefficient of independent validation（Rv2）and standard error of prediction（SEP） were 0.744～0.929 and 0.043～0.346. Conclusion The establishment of the new near infrared diffuse reflectance spectroscopy method can be used to analyze the six alkaloids, which can provide a rapid, exact and reliable method for determining the main alkaloids in C. chinensis Franch.

【中文名称】白刺红色素食品添加剂新产品研发

【英文名称】New product research and development of Nitraria tangutorun red pigment for food additives

【研究起始时间】2007-08

【研究终止时间】2010-12

【中文关键词】白刺;色素;毒理学; 质量标准;生产工艺规程

【英文关键词】Nitraria sibirica; pigment; toxicology; quality standards; technological process of production

【中文摘要】本研究完成了天然白刺红色素原料来源;提取工艺;化学结构及理化特性;试验性使用效果报告;食品中该种食品添加剂的检验方法;卫生学检验报告;毒理学安全性评价等关键技术研究。确定了白刺红色素的最大吸收波长及色价,进行了白刺红色素的抗氧化活性研究。生产方面,制订了唐古特白刺红色素的质量标准。对色素生产所涉及的工序,全程采用HACCP (Hazard Analysis Critical Control Point) 体系和原理对生产过程进行危害分析,确定关键控制点和控制措施。采用分光光度法对色素生产进行质量控制。制定了严格的生产标准操作规程及生产工艺规程。

【英文摘要】The sources of raw materials, extraction process, chemical structure and physicochemical properties of natural Nitraria sibirica red pigment were completed in the present research. In addition, the corresponding key technologies about the experimental performance reports, the testing methods of this kind of food additive in food, hygiene inspection reports, and toxicology safety evaluation were also investigated. Furthermore, the maximum absorption wavelength and color value of the Nitraria sibirica red pigment were identified, and its antioxidant activity was carried out in our study. On the production side, the quality standards of the Nitraria tangutorum Bobr. red pigment were developed. In addition the hazard analysis of the processes involved in pigment production were studied by using HACCP (Hazard the Analysis of the Critical Control Point) system, which could determine the

critical control points and control measures. The quality of pigment production was controlled through the spectrophotometric method. Moreover, the stringent production standard operating procedures and technological process of production were developed

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【中文名称】有机食品 白刺原果汁生产关键技术研究
【英文名称】Organic food the original fruit juice The key technology for the original fruit of Nitraria research
【研究起始时间】2007-09
【研究终止时间】2010-12
【中文关键词】白刺原果汁 生产关键技术 质量控制技术
【英文关键词】Nitraria original juice; key technology in production; Quality Control Technology
【中文摘要】有机食品白刺原果汁关键生产技术研究,主要解决问题:①不添加澄清剂;②不添加防腐剂;③膜澄清过程造成的营养成分及抗氧化成分的损失;④质量控制技术。
【英文摘要】To establish the organic food the original fruit juice the key technology for the original fruit of Nitraria research, mainly to solve following problems:①Do not add clarifying agent;②Do not add preservatives;③nutrients and antioxidant content loss in the clarify process;④ Quality Control Technology

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【中文名称】黑果枸杞营养成分、质量控制技术及抗氧化活性研究
【英文名称】The Lycium nutrients quality control technology and nutrition antioxidant activity research
【研究起始时间】2007-09
【研究终止时间】2010-12
【中文关键词】黑果枸杞 营养成分 质量控制 抗氧化
【英文关键词】Lycium Ruthenicum Murr; Nutrient Composition; Quality Control; antioxidant
【中文摘要】对柴达木地区黑果枸杞干果营养成分,抗氧化活性成分原花青素、总多酚等及抗氧化能力进行了系统的研究。黑果枸杞营养成分、质量控制技术及抗氧化活性。研究主要解决的问题:①柴达木地区黑果枸杞各成分未知;②黑果枸杞质量控制技术;③明确黑果枸杞的抗氧化能力及抗氧化活性成分。
【英文摘要】Study for nutrients, anti-oxidation of the active ingredients proanthocyanidins, polyphenols and antioxidant capacity of Lycium in Qaidam. Nutrient component, Quality control process and antioxidant activity in Lycium Ruthenicum Murr, this research mainly discussed following problems: ① The components of Lycium Ruthenicum Murr are unknown in chaidamu. ;②Lycium Ruthenicum Murr quality control technology of Lycium Ruthenicum Murr;③ clear and definite the oxidation resistance and antioxidant activity ingredients of Lycium Ruthenicum Murr

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【中文名称】抗氧化黑果枸杞活性成分提取关键技术
【英文名称】Antioxidant black fruit extract the key technology of Chinese wolfberry active ingredients
【研究起始时间】2007-07
【研究终止时间】2010-12
【中文关键词】黑果枸杞 抗氧化 活性成分 提取
【英文关键词】Lycium Ruthenicum Murr; antioxidant; active ingredients; extract
【中文摘要】抗氧化黑果枸杞活性成分提取技术,解决了的关键技术问题:①确定提取、纯化工艺参数;②确定黑果枸杞抗氧化提取物以原花青素含量为工艺考核指标及质量控制指标。
【英文摘要】extracting technology for antioxidant active components from Lycium Ruthenicum Murr, The key technology have been solved as follows:①Determine the extraction and purification process parameters; ②To study and formulate the quality control index of the Lycium Ruthenicum Murr extract proanthocyanidins content for antioxidant;

【中文名称】白刺抗氧化活性成分提取关键技术及亚临界萃取白刺籽油工艺研究 白刺抗氧化活性成分提取关键技术及亚临界萃取白刺籽油 工艺研究
【英文名称】key technology Research in the Nitraria antioxidant active ingredients extracted and Subcritical extraction Nitraria Seed Oil
【研究起始时间】2007-09
【研究终止时间】2010-12
【中文关键词】白刺 抗氧化 活性成分 提取 亚临界 白刺籽油

【英文关键词】Nitraria tangutorum Bobr. Antioxidant; active ingredient; extract; subcritical; Nitraria Seed Oil

【中文摘要】抗氧化白刺活性成分提取技术及亚临界萃取白刺籽油工艺研究,解决的关键技术问题:①确定提取、纯化工艺参数;②确定白刺抗氧化提取物以原花青素含量为工艺考核指标及质量控制指标;③对白刺抗氧化活性成分提取生产过程产生的剩余产物白刺籽进行了亚临界萃取白刺籽油工艺研究,达到中试水平。

【英文摘要】the Nitraria antioxidant active ingredients extracted and Subcritical extraction Nitraria Seed Oil Research solve these problems: ①Determine the extraction and purification process parameters; ② To study and formulate the quality control index of the Nitraria extract proanthocyanidins content for antioxidant; ③The Nitraria antioxidant components to extract the remaining product than for of the production process of Nitraria seed subcritical extraction Nitraria seed oil, and level of pilot.

【中文名称】极端气候条件对心血管疾病的影响、作用机制及干预研究

【英文名称】Research report about the effect, mechanism and intervention of extreme climate conditions on cardiovascular diseases

【研究起始时间】2008-05

【研究终止时间】2010-12

【中文关键词】极端气候;心血管疾病;冷应激;热应激

【英文关键词】extreme climate; cardiovascular disease;
cold stress; hot stress;

【中文摘要】应用分子遗传学、分子生物学、免疫学和电生理学等相关技术和平台,在现有研究基础上,从整体、器官、细胞、通道等不同水平,以冠心病、高血压病及心力衰竭为研究核心,以信号转导分子、代谢、遗传基因和电生理参数等为观察指标,观察在冷热应急条件下,上述疾病的病理生理变化和发生发展机理。阐明它们发病的心肌细胞损伤和保护的分子和遗传机制,提出极端气候条件下这些疾病的早期预警和干预措施。成功建立了冷热应激条件下动物高血压、心肌梗死、心衰模型,发现造成心肌损伤发生过程中起关键调节作用的生物分子Bim,血红素氧合酶-1(HO-1),其可能依赖的信号通路为:PI3K/Akt/SK-β,ERK5-MAPK等。寒冷、高盐刺激均能引起血压升高,并导致主动脉和肾脏损害,且二者复合刺激损害更为明显。EPO能通过激活PI3K/Akt途径,增加hsp70的表达、下调炎性因子等而保护受损的心肌抵抗冷应激。MiRNA-21可能通过介导PTEN-AKT-FOXO3a通路对冷应激心衰大鼠起保护作用。总结了冷热应激条件对高血压患者的影响,提出了针对冷热应激条件下高血压及急性心肌梗死可能的干预措施,观察了血压与气温的关联,发现即

