2019 中华口腔医学会“新星秀”壁报交流汇编

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二甲双胍作为抗衰老药物增强 CDK4/6 抑制剂对口腔鳞癌的抗肿瘤效应

胡钦朝　夏　娟　程　斌　中山大学附属口腔医院

【摘要】 目的：细胞衰老及衰老相关分泌表型（Senescence-associated secretory phenotype, SASP）是 CDK4/6 抑制剂用药后的主要结局，发挥抑癌、促癌的双向作用。本研究拟探讨抗衰老药物二甲双胍联合 CDK4/6 抑制剂在口腔鳞癌中应用的可行性及其机制，为口腔鳞癌的治疗提供新的思路。

方法：通过体外细胞系实验、体内移植瘤模型、PDX 模型等检测 CDK4/6 抑制剂（LY2835219）联合二甲双胍对口腔鳞癌的抑制作用；SA-β-gal 染色、蛋白芯片等检测二甲双胍对 LY 所诱导的细胞衰老及 SASP 的影响；细胞成球实验、体内成瘤实验等检测二甲双胍调控 SASP 对肿瘤干性的影响；通过 TCGA 数据库分析 SASP 因子及干性相关指标与患者预后的关系。

结果：LY 和二甲双胍联合上调 p21、下调 pRb，诱导细胞周期阻滞，在体内体外协同抑制口腔鳞癌增殖。联合应用二甲双胍对 LY 所诱导的衰老细胞比例无影响，但改变了 LY 所诱导的 SASP 表达谱：LY 上调 IL6、IL8、MCP1、GRO 等 SASP 因子，而联合二甲双胍可抑制这些因子的表达上调。进一步，证实二甲双胍通过抑制 stat3/mTOR 通路调控上述 SASP 因子。细胞成球实验及体内成瘤实验表明，二甲双胍通过阻断 IL6-stat3 轴的激活，抑制了 SASP 对肿瘤干性的促进作用。生存分析结果显示，SASP 因子 IL6 及肿瘤干性指标 CD44、ALDH1A1 的高表达与患者不良预后相关。

结论：二甲双胍通过调控 SASP 增强 CDK4/6 抑制剂对口腔鳞癌的抑制作用。

【关键词】 口腔鳞癌；CDK4/6 抑制剂；二甲双胍；衰老相关分泌表型；肿瘤干性

Immunocompetence and mechanism of the DRibble-DCs vaccine for oral squamous cell carcinoma

苏　航　同济大学附属口腔医院
牟永斌　南京大学附属口腔医院

【摘要】 Background: Due to the high-quality immunogenicity of tumor-derived autophagosomes (DRibbles), we aimed to explore the antitumor ability and mechanism of DRibble-loaded dendritic cells (DRibble-DCs).

Materials and methods: DRibbles extracted from the oral squamous cell carcinoma cell line SCC7 express specific LC3-II and ubiquitination marker. Immunization of mice with the DRibble-DCs vaccine led to the proliferation and differentiation of CD3+CD4+IFN-γ+ and CD3+CD8+IFN-γ+ T cells. The expression of proteins in endoplasmic reticulum stress (ERS) pathways was determined by Western blotting. Additionally, the functional properties of the DRibble-DCs were examined in mice, and regulatory T cells were measured by flow cytometry.

Results: Excellent biocompatibility was observed in vitro when DCs were loaded with DRibbles. T cells of lymph nodes and spleens from mice immunized with DRibble-DCs had cytotoxic effects on SCC7 cells. DCs homeostasis and ERS-related proteins were affected by DRibbles. Moreover, the DRibble-DCs vaccine achieved significantly better antitumor efficacy than DRibbles and tumor cell lysate-loaded DCs.

Conclusion: The results validated the antitumor immune responses to the DRibble-DCs vaccine in vivo and in vitro. The ERS pathway can be affected by DRibbles.

【关键词】 dendritic cells；oral squamous cell carcinoma；endoplasmic reticulum stress；antigen cross-presentation；vaccine

Periodic Oxaliplatin Administration in Synergy with PER2-mediated PCNA Transcription Repression Promotes Chronochemotherapeutic Efficacy of OSCC

唐清明　华中科技大学同济医学院附属协和医院

【摘要】 Developing chemotherapeutic resistance affects clinical outcomes of oxaliplatin treatment on various types of cancer. Thus, it is imperative to explore alternative therapeutic strategies to

improve the efficacy of oxaliplatin. Here we show that circadian regulator PER2 (period 2) can potentiate the cytotoxicity of oxaliplatin and boost the cell apoptosis via inhibiting DNA adducts repair in human OSCC (oral squamous cell carcinoma) cells. Our mechanistic studies show that PER2 can periodically suppress PCNA transcription by pulling down CLOCK-BMAL1 heterodimer from PCNA promoter in a CRY1/2-dependent manner, which subsequently impedes oxaliplatin-induced DNA adducts repair. Similarly, we find that PER2 is capable of improving the efficacy of classical DNA-damaging chemotherapeutic agents. In summary, our results indicate the PER2 can be deployed as an oxaliplatin administration timing biomarker. Importantly, there results demonstrate that the chronochemotherapeutic strategy matching PER2 expression rhythm can efficiently improve the oxaliplatin efficacy of OSCC.

【关键词】 Chronochemotherapeutic strategy; Oxaliplatin; Circadian clock genes; DNA-damaging repair; Oral squamous cell carcinoma

头颈部腺样囊性癌的 CT 诊断

伍丹丹　空军军医大学

【摘要】 目的：加强对头颈部腺样囊性癌（ACC）的认识，提高术前 CT 诊断率。方法：回顾性分析 99 例经病理证实的头颈部原发 ACC CT 影像资料，其中 35 例行平扫，64 例行平扫及增强扫描。结果：病变主体位于腭部、口底各 34 例，上颌窦、面颊部、腮腺各 8 例，下颌骨 4 例，下颌下腺 3 例。病变累及邻近 2 个以上解剖结构者 67 例。CT 表现：受累部位见类圆形、条形或不规则形软组织肿块，边界不清 82 例，侵犯破坏邻近骨质 52 例，骨质呈压迫性改变 3 例。平扫或增强扫描见筛样改变 52 例。42 例病变主体位于腭部及上颌窦者，19 例见腭大孔扩大，18 例见翼腭窝增宽或密度增高。4 例发生于下颌骨者均可见大范围虫蚀状骨质破坏。结论：（1）低密度筛样改变为 ACC 特征性 CT 改变。（2）腭大孔扩大、翼腭窝增宽及密度增高有助于 ACC 的诊断。（3）CT 可清晰显示骨质破坏情况，但对病变侵犯范围评估不足。（4）原发于下颌骨者骨质破坏范围大。

【关键词】 头颈部肿瘤；腺样囊性癌；体层摄影术；X 线计算机

材　料

打磨和上釉对超透牙科氧化锆机械性能的影响

尹　倩　烟台市口腔医院

【摘要】 随着口腔修复技术的不断更新以及口腔材料学的发展，全瓷修复技术逐渐成为口腔修复治疗中理想的修复方式。在众多的全瓷修复材料中，氧化锆强度高、韧性及生物相容性好，广泛应用于口腔医学领域，如牙体及牙列缺损的冠、桥修复，以及颌面部组织缺损修复。近年来，随着人们对美学要求越来越高，口腔修复治疗的美观性也成为评价修复治疗成功与否的关键标准。超透牙科氧化锆透光性好，符合天然牙的色泽，因此在口腔美学修复中具有优势。研究表明，使用车针打磨超透牙科氧化锆，或在表面上釉，会影响其机械性能，但原因尚存争议。本文通过对超透牙科氧化锆进行小粒度 / 超小粒度打磨和上釉观测表面形貌、挠曲强度、相变量等的改变，以及通过水热处理模拟其在口内使用情况观测抗时效性的改变，探讨小粒度 / 超小粒度打磨与上釉对超透牙科氧化锆机械性能的影响。

【关键词】 超透牙科氧化锆；打磨；上釉；机械性能

儿童口腔医学

Mechanical Stress Modulate the RANKL/OPG system of Periodontal Ligament Stem Cells via α7 nAChR in Human Deciduous Teeth - an in vitro study

陈宇江　空军军医大学口腔医院　Yang Kuan　西安交通大学口腔医院

【摘要】 Objectives: The aim of this study was to investigate the mechanism by which periodontal ligament stem cells (PDLSCs) modulate root resorption of human deciduous teeth under mechanical stress.

Methods: In this investigation, the PDLSCs were derived from deciduous and permanent teeth at different stages of root resorption. A cyclic hydraulic pressure was applied on the PDLSCs to mimic

chewing forces in the oral environment. The cultured cells were characterized using osteogenic and adipogenic differentiation assays, quantitative real time polymerase chain reaction (qRT-PCR) and Western blotting analysis.

Results: The PDLSCs exhibited the ability to induce osteoclast differentiation under certain mechanical stress. As the expression of Runx2, alkaline phosphatase (ALP) and osteoprotegerin (OPG) were significantly reduced, the receptor activator of nuclear factor kappa-B ligand (RANKL) was up-regulated increasing the RANKL/OPG ratio. Under hydrodynamic pressure at 0-135 KPa, the expression of alpha 7 nicotinic acetylcholine receptors (α 7 nAChR), p-GSK-3β, and active-β-catenin were markedly up-regulated in PDLSCs from unresorbed deciduous teeth. Treatment with α 7 nAChR inhibitor, alpha-bungarotoxin (α-BTX), and Wnt pathway inhibitor, DKK1, may reverse the mechanical stress induced up-regulation of RANKL and reduction of Runx2, ALP, and OPG. Alizarin red staining confirmed these results.

Conclusions: The mechanical stress applied on the deciduous teeth PDLSCs can induce osteoclastic effects through up-regulation of α 7 nAChR and activation of the canonical Wnt pathway. It can be suggested that chewing forces may play a major role at the beginning of physiological root resorption of deciduous teeth.

【关键词】 periodontal ligament stem cells; mechanical stress; human deciduous teeth; root resorption

Epiregulin enhances odontoblastic differentiation of dental pulp stem cells via activating MAPK signaling pathway

崔迪新　四川大学华西口腔医学院

【摘要】 Objectives

The odontoblastic differentiation of dental pulp stem cells (DPSCs) contributes to tertiary dentin formation. Our previous study indicated that epiregulin (EREG) enhanced odontogenesis potential of dental pulp. Here we explored the effects of EREG during DPSCs odontoblastic differentiation.

Methods

The changes of EREG were detected during tertiary dentin formation. DPSCs were treated with recombinant human EREG (rhEREG), EREG receptor inhibitor gefitinib, and short hairpin RNAs. The odontoblastic differentiation was assessed with ALP staining, ALP activity assay, alizarin red S staining and real-time RT-PCR of DSPP, OCN, RUNX2, and OSX. Western blot was conducted to examine levels of p38 mitogen-activated protein kinase (p38 MAPK), c-Jun N-terminal kinase (JNK), and extracellular signal-regulated kinase 1/2 (Erk1/2). Expression of EREG and odontoblastic

differentiation related markers were investigated in human dental pulp from teeth with deep caries and healthy teeth.

Results

EREG was up-regulated during tertiary dentin formation. rhEREG enhanced the odontoblastic differentiation of DPSCs following up-regulated p38 MAPK and Erk1/2 phosphorylation, but not JNK, whereas depletion of EREG suppressed DPSCs differentiation. Gefitinib decreased odontoblastic differentiation with decreased phosphorylation of p38 MAPK and Erk1/2. And suppression of p38 MAPK and Erk1/2 pathways attenuated DPSCs differentiation. In human dental pulp tissue, EREG up-regulation in deep caries correlates with odontoblastic differentiation enhancement.

Conclusion

EREG is released during tertiary dentin formation. And EREG enhanced DPSCs odontoblastic differentiation via MAPK pathways.

【关 键 词】 epiregulin；dental pulp stem cells；odontoblastic differentiation；MAPK signaling pathway

Early-life Exposure to bisphenol A Disrupts Enamel Formation via EZH2-mediated H3K27 Trimethylation

万　冕　四川大学华西口腔医院

【摘要】 Background: Molar-incisor hypomineralization(MIH) is a common developmental enamel defect defined as hypomineralization of one or more permanent first molars, frequently associated with affected incisors. MIH is increasing concurrently with bisphenol A(BPA), which has led us to investigate the effect of BPA on enamel formation. Although a number of transcription factors and pathways have been implicated in MIH, the role of epigenome in this process within dental epithelial compartment remains unclear.

Objectives: The aim was to identify the epigenetic regulator involved in amelogenesis and to determine epigenetic mechanisms involved in BPA-induced MIH.

Methods: Experimental animal model that replicates MIH was induced by early-life BPA exposure. Incisor labial cervical loop and dental epithelial stem cells (DESCs) were harvested. Genome-wide mRNA and histone modification (H3K27me3) profiles were established with high-throughput sequencing. The H3K27 methyltransferase EZH2 and DESCs fate choice regulator Lrig1 were selected as research objects. Gain and loss of function analyses were conducted to explore their roles in regulating DESCs fate choice.

Results: Early-life exposure to BPA significantly suppressed enamel formation and promoted

DESCs proliferation in offspring following with down-regulation of stem cell-associated markers Lrig1 and Lgr5 and significantly upregulated expression of DESCs proliferation markers Cldn10, Steap1, Ank2, and Ccnb1. Chromatin immunoprecipitation sequencing (ChIP-seq)，ChIP-qPCR and IF staining revealed that this effect is associated with a global increase of the repressive mark H3k27me3 enrichment across the promoter region in DESCs，especially DESCs fate choice-associated genes Bmi1 and Lrig1. A strong reverse relationship was apparent between H3K27me3 mark and the expression of gene Lrig1, which indicates that the epigenome has an important role in directing cell-fate changes from DESCs to ameloblasts. The expression of EZH2 coincided with H3K27me3 modifications. And ChIP-qPCR demonstrated that the enrichment of EZH2 and H3K27me3 were up-regulated at the Lrig1 promoter in DESCs exposed to BPA. Depletion of EZH2 fully alleviated the reduction of Lrig1 expression level and up-regulated DESCs proliferation induced by BPA.

Conclusions: Together, our results demonstrate the central role of repressive histone modification H3K27me3 in developmental enamel defects elicited by BPA. And EZH2 methyltransferase is required for BPA’s epigenetic effects.