【英文摘要】

【中文名称】综合康复治疗汶川地震脊髓损伤伤员的试验研究

【英文名称】The effects of Comprehensive rehabilitation on spinal cord injury

【研究起始时间】2008-06

【研究终止时间】2010-06

【中文关键词】脊髓损伤;综合康复;汶川地震

【英文关键词】WenChuan earthquake; spinal cord injury;comprehensive Rehabilitation

【中文摘要】目的:探讨5.12汶川地震致脊髓损伤患者的最佳康复治疗方法。方法:通过对26例脊髓损伤患者采用包括物理治疗,作业治疗,膀胱控制训练,针灸治疗的综合康复治疗,观察综合康复治疗对脊髓损伤患者全面了康复的疗效。结果:经6个月的综合系统性康复治疗,脊髓损伤患者在治疗前后肌力无统计学意义;治疗前后坐位平衡/站位平衡能力;步行能力ADL能力有明显提高。神经源膀胱症状经过综合性康复治疗后,有部分患者恢复自主性排尿,间歇性导尿未出现尿失禁或尿路感染症状,膀胱容量维持良好。有尿失禁的患者治疗后均有不同程度改善。结论:物理治疗、作业治疗、膀胱控制训练及针灸治疗等综合康复治疗措施使汶川地震脊髓损伤患者的功能障碍得到了极大的改善,最大限度的促进患者的功能恢复,为其重返社会创造了条件。

【英文摘要】Objective: To investigate the optimal rehabilitative managements for the spinal cord injured patients in 5.12 WenChuan earthquake. Methods: 26 spinal cord injured patients were included. The comprehensive rehabilitation intervention including physical therapy、occupational therapy、bladder control training、acupuncture.Result: the muscle strength haven't been improved significantly,The abilities of balance and walking were significantly improved,Neurognic bladders have been improved in varying degrees. The activities of daily living is improved and the patients were more independently. Conclusion: the comprehensive rehabilitation management is very useful to spinal cord injury patients wounded in Wenchuan earthquake,with the role of improve the life of quality and reduce mortality and finally help return to the society.

【中文名称】类固醇激素受体辅激活子3(SRC-3)促进肝癌的增殖和侵袭

【英文名称】Steroid Receptor Coactivator 3 promotes Heptocarcinoma cell proliferation and invasiveness
【研究起始时间】2008-03
【研究终止时间】2010-04
【中文关键词】类固醇激素受体辅激活子3,肝细胞癌,细胞增殖,细胞侵袭
【英文关键词】Steroid receptor coactivator 3 ; Hepatocellular carcinoma;Cell proliferation;Cell invasion
【中文摘要】SRC-3(Steroid receptor coactivator 3),是p160共激活子家族的一员。SRC-3被报道在多种肿瘤的恶化过程中起到重要的作用,如乳腺癌和前列腺癌。然而SRC-3在人肝癌中的功能尚不清楚。在本研究中,我们发现SRC-3蛋白在68%(34例中24例)的肝癌病人样品中高表达。通过siRNA降低肝癌细胞株SRC-3表达水平可以抑制肝癌细胞的增殖、迁移、侵袭、克隆形成和裸鼠体内成瘤能力,这些作用归因于SRC-3沉默引起的p21CIP/WAF1水平上调,Akt活性、PCNA、MMP-9水平下调。临床样品研究与我们体外实验的结果相一致:SRC-3阳性的肿瘤样品相比SRC-3阴性的肿瘤样品有更高的PCNA表达水平,表明SRC-3起到促进细胞增殖的作用;另外,MMP-9在SRC-3阳性肿瘤中表达水平显著高于SRC-3阴性肿瘤,表明SRC-3阳性的肿瘤具有更高的侵袭性。总之,我们的研究结果证明SRC-3的过表达可以通过增强细胞的增殖和侵袭来促进人肝细胞肝癌发展。因此,SRC-3是人肝细胞肝癌生长的一个重要调节因子,并可能成为肝癌诊断和治疗的有效分子靶点。
【英文摘要】Steroid receptor coactivator 3 (SRC-3), is a member of p160 coactivator family and plays an important role in malignancy of several cancers such as breast and prostate cancers. However, its involvement in human hepatocellular carcinoma (HCC) progression remains unclear. Here, we found that SRC-3 protein was overexpressed in 23 of 34 human HCC specimens (68%). Down-regulation of SRC-3 reduced HCC cell proliferation, migration, invasion, colony formation ability and tumorigenic potential in nude mice. These phenotypic changes caused by SRC-3 knockdown correlated with increased expression of the cell cycle inhibitor p21CIP/WAF1 and decreased Akt activation and the expression of proliferating cell nuclear antigen (PCNA) and matrix metallopeptidase MMP-9. In agreement with these findings, clinical SRC-3-positive HCC expressed higher levels of PCNA than SRC-3-negative HCC. A positive correlation was established between the levels of SRC-3 protein and PCNA protein in HCC, suggesting that SRC-3 may contribute to HCC cell proliferation. In addition, MMP-9 expression in SRC-3-postive HCC was significantly higher than that in SRC-3-negative HCC, suggesting that SRC-3-postive HCC may be more invasive. Collectively, our results demonstrate that overexpression of SRC-3 promotes human HCC progression by enhancing cell proliferation and invasiveness. Therefore, SRC-3 is a master regulator of human HCC growth and might be a useful molecular target for HCC prognosis and treatment.

【中文名称】高比活葡聚糖酶的高效表达及发酵研究
【英文名称】null
【研究起始时间】2006-12
【研究终止时间】2008-12
【中文关键词】葡聚糖酶,高比活,表达,发酵工艺
【英文关键词】null
【中文摘要】研制的饲料用酶具有优良的特性, 包括热稳定性好而同时在常温下又具有高活性; 最适pH在酸性同时在整个酸性和中性的pH范围内又能维持较高活性; 对动物胃、胰蛋白酶和其它蛋白酶具有较好的抗性等综合性质。具有这些优良性质的酶还未曾有过报道。在构建的重组菌株中,葡聚糖酶的表达量达到4.2 mg/mL发酵液,处于国际领先的地位,较研究初期完成的生产技术提高了2.8倍, 也远远高于国外目前的生产技术。建立了稳定成熟的毕赤酵母高细胞密度发酵新工艺, 在缩短发酵周期的基础上, 酶的表达量得到提高, 并且具有发酵方法简便, 发酵原料易得, 节省能源,成本低, 适合大、中、小型发酵企业生产的特点。
【英文摘要】无

【中文名称】聋儿言语障碍矫治的使用方法操作指南
【英文名称】Guidness for therapy of Speech Disorder of Deaf Children
【研究起始时间】2008-07
【研究终止时间】2010-12
【中文关键词】听障儿童，言语治疗方案
【英文关键词】Hearing Impaired
【中文摘要】聋儿言语障碍矫治的使用方法操作指南
【英文摘要】Guidness for therapy of Speech Disorder of Children with hearing impairment

【中文名称】MACO模型大鼠脑组织氯化三苯四氮唑(TTC)染色法
【英文名称】TTC staining
【研究起始时间】2007-07
【研究终止时间】2010-06
【中文关键词】氯化三苯四氮唑，染色
【英文关键词】TTC, staining
【中文摘要】用氯化三苯四氮唑染色法定量测定MACO模型大鼠梗死脑组织
【英文摘要】To examine the volume of brain infarction tissue in MCAO rats

【中文名称】MACO模型鼠脑组织光镜观察
【英文名称】Histological change of brain infarction tissue with HE staining in MCAO rats
【研究起始时间】2007-07
【研究终止时间】2010-06
【中文关键词】光学显微镜，HE染色
【英文关键词】light microscope, HE staining
【中文摘要】用光学显微镜观察MACO模型大鼠梗死脑组织HE染色切片
【英文摘要】To examine histological change of brain infarction tissue with HE staining in MCAO rats