【关键词】 dental enamel；molar-incisor hypomineralization(MIH)；bisphenol A (BPA)；epigenetics；EZH2

年轻恒牙挫入的动物模型建立及组织学观察

王　楠　赵玉鸣　北京大学口腔医院

【摘要】 目的：牙齿挫入是年轻恒牙外伤中较严重的一型，常常会带来牙髓坏死、牙髓钙化、替代性吸收、边缘牙槽嵴丧失等并发症，但其发生机制目前并不清楚。本研究旨在于通过建立年轻恒牙挫入的动物模型，观察其预后及牙髓牙周组织学变化。

方法：选用 3 周龄雄性 SD 大鼠 30 只，利用改良耳钉枪与传力杆对大鼠右上第二磨牙挫入，左上第二磨牙做对照，观察 3d，7d，14d，30d，60d，90d，每时间点取 2 只行 Micro CT 扫描，所有样本进行 HE 染色。

结果：30 只大鼠成功完成牙齿完全挫入，3 只因颅脑损伤或过度出血死亡，实验成功率 90%。从第 7 天开始有自发萌出，14 天萌出率达到最高，第 30 天有所下降。牙髓组织病变主要表现为纤维性变、网状萎缩、炎症细胞浸润以及牙髓钙化，第 30d 时牙髓钙化充满髓腔，呈现成骨样改变，钙化中心可见成骨细胞与多核破骨细胞。牙周组织病变表现为牙齿固连、替代性吸收以及边缘牙槽嵴丧失。

结论：本研究利用改良耳钉枪成功建立了对年轻大鼠磨牙挫入的动物模型，观察到与临床牙挫入相似的各种并发症，为今后并发症机制的探索提供了基础。

【关键词】 牙挫入；年轻恒牙；动物模型；并发症；组织学表现

含银生物陶瓷 / 壳聚糖水凝胶对炎症反应性牙髓修复作用及机制的研究

朱宁馨　王媛媛　秦　满　北京大学口腔医学院

【摘要】 研究目的：本研究的目的是通过设计合成含银生物陶瓷 / 壳聚糖水凝胶（Silver-doped bioactive glass/chitosan hydrogel，Ag-BG/CS），探究其对于炎症反应性牙髓的修复效果和作用机制，为弥漫性牙髓炎的活髓保存治疗提供新的思路。

研究方法：将含银生物陶瓷（Silver-doped bioactive glass，Ag-BG）颗粒分散混合于壳聚糖（Chitosan，CS）水凝胶，合成新型材料含银生物陶瓷 / 壳聚糖水凝胶（Ag-BG/CS）。研究 Ag-BG/CS 的物理特性及抗菌性能，并评价 Ag-BG/CS 对人牙髓干细胞（Human dental pulp stem cells，hDPSCs）生长黏附的影响。应用大肠杆菌脂多糖（Escherichia coli lipopolysaccharide，LPS）诱导 hDPSCs，在体外建立炎症反应性牙髓干细胞（Inflamed human dental pulp stem cells，iDPSCs）模型，评价 Ag-BG/CS 对 iDPSCs 炎症因子表达和成骨 / 成牙本质分化的影响。第四，通过裸鼠皮下包埋实验和大鼠实验性弥漫性牙髓炎盖髓实验来评价 Ag-BG/CS 的体内生物活性，并初步探索 Ag-BG/CS 抗炎及促进炎症反应性牙髓修复的机制。

研究结果：1）Ag-BG/CS 的物理性能检测结果中，能谱分析结果表明，Ag-BG 颗粒成功负载于 CS 水凝胶内部，在扫描电镜下可见 Ag-BG/CS 呈均一的多孔结构；原子吸收光谱仪测定结果显示，在 72 小时内 Ag-BG/CS 可缓慢稳定释放银离子。2）抗菌实验结果表明，Ag-BG/CS 可明显抑制致龋菌 S. mutans 和 L. casei 的生长。3）体外实验结果显示，Ag-BG/CS 处理后的 hDPSCs 仍可稳定增殖和黏附。Realtime-PCR 及 western blot 结果显示，经 Ag-BG/CS 浸提液处理后的 iDPSCs 中相关炎症因子的 mRNA 及蛋白表达水平明显降低；TNAP 染色结果显示 Ag-BG/CS 浸提液可上调成骨诱导后 iDPSCs 的碱性磷酸酶活性；免疫化学染色、realtime-PCR 及 western blot 结果显示，经 Ag-BG/CS 浸提液处理的 iDPSCs 中成骨 / 成牙本质分化相关标记物的表达水平高于未处理的 iDPSCs。4）体内实验中的裸鼠皮下包埋实验结果显示，Ag-BG/CS 可促进牙髓牙本质复合体样结构的形成。大鼠盖髓实验结果显示，Ag-BG/CS 组和 MTA 组在术后 8 周均能形成硬组织屏障。经 Ag-BG/CS 盖髓后牙髓组织中可见成牙本质、成血管、成神经相关因子的阳性表达，根尖区牙髓组织维持其基本结构，根尖发育完全；而 MTA 组牙髓组织弥漫性变性，根尖处大面积钙化。5）对于 Ag-BG/CS 的作用机制，免疫荧光实验及 western blot 结果显示 Ag-BG/CS 能抑制 p65 磷酸化及转移入核，从而阻断了 NF-κB 信号通路激活的同时，Ag-BG/CS 可上调 p38 和 ERK1/2 的磷酸化，提示 Ag-BG/CS 通过抑制 NF-κB 通路、激活 MAPKs 信号通路控制牙髓炎症反应并促进牙髓组织修复。

研究结论：Ag-BG/CS 具有良好的生物活性、抗菌性、抗炎及促成牙本质分化的能力，可在体内促进牙髓牙本质复合体样结构形成。Ag-BG/CS 可通过抑制 NF-κB 通路、激活 MAPKs 通路，

实现抑制炎症漫延、保存根方牙髓组织活性的目的。由此表明 Ag-BG/CS 具有应用于弥漫性牙髓炎活髓保存治疗的潜能。

【关键词】 含银生物陶瓷 / 壳聚糖水凝胶；活髓保存；弥漫性牙髓炎；牙髓炎症修复

数字化技术在牙外伤松动固定术中的应用

汪晓彤　北京大学口腔医院
白　洁　北京大学口腔医院

【摘要】 外伤导致的牙齿松动或移位，临床治疗应对外伤牙进行复位和弹性固定。在多个邻牙缺失或萌出高度不足，无法借助邻牙进行弹性固定时，全牙列殆垫是首选方案。殆垫对外伤牙有固定保护作用和咬合功能刺激，有利于牙周和牙髓组织的恢复，有助于防止牙根固连。传统全牙列殆垫制作需要利用印托盘及印膜材在患者口内取印模，灌制模型后制作，在取下托盘时，可能会造成外伤牙齿移位甚至脱出，引起医源性损伤，为避免该情况需要先对外伤牙进行临时固定再取印模，增加了临床操作时间和成本，也增加了患者的不适。

采用扫描仪（3shape TRIOS T12A）直接进行口内扫描，软件（3shape TRIOS 椅旁版）处理后获取数字化印模，通过 3D 打印技术获取模型，即可压制殆垫。本技术避免了传统印模方法对外伤牙造成的二次损伤，在临床上省去选择托盘、调制印模材料、材料消毒、灌制石膏等步骤；同时较少引起传统托盘取模时的恶心、不适、牙齿敏感甚至呼吸困难等问题。

北京大学口腔医院急诊科将数字化印模技术和 3D 打印技术相结合，已成功对 14 名患者进行了外伤恒牙全牙列殆垫固定术，简化临床操作步骤和时间，减轻患者痛苦，并取得良好的临床效果。

【关键词】 牙；外伤；松动牙；殆垫；3D 打印技术

儿童上颌第一乳磨牙牙冠与其不锈钢预成冠形态差异研究

周永川　河北医科大学口腔医院
卢晓燨　周乐迪　河北医科大学

【摘要】 目的：本研究拟利用三维扫描技术建立来我院就诊儿童上颌第一乳磨牙临床牙冠及其金属预成冠 3D 模型，以 3D 重合与测量技术比较其形态上的差异　方法：收集 116 例上颌第一乳磨牙石膏模型与其金属预成冠（韩国轩宇，美国 3M）。三维扫描仪 D500 扫描其组织面数据得到 3D 图像，计算上颌第一乳磨牙形态数据医学参考值范围及其频数表。利用 Geomagic Wrap2015 3D 重合上颌第一乳磨牙模型韩国轩宇金属预成冠（a 组）和上颌第一乳磨牙模型与美国 3M 金属预成冠（b 组），计算未重合面积。利用 Creo 软件测量 3D 图像的最大近远中径（冠宽）、颊侧

平均近远中径（颊侧冠宽）、舌侧平均近远中径（舌侧冠宽）、颊舌径、牙冠高度（近中面、远中面、颊面、舌面）、冠周径（殆面周径、最大周径、龈缘周径）、颊面曲率、舌面曲率。结果：a 组未重合面积较小，有统计学差异。a 组在最大近远中径、颊舌径、颊舌侧平均近远中经比、最大近远中径与颊舌径比、冠高、最大周径、龈缘周径存在统计学差异。b 组在最大近远中径、颊舌径、最大近远中径与颊舌径比、冠高、殆面周径、龈缘周径、舌侧面曲率均存在统计学差异。结论：上颌第一乳磨牙牙冠颈部无明显收缩，冠高明显较小，与韩国轩宇金属预成冠形态较接近，临床操作难度相对较小

【关键词】 乳磨牙；金属预成冠；计算机辅助设计

口腔病理学

Dietary nitrate protects skin flap against ischemia injury in rats via enhancing blood perfusion

崔　浩　青岛大学附属医院

【摘要】 Insufficient blood supply is associated with high levels of necrosis in reconstructive surgery. Restoring blood flow to undersupplied ischemic tissue is the most important impact factor determining skin flap viability. Dietary nitrate, a significant source of nitric oxide, has multiple physiological functions, including regulator of blood flow, angiogenesis, and vasodilatation. However, the effects of dietary nitrate on ischemic skin flap remain unknown. The present study evaluated whether dietary nitrate supplementation altered blood flow of ischemic skin flap in rats. Our results showed that nitrate treatment significantly enhanced ischemic tissue survival. Mechanistically, nitrate therapy significantly increased serum nitrate and nitrite levels, blood perfusion, and angiogenesis. In addition, the circulating levels of Inflammatory mediators were decreased by nitrate supplementation. In conclusion, we demonstrated that dietary nitrate supplementation protected ischemic skin flap by enhancing ischemia-induced revascularization.

【关键词】 Nitrate; Nitric oxide; Blood perfusion; Skin flap; Microvascular density

Genetic polymorphisms associated with cleft alveolar of non-syndromic cleft lip with/without palate in Western Han population

段世均　West China College of Stomatology, Sichuan University
Zhonglin Jia　West China College of Stomatology, Sichuan University
Bing Shi　West China College of Stomatology, Sichuan University

【摘 要】 Objective: Cleft lip and palate often accompanied with cleft alveolar, which seriously affects the growth and development of the maxilla. The aim of this study is to assess the association between susceptibility genes of non-syndromic cleft lip with/without palate (NSCL/P) and cleft alveolar in Western Han Chinese population.

Methods: We recruited 228 trios of NSCL/P with cleft alveolar (156 males and 71 females). The 47 SNPs were genotyped by SNPscan method; Hardy–Weinberg equilibrium test, allelic TDT, parent-of-origin effect, and linkage disequilibrium analysis were performed by PLINK, FBAT and Haploview software.

Results: The genotypic distribution of these SNPs were not deviated from the Hardy-Weinberg equilibrium ($P > 0.01$). Allelic TDT analysis revealed allele A at rs894673 of FOXE1, and allele T at rs3758249 of FOXE1 were under-transmitted (P=0.0071，ORtransmission=0.35, 95%CI: 0.16–0.78; P=0.0071，ORtransmission=0.35, 95%CI: 0.16–0.78; respectively). Parent-of-origin effect analysis revealed a paternal special under-transmission of allele A at rs894673, allele T at rs3759249, and allele T at rs4460498 of FOXE1 (P=0.039; P=0.039; P=0.039; respectively). Pair-wise LD analysis showed strong LD among rs894673, rs3759249, and rs4460498 ($r2 > 0.95$).

Conclusion: Our findings indicated that the target SNPs at FOXE1 were associated with cleft alveolar in Western Han population.

【关键词】 cleft alveolar; non-syndromic cleft lip with/without palate; susceptibility gene; association study

口服短双歧杆菌促进机体抗肿瘤免疫抑制头颈部鳞癌生长

李庆祥　王　琳　郭传瑛　北京大学口腔医院

【摘要】 目的：探究口服短双歧杆菌对头颈部鳞癌的抑制作用及其机制。

方法：选用 C3H/HeN 小鼠及 SCC VII 鼠源鳞癌细胞系，制备皮下移植瘤模型，约 1 周后成瘤，将小鼠随机分为对照组及实验组。两组分别灌胃给予生理盐水、短双歧杆菌 B.breve，隔日测量肿瘤体积。2-3 周后，处死小鼠，收取肿瘤、脾脏、肠内容物。利用 TUNEL 染色及 Western Blot 检测肿瘤细胞凋亡情况；免疫组化染色及流式细胞术检测肿瘤浸润淋巴细胞（TIL）；流式细胞术检测脾脏调节性 T 细胞（Treg）比例；对肠内容物进行微生物多样性测序分析。制备回肠末段结扎环（loop）模型，B.breve 或其 GFP 转化株 B.breve-GFP 处理后，收取肠段，前者应用 qRT-PCR 技术检测趋化因子及通路改变，后者应用免疫荧光染色检测 B.breve-GFP 定位、趋化因子表达水平及树突状细胞（DC）数量变化。体外诱导 BMDC 细胞，B.breve 刺激后 qRT-PCR 检测相关基因表达水平。

结果：口服 B.breve 可抑制小鼠移植瘤生长，促进肿瘤细胞凋亡。TIL 细胞增多，Treg 细胞减少。小鼠肠道菌群改变，多样性增加。局部施用 B.breve 后，肠上皮 CCL20 表达上调，肠绒毛内 DC 数量增多。免疫荧光染色显示 B.breve-GFP 位于肠上皮内。体外 B.breve 促进 DC 成熟。

结论：口服 B.breve 可以激活 DC 介导的肠黏膜免疫，引起全身及肿瘤局部 Treg 细胞减少，TIL 增多，促进肿瘤细胞凋亡，抑制肿瘤生长，菌群改变可能起到协同作用。

【关键词】 短双歧杆菌；头颈部鳞癌；树突状细胞；肿瘤浸润淋巴细胞；肠道菌群

MTH1 在口腔鳞癌中的表达及其对预后的影响

沈禹辰　李吉辰　哈尔滨医科大学口腔医院

【摘要】 目的：研究 MutT 同源酶 1（MTH1/NUDT1）在口腔鳞状细胞癌（简称口腔鳞癌）组织中的表达及表达情况对患者预后的影响。方法：应用免疫组织化学方法对 62 例口腔鳞癌患者的石蜡切片进行检测并对患者的预后情况进行随访，应用 Kaplan-Meier 法进行生存率分析，并应用 Cox 回归进行多因素分析，应用蛋白质免疫印记实验和 qRT-PCR 对 31 例口腔鳞癌患者的新鲜组织进行检测。结果：蛋白质免疫印迹实验与 qRT-PCR 发现肿瘤组织中 MTH1 的的表达水平均高于正常组织，且伴随着口腔鳞癌组织的分化程度降低，MTH1 的表达水平升高；免疫组织化学检测发现 MTH1 的表达程度与肿瘤浸润深度、淋巴结转移情况及肿瘤分化程度有明显关系，且 MTH1 高表达组患者五年总生存率及肿瘤特异性生存率均低于 MTH1 低表达组患者（$P < 0.0001$）。通