【中文名称】MACO模型鼠脑组织血流动力学的研究
【英文名称】Examination of the regional cerebral blood flow(rCBF), the diameter of the microcirculation of brain infarction tissue in MCAO rats
【研究起始时间】2007-07
【研究终止时间】2010-06
【中文关键词】DRT4激光多普勒血流仪，局部脑血流量，微循环管径
【英文关键词】DRT4 laser Doppler device, regional cerebral blood flow, diameter of the microcirculation
【中文摘要】用DRT4激光多普勒血流仪测定软脑膜的微循环血流量、微循环输入枝和输出枝管径
【英文摘要】To examine the regional cerebral blood flow(rCBF), the diameter of the microcirculation of brain infarction tissue in MCAO rats

【中文名称】MACO模型大鼠评分与针刺
【英文名称】Examination of the neurological deficits scores in MCAO rats and acupuncture stimulation
【研究起始时间】2007-07
【研究终止时间】2010-06
【中文关键词】Zausinger法， Garcia 法，神经功能缺损评分，针刺干预
【英文关键词】Zausinger method, Garcia method，neurological deficits scores，acupuncture stimulation
【中文摘要】用Zausinger 和 Garcia 法测定MACO模型大鼠神经功能缺损评分及针刺干预
【英文摘要】To examine the neurological deficits scores in MCAO rats with Zausinger and Garcia method

【中文名称】MACO模型大鼠造模
【英文名称】Establishment of focal ischemic model with Longa Suture Method in rats
【研究起始时间】2007-07
【研究终止时间】2010-06
【中文关键词】Longa线拴法，局灶性脑缺血, 模型
【英文关键词】Longa Suture Method,focal cerebral ischemic,model
【中文摘要】用Longa线拴法建立局灶性脑缺血模型大鼠
【英文摘要】To establish focal cerebral ischemic model with Longa Suture Method in rats

【中文名称】肺癌早期检测试剂盒主要原材料研究报告
【英文名称】Research report of the main raw material
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】材料 研究 报告
【英文关键词】material,Research ,report
【中文摘要】本报告对肺癌检测试剂盒的主要原材料研究进行了汇报
【英文摘要】The main raw material of lung cancer detection kit were reported .

【中文名称】肺癌早期诊断试剂盒 主要生产工艺及反应体系研究资料
【英文名称】Studies of early stage lung cancer diagnostic kit production process and reaction system
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】生产工艺 反应体系 研究
【英文关键词】production process,reaction system,Studies
【中文摘要】本报告主要对肺癌检测试剂盒的生产工艺及反应体系研究进行汇报。
【英文摘要】This report mainly report the lung cancer detection kit production process and the reaction system .

【中文名称】肺癌早期检测试剂盒稳定性研究报告
【英文名称】Stability study report
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】稳定性 研究
【英文关键词】Stability,study
【中文摘要】本报告对肺癌检测试剂盒的稳定性研究情况进行汇报。
【英文摘要】The report on the stability studies of lung cancer detection kit

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【中文名称】肺癌早期检测试剂盒分析性能评估资料
【英文名称】Analysis of performance evaluation data
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】分析 性能 评估
【英文关键词】Analysis ,performance ,evaluation
【中文摘要】本报告对肺癌检测试剂盒的性能进行了分析评估。
【英文摘要】This report on the analytical performance of the lung cancer detection kit, the assessment report.

【中文名称】胃肠癌快速检测试剂盒研发技术报告
【英文名称】Project R & D Technical Report
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】研发 技术 报告
【英文关键词】R & D ,Technical ,Report
【中文摘要】本报告对胃肠癌检测试剂盒项目研发技术进行总结汇报
【英文摘要】This report summary report on the project technology research and development of gastrointestinal cancer detection kit

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【中文名称】胃肠癌检测试剂盒主要原材料研究报告
【英文名称】Research report of the main raw material
【研究起始时间】2007-08
【研究终止时间】2009-07

【中文关键词】原材料 研究
【英文关键词】raw material,Research
【中文摘要】本报告主要对胃肠癌检测试剂盒的主要原材料研究内容进行汇报。
【英文摘要】This report is mainly about gastrointestinal cancer detection kit, the main raw material research report.

【中文名称】胃肠癌检测试剂盒生产工艺及反应体系研究报告
【英文名称】Study of gastrointestinal cancer detection kit production process and the reaction system
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】生产工艺 反应体系 研究
【英文关键词】production process,reaction system,study
【中文摘要】本报告对胃肠癌检测试剂盒的生产工艺及反应体系研究进行了报告。
【英文摘要】This report is on the production process of the gastrointestinal cancer detection kit and the reaction system。

【中文名称】胃肠癌检测试剂盒稳定性研究报告
【英文名称】Stability study of gastrointestinal cancer detection kit
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】稳定性 研究
【英文关键词】Stability ,study
【中文摘要】本报告对胃肠癌检测试剂盒的稳定性性能研究进行了汇报。
【英文摘要】The stability properties of gastrointestinal cancer detection kit were reported.

【中文名称】胃肠癌检测试剂盒分析性能评估资料
【英文名称】Gastrointestinal cancer detection kit performance evaluation data
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】性能 评估
【英文关键词】performance ,evaluation
【中文摘要】本报告对胃肠癌检测试剂盒的分析性能评估情况进行汇报。
【英文摘要】This report is to report the analytical performance evaluation of gastrointestinal cancer detection kit.

【中文名称】卵巢癌检测试剂盒分析性能评估资料
【英文名称】Ovarian cancer detection kit performance evaluation data
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】分析 性能 评估
【英文关键词】Analysis, performance, evaluation
【中文摘要】本报告对卵巢癌检测试剂盒的分析性能评估进行汇报
【英文摘要】This report on the analysis of ovarian cancer detection kit performance evaluation report

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【中文名称】卵巢癌检测试剂盒技术研究报告
【英文名称】Research reports of ovarian cancer detection kit
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】技术 研究 报告
【英文关键词】Technical,Research,Report
【中文摘要】本报告对卵巢癌检测试剂盒的技术研究进行总结汇报。
【英文摘要】This report, summary report on the technical research for ovarian cancer detection kit.

【中文名称】卵巢癌检测试剂盒原材料研究报告
【英文名称】Raw materials, research reports of ovarian cancer detection kit
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】原材料 研究
【英文关键词】Raw materials, research
【中文摘要】本报告对卵巢癌检测试剂盒的原材料研究进行总结汇报。
【英文摘要】This report, summary report on the raw materials research for ovarian cancer detection kit.

【中文名称】卵巢癌早期诊断试剂盒 主要生产工艺及反应体系研究资料
【英文名称】Studies of early ovarian cancer diagnostic kit production process and reaction system
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】生产工艺 反应体系 研究
【英文关键词】production process,reaction system,research
【中文摘要】本报告主要对卵巢癌检测试剂盒的生产工艺及反应体系研究进行总结汇报。
【英文摘要】This report mainly on the production process of the ovarian cancer testing kit and the reaction system summary report.

【中文名称】卵巢癌检测试剂盒稳定性研究报告
【英文名称】Stability study of ovarian cancer detection kit
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】稳定性 研究
【英文关键词】Stability ,study
【中文摘要】本报告对卵巢癌检测试剂盒的稳定性研究内容进行汇报。
【英文摘要】This report is to report the stability of the contents of ovarian cancer detection kit.

【中文名称】智能化定量分析系统的研究报告
【英文名称】Research reports of intelligent quantitative analysis system
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】智能化定量分析系统 研究 报告
【英文关键词】intelligent quantitative analysis system ,Research, reports
【中文摘要】本报告对智能化定量分析系统的研究内容进行了系统汇报。
【英文摘要】The reporting system to report research of intelligent quantitative analysis system.

【中文名称】智能化定量分析系统风险分析报告
【英文名称】risk analysis report of intelligent quantitative analysis.
【研究起始时间】2007-08
【研究终止时间】2009-07
【中文关键词】风险分析 报告
【英文关键词】risk analysis,report
【中文摘要】本报告对智能化定量分析系统的风险分析进行了详细汇报。
【英文摘要】This report a detailed report on risk analysis of the intelligent quantitative analysis.