过单因素及多因素 Cox 回归分析发现 MTH1 在口腔鳞癌中可以作为独立的影响因素（P=0.011）以判断患者的预后情况。结论：MTH1 的表达情况从一定程度上反映了口腔鳞癌疾病的严重程度，并提示口腔鳞癌患者的预后情况，MTH1 有望成为诊疗中对口腔鳞癌患者预后进行评估的新指标。

【关键词】 口腔鳞状细胞癌；MutT 同源酶 1；免疫组织化学；单因素分析；多因素回归分析；蛋白质免疫印记实验

抑制 6- 磷酸葡萄糖脱氢酶通过激活 JNK 通路抑制口腔鳞状细胞癌颈淋巴转移

王逸飞　王　琳　郭传瑛　北京大学口腔医院

【摘要】 目的：探究 6 磷酸葡萄糖脱氢酶（G6PD）在口腔鳞状细胞癌（OSCC）颈淋巴转移中的作用及机制。

方法：通过免疫组化染色检测 105 例 OSCC 患者的肿瘤组织中 G6PD 的表达水平，并分析与患者颈淋巴转移及预后的相关性。在 OSCC 细胞系中，通过 siRNA 抑制 G6PD 表达，检测细胞迁移、侵袭和上皮间质转化（EMT）的变化；通过流式细胞术和 Westernblot 分别检测 ROS-JNK 的激活情况，使用 JNK 抑制剂 SP600125 进行“拯救实验”，检测是否可以逆转敲低 G6PD 介导的肿瘤侵袭、迁移和 EMT 抑制；通过裸鼠舌鳞癌原位移植瘤模型，进一步验证 G6PD 抑制剂 DHEA 对 OSCC 转移的影响，以及 JNK 通路在其中的作用。

结果：G6PD 的高表达与患者颈淋巴转移存在显著相关性（P ＜ 0.001），与患者的三年总体生存率存在相关性（P<0.05）。在 OSCC 细胞系中，抑制 G6PD 的表达或活性，可抑制肿瘤细胞的迁移、侵袭和 EMT 进程。敲低 G6PD 可激活 ROS-JNK 通路。SP600125 可逆转敲低 G6PD 导致的细胞迁移、侵袭和 EMT 抑制。裸鼠舌鳞癌原位移植瘤模型表明，对照组转移率为 100%（n=6，下同），DHEA 组转移率为 16.67%，SP600125+DHEA 组转移率为 66.67%。

结论：G6PD 表达与 OSCC 颈淋巴转移和预后相关；抑制 G6PD 的表达或活性可抑制 OSCC 的 EMT 进程和原位荷瘤动物模型颈淋巴转移，这一过程可能通过激活 JNK 通路发挥作用。

【关键词】 6- 磷酸葡萄糖脱氢酶；口腔鳞状细胞癌；颈淋巴转移；JNK 通路；上皮间质转化

Cdc42 缺失引起牙源性上皮囊性变和釉质发育异常

郑金绚　曹　阳　毛　剑　中山大学附属口腔医院

【摘要】 目的：探讨 Cdc42 在成釉器发育过程中的调控作用及可能机制，为研究 Cdc42 在牙发育中的功能及 Cdc42 缺失可能引起的相关疾病模型提供理论依据。

材料与方法：采用免疫荧光法检测 Cdc42 在牙发育过程中的表达模式，继而应用 K14-cre 与 Cdc42loxp/loxp 转基因鼠构建牙源性上皮特异性敲除 Cdc42 的转基因小鼠 K14-cre; Cdc42loxp/loxp。组织学检查和裸鼠肾背囊下移植分析 Cdc42 敲除鼠第一磨牙表型；透射电镜观察成釉器细胞超微结构变化；TUNEL 试验、免疫荧光染色、qRT-PCR 和原位杂交技术分别检测成釉器细胞凋亡、增值和牙发育过程中重要信号分子的变化。

结果：

1. Cdc42 高表达于胚胎期牙源性上皮（成釉器），出生后表达降低，表明 Cdc42 参与成釉器发育。

2. 上皮特异性敲除 Cdc42 导致牙源性囊肿形成。K14-cre; Cdc42loxp/loxp 小鼠出生后 24 小时内死亡，出生时，第一磨牙形态异常伴有囊肿；胚胎期组织学检查发现，囊性变始于 E15.5 天左右，发展至 E18.5 时为具有上皮衬里和基底膜的真性囊肿。将 K14-cre; Cdc42loxp/loxp 小鼠第一磨牙牙胚于裸鼠肾背囊下移植 5 周后发现，Cdc42 缺失导致磨牙牙源性囊肿。

3. 敲除 Cdc42 后，成釉器细胞伪足减少、细胞连接数目减少伴有结构异常、细胞内自噬小体数目增加同时 Lc3b 基因表达增加。与对照鼠牙胚相比，上皮 - 间充质之间的基底膜不完整。

4. Cdc42 的缺失，引起胚胎期成釉器细胞凋亡增加；次级釉结相关标记物 shh 表达降低，Sox2 阳性细胞异位表达。此外，敲除 Cdc42 导致胚胎后期成釉器增生减少、体积减小。

5. 敲除 Cdc42 引起成釉器发育过程中 Wnt/β-catenin 激活减少。

结论： Cdc42 的缺失导致牙源性囊肿形成，Cdc42 是成釉器发育的重要调节因子，其通过调节成釉器凋亡、增生、成牙相关信号通路 Wnt/β-catenin 和 shh 参与成釉器发育，可能参与自噬。K14-cre; Cdc42loxp/loxp 小鼠可能为牙源性囊肿的动物模型提供理论依据。

【关键词】 Cdc42；成釉器；牙发育；牙源性囊肿；釉质

褪黑素对变应性鼻炎大鼠颌下腺的作用

周　凯　青岛大学附属医院

【摘要】 目的：研究褪黑素对变应性鼻炎大鼠颌下腺唾液减少和氧化应激的影响。

方法：111 诱导的变应性鼻炎的大鼠给予褪黑素治疗 4 周后，检测褪黑素对变应性鼻炎大鼠唾液分泌，颌下腺组织形态学及氧化应激水平的影响。

结果：与正常对照组大鼠比较，变应性鼻炎大鼠唾液分泌减少，免疫球蛋白 E 升高，饮水量增加，同时颌下腺组织丙二醛（MDA）含量显著增加，而抗氧化酶包括超氧化物极化酶（SOD）、谷胱甘肽过氧化物酶（GSH），活性显著降低。褪黑素治疗可明显增加唾液分泌量，增加颌下腺 SOD 和 GSH 活性，降低 MDA 含量。

结论：褪黑素有效抑制变应性鼻炎大鼠颌下腺氧化应激反应，改善颌下腺功能。颌下腺内在的抗氧化酶缺乏可能在变应性鼻炎颌下腺损伤的发生发展过程中起着重要作用。

【关键词】 褪黑素；变应性鼻炎；氧化应激；口干；颌下腺

人工智能自动定量分析胞核性状的初步应用

池彦廷　北京大学口腔医院

【摘要】 医学大数据具有“大量、高速、多样、价值”的特点，它正在改变着医学研究与实践，在服务人群健康管理、疾病预防、疾病早期检测、疾病诊断、疾病治疗及预后评估等方面发挥巨大作用。

病理学作为医学中的基础学科，是疾病诊断的金标准。病理学数据库极为庞大，图像中存在众多肉眼难以辨别的亚视觉图像信息。为了区分视觉上难以辨别的微小图像模式，需要先进的计算机技术。人工智能在病理学中广泛应用，病理组学的概念应运而生；病理组学需要更加全面详细的病理图像数据特征，这些工作单由病理医生来进行人工标记是不现实的，所以需要运用多种人工智能分析算法来学习并且提取病理图像中的特征信息，深度挖掘亚视觉信息，以病理数据为核心融合多种原始数据（如影像、临床数据、分子数据等），用于疾病的预防、检测、诊断及预后评估，从而为患者制定最优的临床决策。医学大数据的不断积累和人工智能研究的不断突破，使得人类对疾病的诊治逐步迈入了精准医学时代。

本研究以测定口腔鳞状细胞癌中细胞核 Ki-67 染色情况为例，通过对多种细胞核自动定量方法的的分析和比较，旨在开发出一种高效率的胞核自动定量分析技术，作为人工智能辅助病理组学中一个重要部分。

【关键词】 人工智能；临床病理；细胞核；定量分析

多点取材法对诊断口腔癌肿瘤内异质性的价值

揭伟萍　池彦廷　李斌斌　北京大学口腔医院

【摘要】 肿瘤内异质性是指一种肿瘤内不同肿瘤细胞间从基因型到表型上存在的差异。肿瘤异质性在时间及空间维度上发展的随意性及不可预测性给肿瘤的个体化精确治疗带来极大的挑战，是精准医学需要破解的一大难题。

肿瘤样本的取材直接影响肿瘤异质性检测结果的可靠性。传统取材方法是在肿瘤异质性尚未纳入临床考虑时建立起来的传统准则。为了高效、准确检测肿瘤异质性，急需对当今取材方法进行适当的改良。

本研究基于“分治算法”的理论依据，研究多点取材方法的建立及多点取材法较传统取材法在口腔癌肿瘤内异质性检测中的优势。

【关键词】 多点取材法；传统取材法；肿瘤内异质性

口腔材料学

Nanotopography on titanium promotes osteogenesis via autophagy-mediated signaling between YAP and β-catenin

李玲婕　杨　生　宋锦璘　重庆医科大学附属口腔医院

【摘要】 Nanostructured titanium implants are recognized for inducing osteogenesis, but the cell signal transductions related to topography are not fully understood. Implant topography is associated with the functionality of osteogenic transcription factors directed by β-catenin in the nucleus, and autophagic flux in the cytoplasm; YAP (Yes-associated protein) is implicated .n the destruction of β catenin in the cytoplasm and is susceptible to autophagic flux. This study investigated whether surface topography of the titanium implant modulates autophagy-lysosome degradation of cytoplasmic YAP. Titanium surfaces were modified with smooth, micro, or nanotopographies. Compared with the smooth and micro surfaces, nanotopography was associated with higher β-catenin nuclear translocation, osteogenic differentiation, and autophagy, and less cytoplasmic YAP. Blockade of the autophagy-lysosome pathway resulted in YAP retention in MC3T3-E1 cells. Cytoplasmic YAP restricted β-catenin nuclear translocation. In the nano surface group, β-catenin accumulation in the nucleus and expression of osteogenesis genes was improved. However, in the absence of cell-cell (confluent) contact, manipulation of YAP and β-catenin localization associated with topography-induced autophagy was lost. In summary, the osteogenesis observed in response to titanium implants with nanotopography involves a signaling link between YAP and β-catenin.

【关键词】 Autophagy; Nano-textured surface; Osteogenesis; Titanium

Lithium-containing biomaterials stimulate bone marrow stromal cell-derived exosomal miR-130a secretion to promote angiogenesis

刘　璐　上海交通大学医学院附属第九人民医院

【摘要】The chemical signals of biomaterials could influence bone marrow stromal cells (BMSCs)-

endothelial cells (ECs) communication during vascularized bone regeneration. However, the underlying mechanisms still remain unknown. Exosomes, a series of extracellular vesicles, have recently emerged as potential paracrine mediators in cell-cell communication. However, whether exosomes and exosomal microRNAs (miRNAs) are involved in the chemical signals of biomaterials-modulated BMSCs-ECs communication are unknown. Hence, in the present study, a model Li-incorporated bioactive glass ceramic (Li-BGC) was applied to explore the chemical signals of biomaterials mediated cell-cell communication between BMSCs and ECs. Our results showed that Li-BGC facilitated the pro-angiogenic capacity of HUVECs by eliciting the expression of exosomal pro-angiogenic miR-130a in BMSCs-derived exosomes, which subsequently leading to the downregulation of PTEN protein and activation of AKT pathway, ultimately resulting in the elevated proliferation, migration and tube formation of endothelial cells, as well as the upregulated expression of pro-angiogenic genes. Our findings may provide new insights into the regulatory roles of the chemical signals of biomaterials in BMSCs-ECs communication via stimulating exo- somal miR-130a secretion and PTEN/AKT signaling pathway in the angiogenic process of bone remodelling.

【关键词】 Exosome；MiR-130a/PTEN/AKT pathway；Lithium；Biomaterial；Angiogenesis

氟离子掺杂促进异种骨内源性阳离子原位释放促进骨再生的体内外作用研究

刘润恒　中山大学附属口腔医院

【摘要】 前言：生物来源羟基磷灰石 (BAp)（异种骨）因具有良好的生物降解性、生物相容性和骨传导性而被广泛应用于骨组织再生领域。微量元素掺杂是常见的改善化学合成羟基磷灰石成骨性能的方法。但是目前利用微量元素掺杂进一步提高生物来源羟基磷灰石 (BAp) 成骨性能的研究较少。在本研究中，我们将氟离子掺入猪骨羟基磷灰石 (pBAp) 中，合成氟化猪骨羟基磷灰石 F-pBAp，并探索氟离子掺杂对 pBAp 理化性能和体内外成骨性能的影响及其机制。

方法：通过热处理化学方法制备 F-pBAp。通过 TEM、SEM、EDS、FTIR、XRD、XPS、ICP 和氮气吸附等温线实验检测氟离子掺杂后 pBAp 理性能的改变。通过 SEM 检测大鼠骨髓间充质干细胞 (rBMSCs) 在 pBAp 和 F-pBAp 材料表面的黏附情况。通过 CCK-8、ALP 活性试剂盒和 qRT-PCR 分别检测 rBMSCs 与 pBAp 和 F-pBAp 材料浸提液共培养后的细胞增殖、ALP 活性以及成骨破骨相关基因表达情况。通过 qRT-PCR、WB、IF 检测 rBMSCs 与 pBAp 和 F-pBAp 材料浸提液共培养后 Wnt/β-catenin 信号通路中关键分子的表达情况。通过大鼠颅骨缺损模型、micro-CT、HE 染色、Trap 染色、Goldner’s 三色染色、免疫荧光染色，评价 pBAp 和 F-pBAp 材料的体内成骨性能及 Wnt/β-catenin 信号通路的激活情况。

结果：本研究的结果证明了氟离子掺入猪骨来源羟基磷灰石材料中，有助于改变材料的晶体

形态、持续释放氟离子，并促进内源性阳离子（如镁和钙）释放进入外周的材料组织微环境中。这种材料周围微环境中的离子平衡状态，不仅可促进 rBMSCs 的增殖和成骨分化，还可通过激活 Wnt / β -catenin 信号通路促进大鼠颅骨缺损中的新生骨形成。

结论：氟离子掺杂促进异种骨材料中的内源性阳离子原位释放，与氟离子的释放共同营造了有利成骨的材料周围组织微环境。

【关键词】 氟离子；异种骨；羟基磷灰石；成骨性能

Antibacterial and remineralizing orthodontic adhesive containing quaternary ammonium resin monomer and amorphous calcium phosphate nanoparticles

刘　奘　空军军医大学第三附属医院

【摘要】 Objective: To evaluate the bonding performance, antibacterial activity, and remineralization effect on enamel of the orthodontic adhesive containing MAE-DB and NACP.