【中文名称】有机食品 枸杞叶养生茶 企业标准
【英文名称】The enterprise standard of an organic food—medlar leaves health tea
【研究起始时间】2007-03

【研究终止时间】2010-12
【中文关键词】有机食品 枸杞叶养生茶 企业标准
【英文关键词】organic food; medlar leaves health food; enterprise standard
【中文摘要】青海红鼎生物工程有限公司于2009年在青海省海西州都兰县察汗乌苏镇东山根建立了200公顷(3000亩)的有机枸杞叶生产基地,进行有机食品枸杞叶养生茶加工。为保证产品质量,指导与规范产品生产,提高本企业标准化生产水平,为产品生产提供标准技术支撑,青海红鼎生物工程有限公司提出建立《有机食品 枸杞叶养生茶》企业技术标准,并与中国科学院西北高原生物研究所共同完成标准的制定,建立了有机食品枸杞叶养生茶生产、加工、产品、包装、销售标准。本标准能够进一步有效指导和促进产品的规范化、标准化、规模化种植和加工。本标准规定了有机食品枸杞叶养生茶技术要求、试验方法、检验规则、标志、标签、包装、贮藏、运输和销售。本标准适用于以枸杞鲜叶为原料,经杀青、揉捻、干燥等工艺制成的有机食品枸杞叶养生茶。
【英文摘要】Qinghai Hongding Biological Engineering Co.,Ltd established a 200 hectares of organic medlar leaves production base in Dulan county of Qinghai province in 2009, for the processing of organic food — medlar leaves health tea. In order to ensure the producti

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【中文名称】《有机食品 黑果枸杞》企业标准
【英文名称】The enterprise standard of an organic food—Lycium ruthenicum Murr.
【研究起始时间】2007-04
【研究终止时间】2010-12
【中文关键词】有机食品 黑果枸杞 企业标准
【英文关键词】organic food; Lycium ruthenicum Murr; enterprise standard
【中文摘要】黑果枸杞(Lycium ruthenicum Murr.)为茄科(Solanceae)枸杞属(Lycium L.)多年生灌木植物,在我国主要分布于分布于西藏、青海、甘肃、宁夏和陕西北部。青海红鼎生物工程有限公司于2009年在青海省海西州都兰县建立了300公顷(4500亩)有机黑果枸杞野生采摘生产基地,进行有机食品黑果枸杞干果加工。为保证产品质量,指导与规范产品生产,提高本企业标准化生产水平,为产品生产提供标准技术支撑,青海红鼎生物工程有限公司提出建立《有机食品 黑果枸杞》企业技术标准,并与中国科学院西北高原生物研究所共同完成标准的制定,建立了有机食品黑果枸杞生产、加工、产品、包装、销售标准。本标准能够进一步有效指导和促进产品的规范化、标准化、规模化野生采摘和加工。本标准规定了有机食品黑果枸杞技术要求、试验方法、检验规则、标志、标签、包装、贮藏、运输和销售。本标准适用于将干燥加工制成的黑果枸杞。
【英文摘要】Lycium ruthenicum Murr, a member of Solanceae family, Lycium genus, is a kind of perennial shrub plants, which mainly distributes in Tibet, Qinghai, Ningxia, Gansu and north Shanxi.Qinghai Hongding Biological Engineering Co.,Ltd established a 300 hectar

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【中文名称】《有机食品 白刺原果汁》企业标准
【英文名称】The enterprise standard of an organic food—original Nitraria tangutorum Bobr juice
【研究起始时间】2007-09
【研究终止时间】2010-12
【中文关键词】有机食品 白刺原果汁 企业标准
【英文关键词】organic food; original Nitraria tangutorum Bobr juice; enterprise standard
【中文摘要】利用青海红鼎生物工程有限公司在青海省海西州都兰县察汗乌苏镇东山根的566.7公顷(8500亩)野生唐古特白刺(Nitarria tnugtorum Bbor.)资源,由中国科学院西北高原生物研究所研制开发出“有机食品 白刺原果汁”,符合GB/T 19630.1~19630.4—2005《有机产品》生产加工要求,不添加澄清剂、防腐剂及色素。为保证白刺原果汁的质量,指导与规范产品的生产,提高本企业标准化生产水平,为白刺原果汁的生产提供标准技术支撑,建立《有机食品 白刺原果汁》企业标准。本标准的制定,对促进维护野生白刺林生态环境,开展白刺生产,促进青海白刺产业发展具有重要意义。这是当前市场经济发展的需要,也是加工企业的需要。本标准规定了有机食品白刺原果汁要求、试验方法、检验规则、标志、标签、包装、贮藏、运输和销售。本标准适用于以白刺新鲜果实为原料,经榨汁、均质、过滤、超高温瞬时灭菌、灌装等工艺制成的清汁型白刺原果汁。
【英文摘要】Making use of the 566.7 hectares of wild Nitraria tangutorum Bobr resources of Qinghai Hongding Biological Engineering Co.,Ltd. in Dulan county of Qinghai province,,Northwest Institute of Plateau Biology, Chinese Academy of Sciences developed the organic

【中文名称】《有机食品 白刺枸杞复合果汁》企业标准
【英文名称】The enterprise standard of an organic food—Nitraria tangutorum Bobr-medlar compound juice
【研究起始时间】2007-08
【研究终止时间】2011-12
【中文关键词】有机食品 白刺枸杞复合果汁 企业标准
【英文关键词】Nitraria tangutorum Bobr-medlar compound juice; enterprise standard
【中文摘要】为进行有机食品系列产品开发,中国科学院西北高原生物研究所进行了“有机食品 白刺枸杞复合果汁”研制,青海红鼎生物工程有限公司生产。由于枸杞果汁口感及口味较差,因此人们在研制枸杞果汁的时候经常加入大量食品添加剂,影响了枸杞果汁原有营养成分的吸收。白刺果汁与枸杞果汁混合,不仅将两者的营养成分无损失的合二为一,而且增加了枸杞果汁的口味及口感。这是一种极具开发前景的复合保健果汁饮料。为保证白刺原果汁的质量,指导与规范产品的生产,提高本企业标准化生产水平,为白刺枸杞复合果汁的生产提供标准技术支撑,建立《有机食品 白刺枸杞复合果汁》企业标准。本标准规定了白刺枸杞复合果汁要求、试验方法、检验规则、标志、标签、包装、贮藏、运输和销售。本标准适用于以白刺、枸杞新鲜果实为原料,经榨汁、均质、过滤、超高温瞬时灭菌、灌装等工艺制成的清汁型白刺枸杞复合果汁。
【英文摘要】For the purpose of the development of a series of organic food, Northwest Institute of Plateau Biological, Chinese Academy of Sciences conducted the development of the organic food—Nitraria tangutorum Bobr-medlar compound juice, which was produced by Qing

【中文名称】青海省地方标准《柴达木地区枸杞》
【英文名称】The Qinghai province local standard of medlar in Qaidam region
【研究起始时间】2007-02
【研究终止时间】2010-12
【中文关键词】柴达木地区 枸杞 企业标准
【英文关键词】Qaidam region; medlar; local standard
【中文摘要】2008年~2009年共采集了青海省所有市场销售的柴达木枸杞及都兰县诺木洪地区、英得尔羊场枸杞样品21个,由农业部枸杞产品质量监督检验测试中心检测了枸杞子多糖、总糖及蛋白质含量。国家标准GB/T 18672-2002《枸杞(枸杞子)》理化指标总糖含量≥24.8%~39.8%,根据检测结果表明,柴达木地区枸杞与国家标准相比较,枸杞多糖及蛋白质含量不具明显优势,但总糖含量明显高于国家标准,因此。本标准将柴达木地区枸杞总糖含量提高到≥42%。《柴达木地区枸杞》青海省地方标准的建立,主要解决的关键技术问题:通过质量标准的提高,以区别其它地区枸杞,实施技术标准战略,突出产品的特点,打造“柴达木地区枸杞”品牌。
【英文摘要】We collected all the 21 medlar samples from all the market in Qinghai province, Nuomuhong region in Dulan county and Yingdeer Sheep Garden in 2008~2009. The polysaccharide, total saccharide and total protein were detected by the Ministry of Agriculture,