Methods: Eighty non-carious human premolars were divided into 3 groups: Transbond XT (TB), PEHB+5% MAE-DB (PD), and PEHB+40% NACP+5% MAE-DB (PND). Premolars were bonded with orthodontic brackets, the first subgroup (n = 10) and the second subgroup (n = 10) were subjected to shear bond strength testing after immersed in water for 24 h and in demineralization solution for 28 days respectively, while the third subgroup (n = 6) was used for microhardness evaluation after aged in demineralization solution for 28 days. For each adhesive, fifty disk samples were prepared for antibacterial study. Specimens measuring 12 mm × 2 mm × 2 mm were fabricated for ion release test.

Results: Shear bond strengths after 28 d of aging (mean ± SD; in MPa) were: 8.9 ± 2.6 (TB), 6.3 ± 1.2 (PD), 8.4 ± 2.3 (PND). The bond strength of PND was almost the same as with TB, but significantly higher than PD. No significant difference in ARI between three groups ($P > 0.05$). Numerous bacteria adhered to TB surface, while PD and PND had minimal bacterial growth. PND showed high levels of Ca and P ions release. The surface roughness of PND was much lower than TB and PD ($P < 0.05$) and showed no significant difference with the sound, control enamel.

Conclusion: PND adhesive with 5% MAE-DB and 40% NACP exhibits antibacterial and remineralizing capabilities, and did not adversely affect bond strength compared to commercial adhesive.

【关键词】 adhesive；antibacterial；orthodontics；remineralization；white spot lesion.

Tracking the Repair Process of Rat Mandible Defect after Inferior Nerve Axotomy

马驷骁　北京大学口腔医院

Li Jiao　Peking University Third Hospital

【摘要】 Trauma and tumor-induced bone defects often accompany nerve injury. Several studies demonstrated that denervation led to over-sized callus and delayed fracture healing in lower limbs. However, there are few studies on the effects of denervation on the repair of maxillofacial bone defects. To track the repair process of mandible defects after denervation, male Sprague-Dawley rats were subjected to bilateral mandible defect surgery. On the left side, resection of 5mm inferior alveolar nerve (IAN) was performed in IAN axotomy group, while the other side of IAN was only separated without damage (sham group). Micro-computed tomography (micro-CT) and histologic staining were applied to track the repair process of mandible defect at 1, 2, 4, 8 weeks after the operation sequentially. The bone volume of both sides increased within 2 weeks after operation, and then gradually decreased even reaching the level of resorption. New bone volume of axotomy group was less than that of sham group at 1, 2, 4 weeks after surgery, whereas with no difference at 8 weeks. There is no significant difference in bone mineral density between two groups during repair process. This study suggests that IAN plays an important role in repair of mandible defect at early stage, but not affect bone remodeling.

【关键词】 Mandibular defect；Inferior alveolar nerve axotomy；Bone repair；Micro-CT

猪源性脱细胞骨基质修复颅面部骨缺损

聂子焱　兰州大学口腔医学院

【摘要】 由于复杂的解剖结构和严格的美学要求，颅面缺损的修复和组织再生具有挑战性，动物源性异种移植是一种很有前途的骨再生方法。为了降低免疫原性，脱细胞技术已被应用于再生医学，其中包括皮肤、血管、肌腱、软骨等。近年来对硬组织脱细胞的研究日益增多，但对猪源性脱细胞的研究较少。本研究采用猪肋骨松质骨部分，研发一种新的脱细胞方法制备了细胞外基质支架。H&E 染色和 DNA 定量显示细胞几乎完全被去除。胶原含量试验和力学强度试验结果表明，脱细胞方法未破坏脱细胞骨基质的成分、力学强度和三维孔隙结构。此外 , 将人类间充质干细胞种植在脱细胞骨基质上，并和人工合成材料 β -TCP 支架对比 , 体外研究脱细胞骨基质的成骨能力。结果表明，脱细胞骨基质能促进间充质干细胞的增殖和成骨分化。甚至脱细胞骨基质在

细胞粘附、增殖和早期成骨分化上比 β-TCP 支架更有优势。所有实验结果表明，猪源性脱细胞骨基质是一种有潜力的骨移植替代物。

【关键词】 脱细胞；猪骨； β-TCP；骨组织工程

Bioinspired Mineralization with Hydroxyapatite and Hierarchical Naturally Aligned Nanofibrillar Cellulose

亓益品　凌均棨　中山大学附属口腔医院

【摘 要】 We used cellulose and a nonclassical mineralization process to fabricate a bioinspired nanohybrid material that exhibited structural features and properties similar to those of human hard tissues. We made a hydrogel with highly compacted and aligned cellulose nanofibers. We thoroughly mineralized the cellulose hydrogel with hydroxyapatite nanocrystals, using poly(acrylic acid) as a soluble template for precursor minerals, which infiltrated the nanocompartments of the aligned cellulose nanofiber network. The ultrastructure and mechanical properties of the mineralized gels were strikingly similar to those of bone and dentin, which supports further use of cellulose-based fibrillary materials as affordable, biocompatible scaffolds for repair and regeneration of hard tissues. The versatility of the bioinspired mineralization processes used here can broaden the applications of these cellulosic nanohybrids.

【关键词】 nanocellulose; biomineralization; hydroxyapatite; biomimetic; dentin

Near-infrared Triggered Titanium Dioxide Nanoparticles with Antibacterial Photodynamic Inactivation against Peri-implantitis-related Pathogens

齐曼霖　吉林大学口腔医学院
王　林　吉林大学口腔学院
周延民　吉林大学口腔医院

【摘 要】 Objectives: The prevalence of peri‐implantitis was in the order of 10% implants and 20% patients during 5-10 years after implantation.[1] Plaque is regarded as the primary role in peri-implantitis occurrence.[2] Therefore, the objectives of this study were to: (1) develop a near-infrared (NIR) light triggered core-shell nanostructure of upconversion nanoparticles and TiO2 (UCNPs@

TiO2), and (2) investigate its inhibitory effects via antibacterial photodynamic therapy (aPDT) against peri-implantitis-related pathogens.

Methods: The core β-NaYF4:Yb3+,Tm3+ were synthesized via thermal decomposition and further modified with the TiO2 shell via a hydrothermal method. The core-shell structure and the upconversion fluorescence-induced aPDT treatment via 980 nm laser were studied. Three peri-implantitis-related pathogens Streptococcus sanguinis (S. sanguinis), Porphyromonas gingivalis (P. gingivalis) and Fusobacterium nucleatum (F. nucleatum) were investigated. The killing activity against planktonic bacteria was detected by a time-kill assay. Single species 4-day biofilms on dentin were tested by live/dead staining, colony-forming units (CFU), and metabolic activity.

Results: The hexagonal shaped UCNPs@TiO2 had an average diameter of 39.7 nm. UCNPs@TiO2 nanoparticles had positively charged (+12.4 mV) surface and were biocompatible and non-cytotoxic. Under the excitation of NIR light (980 nm), the core NaYF4:Yb3+,Tm3+ UCNPs could emit intense ultraviolet (UV) light, which further triggered the aPDT function of the shell TiO2 via energy transfer, thereby realizing the remarkable antibacterial effects against planktons and biofilms of peri-implantitis-associated pathogens. NIR-triggered UCNPs@TiO2 achieved much greater reduction in biofilms than control ($p < 0.05$). Biofilm CFU was reduced by 3-4 orders of magnitude via NIR-triggered aPDT. The killing efficacy of UCNPs@TiO2-based aPDT against the three species was ranked to be: S. sanguinis < F. nucleatum = P. gingivalis. Metabolic activities of biofilms were also greatly reduced via NIR-triggered aPDT ($p < 0.05$).