【中文名称】青海省地方标准《有机食品 柴达木地区枸杞生产技术规程》
【英文名称】Qinghai local standard of an organic food-the Technical Specification of Qaidam region medlar production
【研究起始时间】2007-02
【研究终止时间】2010-12
【中文关键词】有机食品 柴达木地区 枸杞 企业标准
【英文关键词】organic food; Qaidam region; medlar; enterprise standard
【中文摘要】枸杞作为经济生态林,在青海柴达木地区栽植时间较长,近年来发展迅速,并取得了较好的经济效益。柴达木盆地所产枸杞具有品质好、糖分含量高、色艳、果大等特性。由于青藏高原特殊的地理环境,高寒缺氧,太阳辐射特别强烈,植物的病虫害少,农牧业区无工业污染,农民很少使用或不使用化肥和农药,容易转换成有机农业生产基地。有机食品的开发上具有得天独厚的优势,我省应立足特色资源,发展有机农业,开发有机食品。开展有机食品枸杞生产,推动青海枸杞生产与国际市场接轨,促进青海枸杞产业进一步升级,是青海枸杞产业所面临的一项紧迫而重要的任务。本标准规定了有机枸杞生产的产地环境条件、种苗选择、育苗、栽培、土肥管理、整形修剪、病虫害防治、鲜果采收、制干、贮存、运输及生产管理体系等。本标准适用于柴达木地区有机枸杞生产。
【英文摘要】Medlar have a long planting history in Qaidam region as an economic and ecological species. It has developed rapidly recent years and has achieved good economic results. The medlar produced from Qaidam basin has good quality, high sugar content,

colorful

【中文名称】有机食品 枸杞叶养生茶生产技术规程
【英文名称】The production Technical Specification of an organic food-the health tea of medlar leaf
【研究起始时间】2007-04
【研究终止时间】2010-12
【中文关键词】枸杞叶养生茶 生产技术规程
【英文关键词】health tea of medlar leaf; the production Technical Specification
【中文摘要】为保证有机食品枸杞叶养生茶的产品质量、指导与规范产品的加工,特制定《有机食品 枸杞叶养生茶生产技术规程》,本标准依据GB/T 1.1—2000《标准化工作则 第1部分:标准的结构和编写规则》、GB/T 1.2—2002《标准化工作则 第2部分:标准中规范性技术要素内容的确定方法》有关规定,以及GB/T 19630—2005《有机产品》有关规定,结合枸杞叶养生茶生产上的特性制定。
【英文摘要】To ensure the products quality, guide and regulate the product processing of the health tea of medlar leaf, we specially make the production Technical Specification of the health tea of medlar leaf. This standard was established according to the relevant

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【中文名称】有机食品 白刺原果汁生产技术规程
【英文名称】Production technical specification of an organic food- Nitraria tangutorum Bobr original juice
【研究起始时间】2007-07
【研究终止时间】2010-12
【中文关键词】白刺原果汁 生产技术规程
【英文关键词】Nitraria tangutorum Bobr original juice; the production Technical Specification
【中文摘要】中国科学院西北高原生物研究所于2007年—2008年开发了“有机食品白刺原果汁”,2009年由青海红鼎生物工程有限公司试生产,2010年进行正式生产,并将投放市场。为规范和指导白刺果汁生产,保证产品质量,特制订本标准。本标准规定了白刺原果汁产地环境条件、加工、包装、成品运输等。本标准适用于青海红鼎生物工程有限公司生产的白刺原果汁。
【英文摘要】Developed by the Northwest Institute of Plateau Biology, Chinese Academy of Sciences in 2007 and 2008, the Nitraria tangutorum Bobr original juice was trialed production in 2009 by Qinghai Hongding Biological Engineering Co. , Ltd. The Nitraria tangutorum

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【中文名称】有机食品 白刺枸杞复合果汁生产技术规程
【英文名称】Production technical specification of an organic food-the mixed juice of Nitraria tangutorum Bobr and medlar
【研究起始时间】2007-09
【研究终止时间】2010-12
【中文关键词】白刺枸杞复合果汁 生产技术规程
【英文关键词】the mixed juice of Nitraria tangutorum Bobr and medlar; the production Technical Specification
【中文摘要】由于枸杞果汁口感及口味较差,因此人们在研制枸杞果汁的时候经常加入大量食品添加剂,影响了枸杞果汁原有营养成分的吸收。白刺果汁与枸杞果汁混合,不仅将两者的营养成分无损失的合二为一,而且增加了枸杞果汁的口味及口感。这是一种极具开发前景的复合保健果汁饮料。为增加有机食品新品种,开辟新的市场,中科院西北高原生物研究所研制了“有机食品 白刺枸杞复合果汁”。为保证有机食品白刺枸杞复合果汁的产品质量、指导与规范产品的加工,特制定《有机食品 白刺枸杞复合果汁生产技术规程》。本标准规定了白刺枸杞复合果汁产地环境条件、加工、包装、成品运输等。本标准适用于青海红鼎生物工程有限公司生产的白刺枸杞复合果汁。
【英文摘要】Abundant food additives were added into the medlar juice because of its poor texture and taste. So it will affect the absorption of the nutrients of the medlar juice. The mixture of Nitraria tangutorum Bobr juice and medlar juice will combine the nutrient

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【中文名称】有机食品 黑果枸杞生产技术规程
【英文名称】Production Technical Specification of an organic food -Lycium ruthenicum Murr
【研究起始时间】2007-09
【研究终止时间】2010-12

【中文关键词】黑果枸杞 生产技术规程
【英文关键词】Lycium ruthenicum Murr; the production Technical Specification
【中文摘要】为保证有机食品黑果枸杞的产品质量、指导与规范产品的加工,特制定本规程。本标准规定了有机黑果枸杞产地环境条件、加工、包装、成品运输等。本标准适用于青海红鼎生物工程有限公司在柴达木地区生产的黑果枸杞。
【英文摘要】We establish this standard to ensure the production quality, guide the processing of the product of the Lycium ruthenicum Murr. This standard rule the environment conditions of producing area, processing, packaging and product transportation of the Lycium

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【中文名称】云南白药一般药理学试验
【英文名称】The study on the general pharmacology of Yunnanbaiyao
【研究起始时间】2009.9.9
【研究终止时间】2010.5.24
【中文关键词】云南白药;精神神经系统;心血管;呼吸系统;体温;影响
【英文关键词】Yunnan Baiyao;psychical nervous system; cardiovascular; respiratory system; hypothermia; influence
【中文摘要】云南白药经小鼠及犬不同剂量给药,小鼠精神神经系统,犬心血管、呼吸系统及体温均无明显影响
【英文摘要】The different doses of Yunnanbaiyao were given by oral for the mice and dogs, there had no significant effects on the psychical nervous system in mice, as well as on the cardiovascular, respiratory and hypothermia in dogs

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【中文名称】大鼠经口与腹腔注射给予云南白药急性毒性试验总结报告
【英文名称】Investigate the acute toxicity of Yunnanbaiyao by Oral and intraperitoneal injection in rats (summary report)
【研究起始时间】2009.9.7
【研究终止时间】2009.10.20
【中文关键词】云南白药;大鼠;急性毒性
【英文关键词】Yunnan Baiyao;Rat;Acute toxicity
【中文摘要】大鼠经口与腹腔注射给予云南白药最大给药量时对大鼠无明显的毒性
【英文摘要】There were no apparent acute toxicity about Yunnanbaiya, which were given with the maximum quantity of oral administration in rats

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【中文名称】大鼠经口给予云南白药六个月毒性试验
【英文名称】The toxicity study of Yunnanbaiyao were orally given six consecutive months in rats
【研究起始时间】2009.7.6
【研究终止时间】2011.1.28
【中文关键词】云南白药;大鼠;长期毒性
【英文关键词】Yunnan Baiyao;Rat;Chronic toxicity
【中文摘要】SD大鼠连续六个月经口给予“云南白药”,能引起类过敏样反应,对神经肌肉和感官有刺激作用,各剂量组反应的严重程度、反应的持续时间与剂量呈正相关
【英文摘要】The Yunnanbaiyao were given to SD rats by oral for six consecutive months, which can cause anaphylactoid-like reaction, stimulation on the neuromuscular and sensory, the responses severity and duration of each dose group are positive correlation to the gi

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【中文名称】小鼠经口与腹腔注射给予云南白药急性毒性试验
【英文名称】Investigate the acute toxicity of Yunnanbaiyao by Oral and intraperitoneal injection in mice
【研究起始时间】2009.9.7
【研究终止时间】2009.10.20
【中文关键词】云南白药;小鼠;急性毒性
【英文关键词】Yunnan Baiyao;mouse;Acute toxicity
【中文摘要】小鼠经口给予云南白药最大给药量时对大鼠无明显的毒性
【英文摘要】There were no apparent acute toxicity about Yunnanbaiya, which were given with the maximum quantity of oral administration in mice

【中文名称】Beagle犬经口给予“云南白药”九个月毒性试验2009.6.27
【英文名称】The toxicity study of Yunnanbaiyao were orally given nine consecutive months in Beagle dogs
【研究起始时间】2009.6.27
【研究终止时间】2011.1.10
【中文关键词】云南白药;Beagle犬;长期毒性
【英文关键词】Yunnan Baiyao;Beagle dog;Chronic toxicity
【中文摘要】Beagle犬分别经口给予“云南白药”不同剂量,未出现明显影响,仅在给药期间出现可逆的稀便、流涎、体重增长减慢,对部分生化学指标(ALT、AST)有升高影响,也未引起动物死亡
【英文摘要】There were significant effects on Beagle dogs, when Yunnanbaiyao were given to them by oral for six consecutive months.Only appears reversible influence, such as loose stools, salivation, weight growth slowed, part of the biochemical indicators (ALT, AST)

【中文名称】“云南白药”中国仓鼠肺成纤维细胞(CHL)染色体畸变试验
【英文名称】The mutagenic study of Yunnanbaiyao on chromosomal aberrations in Chinese hamster lung fibroblasts
【研究起始时间】2009.7.26
【研究终止时间】2010.4.5
【中文关键词】云南白药;中国仓鼠;肺成纤维细胞染色体畸变
【英文关键词】Yunnan Baiyao;China hamster;aberration of lung fibroblasts chromosome
【中文摘要】云南白药对中国仓鼠肺成纤维细胞的染色体畸变诱发作用为阴性
【英文摘要】The mutagenic effects of Yunnanbaiyao on chromosomal aberrations in Chinese hamster lung fibroblasts were negative

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【中文名称】“云南白药”小鼠微核试验
【英文名称】The study of Yunnanbaiyao on mice micronucleus
【研究起始时间】2009.10.29
【研究终止时间】2010.4.5
【中文关键词】云南白药;ICR小鼠;骨髓嗜多染红细胞;微核
【英文关键词】Yunnan Baiyao;ICR mouse;Bone marrow polychromatic erythrocytes; micronucleus
【中文摘要】ICR小鼠分别经口给予“云南白药”不同剂量,对小鼠骨髓嗜多染红细胞未见诱发微核的作用
【英文摘要】ICR mice were orally administered different doses of the Yunnanbaiyao, which were no induced micronuclei in mouse bone marrow polychromatic erythrocytes

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【中文名称】“云南白药”微生物回复突变(Ames)试验
【英文名称】The study of Yunnanbaiyao on microbial reverse mutation (Ames) test
【研究起始时间】2009.10.30
【研究终止时间】2010.4.5
【中文关键词】云南白药;菌株;Ames试验
【英文关键词】Yunnan Baiyao;Strains; Ames test
【中文摘要】云南白药不同剂量对各菌株均未见致回复突变作用,Ames试验结果为阴性
【英文摘要】The effect of different doses of Yunnan baiyao on each strains were not seen revertant mutation, Ames test results were negative

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【中文名称】大鼠经口给予“云南白药”生育力与早期胚胎发育毒性试验
【英文名称】The study of Yunnanbaiyao orally administered on fertility and early embryonic development toxicity in rats
【研究起始时间】2009.10.19
【研究终止时间】2010.2.26
【中文关键词】云南白药;SD大鼠;生殖毒性试验
【英文关键词】Yunnan Baiyao;SD rat;Reproductive toxicity tests
【中文摘要】雌性、雄性SD大鼠分别经口给予云南白药不同剂量,SD大鼠仅表现出一定的母体毒性(高剂量组反应明显,中、低剂量组较轻),对生育力及早期胚胎发育无明显毒性

【英文摘要】The different dose of Yunnanbaiyao were orally administered to female and male SD rats, SD rats only show some maternal toxicity (high dose group was significantly, less low-dose group), no significant effects on fertility and early embryonic development

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【中文名称】大鼠经口给予“云南白药”胚胎-胎仔发育毒性试验
【英文名称】The study of Yunnanbaiyao orally administered on embryonic-fetal developmental toxicity in rats
【研究起始时间】2009.10.23
【研究终止时间】2010.3.18
【中文关键词】云南白药;SD大鼠;胚胎发育毒性试验
【英文关键词】Yunnan Baiyao;SD rat;Embryonic development toxicity tests
【中文摘要】妊娠SD大鼠分别经口给予云南白药不同剂量,对SD大鼠有一定的母体毒性(主要为高、中剂量),对胎鼠体重(高、中剂量)有减轻影响,但未见其他明显胚胎-胎仔发育毒性,无明显致畸作用
【英文摘要】The different dose of Yunnanbaiyao were orally administered to pregnancy SD rats, SD rats have certain maternal toxicity (mainly in high and medium dose group), the weight of fetal rats (in high and medium dose group) were mitigation, but did not see the

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【中文名称】云南白药胶囊临床试验总结(五官科)
【英文名称】The summary report of Yunnanbaiyao capsule Clinical Trial on ophthalmology and otorhinolaryngology
【研究起始时间】2009.4.9
【研究终止时间】2011.5.20
【中文关键词】云南白药;鼻内镜手术;术中出血;疗效观察
【英文关键词】Yunnan Baiyao;Nasal endoscopic surgery. Intraoperative hemorrhage;Investigation of curative effects
【中文摘要】云南白药胶囊用于慢性鼻窦炎/鼻息肉鼻内镜手术促进鼻腔粘膜愈合、减少术中出血,对促进鼻腔粘膜愈合,减少术中出血安全、有效
【英文摘要】Yunnan baiyao capsules used for remedy nasal endoscopic surgery on chronic sinusitis or nasal polyps were safe and effective, which could promote nasal membrane healing, reducing intraoperatie bleeding

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【中文名称】云南白药胶囊临床试验总结(骨科)
【英文名称】The summary report of Yunnanbaiyao capsule Clinical Trial on orthopedics
【研究起始时间】2009.7.28
【研究终止时间】2011.5.8
【中文关键词】云南白药;骨折愈合;疗效观察
【英文关键词】Yunnan Baiyao;Fracture healing; Investigation of curative effects
【中文摘要】云南白药胶囊促进骨折愈合有效性和安全性均优于安慰剂
【英文摘要】The efficacy and safety of Yunnan baiyao capsules promote fracture healing are superior to placebo

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【中文名称】云南白药胶囊临床试验总结(骨科、围手术期)
【英文名称】The summary report of Yunnanbaiyao capsule Clinical Trial on orthopedics during perioperative period
【研究起始时间】2009.7.28
【研究终止时间】2011.5.8
【中文关键词】云南白药;颈椎椎管;骨折;围手术期
【英文关键词】Yunnan Baiyao;Cervical spinal canal; fracture; the perioperative period
【中文摘要】云南白药胶囊减少颈椎椎管减压术、锁骨骨折切开复位术围手术期出血疗效显著,安全性良好
【英文摘要】The significant curative effect and security of Yunnanbaiyao capsules on reducing the cervical spinal canal decompression and perioperative bleeding of clavicle fractures for the reset

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【中文名称】云南白药胶囊临床试验总结(牙科)
【英文名称】The summary report of Yunnanbaiyao capsule Clinical Trial on dentistry
【研究起始时间】2009.4.22

【研究终止时间】2011.5.20
【中文关键词】云南白药;第三磨牙;拔牙;槽骨改建;
【英文关键词】Yunnan Baiyao;The third molar; exelcymosis; Reconstruction of alveolar bone
【中文摘要】口服云南白药胶囊对下颌第三磨牙拔牙槽骨改建影响的有效性和安全性
【英文摘要】The effectiveness and safety of oralYunnanbaiyao capsules reconstruction mandible alveolar bone after mandibular third molar exelcymosis

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【中文名称】国家科技支撑计划课题验收申请表
【英文名称】null
【研究起始时间】2006-12
【研究终止时间】2009-12
【中文关键词】机械设计,防褥疮床垫,生理指标检测,信息交互,模块化,小批量生产
【英文关键词】null
【中文摘要】根据对功能障碍者的护理要求,研究和开发新型的、经济实用的、系列化的残障人专用生活起居床。该残障人专用生活起居床符合人机工程学要求,配置不同功能模块,可实现起身、曲腿、左右翻身、辅助解便、污物后处理、起居床原位旋转、起居床的折叠和移动、生理参数智能检测和生理参数超标分析、自动定时模式、人机交互与紧急报警等功能,产品性能指标达到国际同类产品的先进水平;通过样机、产品开发、临床验证、应用推广,促进技术规范与产业标准、自主知识产权的形成和行业的发展,为我国残障人专用生活起居床的完善与产业化做出贡献。
【英文摘要】无

【中文名称】枸杞优异资源挖掘与评价研究
【英文名称】null
【研究起始时间】2010-01
【研究终止时间】2012-12
【中文关键词】种质资源;抗旱;花粉活性;分子标记;光合作用
【英文关键词】null
【中文摘要】从国内枸杞主产区搜集整理枸杞种质资源,并枸杞种质抗旱性研究、枸杞花粉活性研究、分子标记技术研究、光合生理研究,对种质资源进行评价。共计引种18份,分别以果形,果色,千粒重分类整理出20份枸杞资源,制作蜡叶标本;并进行了种子采集,采集后种子经晾干、除杂、称重、装袋和统一编号,分别保存在枸杞中心保存库和中国药用植物研究所中长期“国家药用植物种子库”;四种种质的抗旱性排序为:红枝枸杞>黄果枸杞>新疆枸杞>中国枸杞;宁1的花粉是供试材料中活性和持久性最强的,其次为YX-04-001和06-03、06-16,再次为宁3,最后为06-02、04-03-32和宁2。
【英文摘要】无

【中文名称】枸杞优良品种选育研究
【英文名称】null
【研究起始时间】2010-01
【研究终止时间】2012-12
【中文关键词】杂交;花药培养;区域试验;宁杞7号
【英文关键词】null
【中文摘要】对现有育种群体进行优良株系的初选,继续开展杂交授粉工作,共选择亲本41个,140个杂交组合,进行了4500个杂交处理,获得杂交种子3万粒;扩大育种群体,共收集枸杞材料约40份,其中丰产性好的6个,坐果率高的5个,适宜机械采摘的(果柄易脱落)2个,早熟的1个,还有具特异性状的枸杞材料15个;建立与优化枸杞花药培养体系,枸杞花药培养中基因型、植物生长调节剂、基本培养基是主要的影响因子;进行枸杞新品系的区域品比试验;2010年12月10日完成“0207”的自治区林木品种委员会的审定,定名为“宁杞7号”。
【英文摘要】无

【中文名称】枸杞规范化种植技术研究与示范
【英文名称】null
【研究起始时间】2010-01

【研究终止时间】2012-12
【中文关键词】配方施肥;节水灌溉;株型;规范化种植
【英文关键词】null
【中文摘要】对枸杞配方施肥、高效节水灌溉技术、优质稳产株型的早期培育技术进行研究,并进行枸杞规范化种植技术集成与示范。结果表明在5个示范园中,存在枸杞种植户根据枸杞行情有盲目施肥的现象,枸杞价格高就多施,枸杞价格低就少施或不施,我们推荐施肥量为处理三,力求达到全年均衡产量;在宁南山区有灌溉条件的地方,枸杞园灌水改传统漫灌为沟灌,可以有效提高灌水均匀度和灌水效率,节水效果明显,节水率提高30%以上,每亩平均节约成本70-90元,同时通过节约灌水时间减少灌水蒸发的损耗,提高灌溉效率,有必要在枸杞生产中大力推广;建立了引黄灌区和旱作区2种不同气候条件下的枸杞整形修剪技术; 建成枸杞科技示范基地10000亩,基地平均亩产200公斤,水肥利用率提高10-20%,亩均节本增效400元。
【英文摘要】无

【中文名称】枸杞生产配套机械装备的研制与应用
【英文名称】null
【研究起始时间】2010-01
【研究终止时间】2012-12
【中文关键词】采摘机;肥料一体机;色选机;驱鸟器;烘干棚
【英文关键词】null
【中文摘要】项目主要针对枸杞生产中存在的问题和生产的实际需要,研制枸杞生产配套机械装备。1、枸杞采摘机械,首先确定采摘机的工作原理为振动原理,通过采果头插入枝条进行振动使果实脱落。机械研制主要研制采摘枪、采果头、调速器、电瓶、电瓶车等,并进行组装配套,将研制出的采摘机进行采摘试验和性能评价、根据评价意见修改完善采摘机,实现枸杞的机械采摘;2、车载式肥料一体机,在原有枸杞喷药器械的基础上,按照一机多用的原则,将研制的2种新型枸杞液体肥料高压施肥枪进行转化,一台机械每天施肥4-6亩,提高劳动工效10倍以上,每年每亩节省劳动成本200元以上;示范应用枸杞色选机、太阳能超声波驱鸟器、太阳能枸杞烘干棚,解决了鸟类危害和加工过程中的难题,促进枸杞产业的发展。
【英文摘要】无

【中文名称】枸杞科技示范基地建设
【英文名称】null
【研究起始时间】2010-01
【研究终止时间】2012-12
【中文关键词】节水高效;经济平衡施肥;GAP基地建设
【英文关键词】null
【中文摘要】在全区各枸杞主产区建立科技示范基地,以宁夏枸杞工程技术研究中心为技术依托,以“龙头企业+科技特派员+基地”的运行模式,按照“生产标准化、服务一体化、产品档次化”的总体要求,在中宁红梧山建立了2000亩枸杞规范化示范基地,在中宁田滩推广骨架牢固、冠层合理、冠幅紧凑、通风透光等树形修剪技术2400亩;同时配套示范推广测土配方平衡施肥、枸杞病虫害统防统治技术5000亩;推广枸杞红瘿蚊覆盖隔离物理防治技术500亩;在中宁杞乡公司建立804亩枸杞GAP基地;在原州区建成3000亩枸杞科技示范基地,改造1000亩银川市西夏区镇北堡枸杞基地和1000亩石嘴山市惠农区枸杞基地。示范推广枸杞新品种、新技术,新装备,促进枸杞产业发展。
【英文摘要】无

【中文名称】短葶山麦冬组织培养技术与机理研究
【英文名称】null
【研究起始时间】2009-11
【研究终止时间】2012-06
【中文关键词】短葶山麦冬;外植体的选择;机理;内源激素;外源激素
【英文关键词】null
【中文摘要】短葶山麦冬Liriope muscari(Decne.)Bailey为百合科山麦冬属植物,集药用、观赏于一体,根内含皂苷、多糖等成分,叶可观赏,是重要的园林地被植物。本研究旨在以短葶山麦冬的优良品种的各个器官为外植体,在前人研究的基础上,对短葶山麦冬组培苗芽诱导机理、愈伤组织诱导机理、继代增殖机理、壮苗机理、生根机理进行探讨,研究添加外源激素(6-BA、NAA、2.4-D等),内源激素含量的变化,通过对其组织培养机理的研究,有效地提高芽的诱导率、继代增殖系数及生根率,形成一系列的短葶山麦冬组织培养体系,以便进行工厂化生产。

【英文摘要】无

【中文名称】雷公藤有效成分与环境效应的关系
【英文名称】null
【研究起始时间】2009-11
【研究终止时间】2012-06
【中文关键词】雷公藤;有效成分;环境效应;质量控制;指纹图谱
【英文关键词】null
【中文摘要】雷公藤(Tripterygium wilfordii Hook.f.) 系卫矛科雷公藤属植物,广泛分布于我国南方省份。其干燥根是传统的中药材,雷公藤药材及其制剂对多种疾病均有良好的疗效,雷公藤植物研究新药已引起医药界的广泛重视,其应用领域正不断拓宽,需求量日渐增大,开发前景非常广阔。但雷公藤又有明确的毒性,它的研究也成为人们关注的焦点和热门研究的课题。雷公藤因其药材来源广泛、生境差异大、生产加工工艺的不同造成药材的质量参差不齐,质量控制也无系统性地研究,这些因素均造成雷公藤中药材及其药剂质量的差异性较大,严重影响了临床应用的安全性和有效性。本文对全国8省26市共32个种源的雷公藤有效成分及指纹图谱研究的基础上,确立有效成分的最佳提取工艺,初步建立各因素与雷公藤质量控制的关系,得出雷公藤不同种源的指纹图谱。
【英文摘要】无

【中文名称】短葶山麦冬的遗传多样性分析及ISSR指纹图谱构建
【英文名称】null
【研究起始时间】2008-10
【研究终止时间】2011-06
【中文关键词】短葶山麦冬;ISSR;遗传多样性;指纹图谱
【英文关键词】null
【中文摘要】短葶山麦冬(Liriope muscari (Decne.) Bailey),百合科山麦冬属,多年生常绿草本植物,主要分布在福建省内,块根具有药用价值,园林绿化上主要作地被用,常年绿色。短葶山麦冬为多年生草本植物,其药用价值一直被人们说认可,但短葶山麦冬的观赏价值近年来才逐渐被人们所认可。本研究为短葶山麦冬的研究、开发、利用,制定它们的育种策略,培育出优良品种提供参考和依据;同时对于进一步进行品种分类和分子辅助育种及研究短葶山麦冬的遗传起源进化及物种形成、分子遗传的基础理论研究都有重要的意义。本研究利用ISSR分子标记研究福建省31个短葶山麦冬种源的遗传多样性,了解这短葶山麦冬的遗传变异水平;进行基于ISSR分子标记的聚类分析,了解短葶山麦冬种源间的亲缘关系,并建立短葶山麦冬的指纹图谱。
【英文摘要】无

【中文名称】雷公藤组织培养技术研究
【英文名称】null
【研究起始时间】2008-11
【研究终止时间】2011-06
【中文关键词】雷公藤 组织培养 愈伤组织 外植体褐变
【英文关键词】null
【中文摘要】雷公藤(Tripterygium wilfordii)作为一种重要的杀虫植物和传统的中药材,近年来在无公害农业生产和医药临床方面的需求不断增加,造成野生资源急剧减少。为保护雷公藤自然资源,实现其资源的可持续利用,有必要对雷公藤组织培养技术体系进行系统研究,还要解决组培过程中材料易褐变的难题,以提高组培成功率。本试验以雷公藤的嫩叶、幼茎及根为外植体,对外植体灭菌、启动培养、继代增殖培养、生根培养、愈伤组织诱导及植株再生、外植体褐化等方面进行了研究,探讨外植体的消毒程序、基本培养基的筛选、最佳植物生长调节剂的浓度及组合等对雷公藤组织培养的影响,外植体褐变的过程和机理及其抑制处理,为雷公藤的组培工厂化育苗奠定基础。
【英文摘要】无

【中文名称】宁夏枸杞质量标准及质量控制方法的化学研究
【英文名称】null
【研究起始时间】2010-01

【研究终止时间】2012-11
【中文关键词】宁夏枸杞 玉米黄素双棕榈酸酯 含量测定方法 甜菜碱 老年黄斑变性
【英文关键词】null
【中文摘要】利用硅胶柱层析、氧化镁柱层析、Sephadex LH-20凝胶和高效液相色谱法对宁夏枸杞化学成分进行分离纯化,通过理化性质和波谱数据分析鉴定化合物结构。从枸杞子中分离得到10个化合物,鉴定了其中的8个化合物,分别为:烟酸(1),棕榈酸(2),正二十烷酸(3),麦角甾醇(4),β-胡萝卜素(5),玉米黄素双棕榈酸酯(6),β-谷甾醇(7),甜菜碱(8)。尤其是明确了玉米黄素双棕榈酸酯(6)在宁夏枸杞中的含量高,还具有良好的活性,为宁夏枸杞的特征性化学成分。建立了玉米黄素双棕榈酸酯的含量测定方法(HPLC法):液相条件:Ultimate Carotenoids(C30)(250×4.6mm, 5μm); 流动相:A:MeOH:MTBE:H2O=81:15:4,B: MeOH:MTBE:H2O=6:90:4;梯度:1-100%B (90min);检测波长:450 nm;流速:1.0 ml/min;柱温:25 ℃。
【英文摘要】无

【中文名称】系列“零农残”制剂防控技术
【英文名称】null
【研究起始时间】2010-01
【研究终止时间】2012-11
【中文关键词】“零农残”防控制剂;检测;未检出
【英文关键词】null
【中文摘要】初步建立有机枸杞病虫害“零农残”防控制剂简易配制中试生产车间1个、中试生产线一条,配制“零农残”1号-19号系列防控制剂开展多点扩大示范。各示范区自主对枸杞集中采样、统一送检,进行第三方检测机构的权威农残检测,确保了检测结果的的客观性与中立性。检测结果表明:各示范区在完全不使用农药的前提下,采用《有机枸杞病虫害‘零农残’防控技术年历》及相应的防控制剂,多种农残扫描(191+项)农药残留均“未检出”,达到了“零农残”水平。全面减少了农药残留污染,根本提升了枸杞产品质量,有效支撑了宁夏枸杞产业健康发展。
【英文摘要】无

【中文名称】宁夏枸杞产地适宜性分析
【英文名称】null
【研究起始时间】2010-01
【研究终止时间】2012-11
【中文关键词】地理信息系统、生态环境特征、宁夏枸杞、因子分析、适宜性分析
【英文关键词】null
【中文摘要】1.利用GIS技术和统计学的方法,对宁夏枸杞的地理空间分布和生态环境特征进行了总结描述,统计出宁夏枸杞的生态环境特征值。由此得知:说明宁夏枸杞是对日照时数和太阳辐射量要求均较高,是一种适应盐碱土生长的植物。2.利用岭回归的方法分别分析了宁夏枸杞甜菜碱含量、多糖含量和总糖含量与环境变量的关系,可知宁夏枸杞的分布趋向于活动积温条件高、土壤PH相对较高的地区。3.对宁夏枸杞生态环境的因子分析表明:宁夏枸杞分布主要受“热量因子和有机质因子”的控制。通过因子分析还得到各因子权重系数及因子得分,这些为进行宁夏枸杞的产地适宜性分析奠定了基础。4.通过对宁夏枸杞适宜分布区的分析表明,100%适宜区中宁夏回族自治区包含的县市数最多,总面积最大,其次为内蒙古自治区和甘肃省;90%-99%适宜区以甘肃省包含的县市最多面积也最大,其次为新疆、宁夏和内蒙古等省区。
【英文摘要】无

【中文名称】宁夏枸杞质量安全检测技术研究与应用
【英文名称】null
【研究起始时间】2010-01
【研究终止时间】2012-11
【中文关键词】农药残留 金属元素 二氧化硫 色谱 质谱 等离子发射光谱
【英文关键词】null
【中文摘要】本研究通过对宁夏、内蒙、新疆、青海、甘肃等枸杞主产区枸杞生产情况的调查,确定枸杞中常用的81种农药,并根据农药性质及仪器相应特征,通过对枸杞多种农药残留预处理研究,建立了81中农药残留前处理的技术平台,同时建立了枸杞中60种农药残留气相色谱-串联质谱(GC-MS-MS)检测方法和56种农药液相色谱-串联质谱(LC-MS-MS)的大通量检测方法,方法的添加回收率为60 % -129.2%,相对标准偏差1.0%~17.7%,81种农药的线性范围在0.002μg/mL ~1.0μg/mL之间,相关系数0.9927~0.9998,定量限为5μg/kg~70μg/kg ,符合农药残留分析方法的要求,并形成《枸杞中50-100种农药多残留气

相色谱-质谱和液相色谱-串联质谱检测方法》标准送审稿;通过标准物质的测定,建立了枸杞样品元素测定的前处理方法—微波消解法。对50种元素的半定量扫描,建立了枸杞中多种金属元素的电感耦合等离子光谱-质谱(ICP-MS)的分析方法。测定误差小于20%,符合ICP-MS分析方法的要求;

【英文摘要】无