【关键词】 titanium dioxide; upconversion nanoparticles; antibacterial; near-infrared; photodynamic therapy

去甲二氢愈创木酸对脱矿牙本质基质生物改性的研究

石　鑫　华中科技大学同济医学院附属同济医院

【摘要】 目的：

以戊二醛（Glutaraldehyde，GA）作为阳性对照，探究石炭酸灌木来源的天然儿茶酚抗氧化剂去甲二氢愈创木 (Nordihydroguaiaretic acid，NDGA) 作为交联剂对脱矿牙本质基质进行生物改性的可行性。

方法：

对脱矿牙本质基质生物化学改性的研究，分别采用干燥质量损失和羟脯氨酸释放、表观弹性模量稳定实验、扫描电镜和透射电镜进行评价；而生物机械性能的检测则分别采用膨胀率和原子力显微镜实验；对于交联机制的探讨，分别进行茚三酮实验和傅里叶变换红外光谱检测。

结果：

本研究发现，20mg/ml NDGA 交联 5min 能够显著增加脱矿牙本质基质对胶原酶的酶解耐受力，降低干燥质量损失和羟脯氨酸释放，维持胶原纤维支架结构稳定性。 在改善脱矿牙本质基质机械性能方面，NDGA 显著降低了膨胀率，并分别在宏观水平和纳米水平提高了弹性模量。NDGA 交联牙本质胶原的机制与儿茶酚基团贻贝仿生氧化和邻醌官能团的氧化偶联有关。另外，还可能涉及儿茶酚基与胶原分子间氢键形成，需要进一步深入的研究。

结论：

NDGA 能够作为脱矿牙本质基质的交联剂在提高其胶原酶酶解耐受力的同时，还能改善其机械性能。本研究首次将 NDGA 用于脱矿牙本质基质交联，为贻贝仿生化学在脱矿牙本质基质保护中的效用提供了佐证，为改善牙本质再矿化和提高牙本质 - 树脂粘接耐久性提供了卓越的前景。

【关键词】 牙本质；胶原交联；儿茶酚化合物；去甲二氢愈创木酸；戊二醛

In situ Gas Foaming Based on Magnesium Particle Degradation: A Novel Approach to Fabricate Injectable Macroporous Hydrogels for Improving Tissue Regeneration

唐艳梅　蒋欣泉　上海第九人民医院

【摘 要】 Injectable hydrogels are attractive biomaterials for cell delivery in tissue engineering. However, the in vivo viability of transplanted cells remains limited. Typically, macroporous structures constructed in hydrogels are utilized to enhance nutrients/waste exchange for cell survival and to promote integration between the material and host tissue. A new gas-foaming method to generate pores was proposed by directly adding Mg particles into cell-laden hydrogel solutions, taking advantage of the H2 gas formed during the degradation of Mg. The optimization design of the size and amount of Mg particles added into the hydrogels was investigated in detail, as well as the morphological, mechanical and chemical properties of the porous hydrogels. A series of experiments demonstrated significantly increased cell viability and proliferation in the porous hydrogel groups. Additionally, Mg2+ ions generated during Mg degradation facilitated the osteogenic differentiation of stem cells encapsulated in hydrogels. A preliminary trial to repair bone defects in the distal femoral sites of rats was performed. Extensive vascularized bone regeneration in the defects revealed that the use of Mg particles as the foaming agent is feasible, endowing injectable hydrogels with optimized porosity and enhanced bioactivity, and providing a new strategy for future designs of porous hydrogels in tissue engineering.

【关键词】 Injectable hydrogel；Magnesium；Cell viability；Vascularized bone regeneration

可变二氧化钛纳米管处理对钛骨结合的影响

徐晓旭　南京医科大学附属口腔医院

【摘要】 骨缺损具有较高致残率，近年来为提高骨代替材料移植成功率，促进诱导成骨，许多研究对钛及其合金进行表面改性如阳极氧化，且已证实纳米管修饰后的钛植入物表面具有比传统加工表面更高的粗糙度和润湿性，可加速成骨细胞的粘附和分化，这对骨与植入物表面的直接结合非常重要。在阳极氧化成二氧化钛的纳米管状结构中加入特定元素、药物或聚合物可以给钛提供一定的性能，但这些技术受药物载药量和释放速率的限制，无法长期保持植入物周围的药物浓度，为改善钛骨结合效果，本项目拟将京尼平交联壳聚糖形成水凝胶灌注进哑铃型二氧化钛纳米管中，控制水凝胶的释放速率。京尼平交联壳聚糖生成水凝胶可有效抑制细菌黏附，有利于细胞的黏附和增殖，为组织再生提供良好的微环境。本项目拟对样品进行形貌表征测试，研究其与 BMSCs 的细胞学效应。研究结果有助于提高骨代替材料植入的稳定性，为临床骨缺损修复材料提供指导。

【关键词】 骨缺损；二氧化钛纳米管；水凝胶；骨结合

Matrix stiffness regulates arteriovenous differentiation of endothelial progenitor cells during vasculogenesis in nude mice

薛昌越　南京医科大学

赵　丹　四川大学华西口腔医学院

【摘要】 Objectives: The aim of the study was to investigate the effect of matrix stiffness on arteriovenous differentiation of endothelial progenitor cells (EPCs) during vasculogenesis in nude mice.

Materials and methods: Dextran hydrogels of differing stiffnesses were first prepared by controlling the crosslinking reaction to generate different thioether bonds. Hydrogels with stiffnesses matching those of the arterial extracellular matrix and venous extracellular matrix were separately combined with mouse bone marrow‐derived EPCs and subcutaneously implanted on either side of the backs of nude mice. After 14 days, artery‐specific marker Efnb2 and vein‐specific marker Ephb4 in the neovasculature were detected to determine the effect of matrix stiffness on the arteriovenous differentiation of EPCs in vivo.

Results: Fourteen days after the implantation of the EPC‐loaded dextran hydrogels, new blood vessels were observed in both types of hydrogels. We further verified that matrix stiffness regulated the arteriovenous differentiation of EPCs during vasculogenesis via the Ras/Mek pathway. Conclusions: Matrix stiffness regulates the arteriovenous differentiation of EPCs during vasculogenesis in nude mice through the Ras/Mek pathway.

【关键词】 stiffness; endothelial progenitor cells; extracellular matrix; arteriovenous differentiation; Ras/Mek pathway

预构血管通道联合血管束植入增强 3D 打印组织工程骨成骨和血管化的实验研究

杨晓彬　李树祎　周　苗　广州医科大学附属口腔医院

【摘要】 目的：研发预构仿生血管通道支架并研究其成骨和血管化的促进作用以及联合血管束植入的方式异位促进成骨和血管化的效果。

方法：采用医学计算机辅助设计与制作软件 3-matic 设计含仿生血管通道结构的支架模型，并采用自动注浆技术制作 10mm×8mm×6mm 的预构血管通道 TCP 支架（Channeled scaffold）和普通支架（Scaffold），体外实验评价其性能，新西兰兔动物模型研究其成骨和成血管化效果，采用明胶包裹技术将 rhBMP-2 复合于支架上。将实验分组为不含血管通道组 (Scaffold 组)、含血管通道组 (Channeled scaffold 组)、植入末端结扎的血管束组 (Channeled scaffold+LVB 组)、植入保持血流顺畅的血管束组 (Channeled scaffold+FVB 组)，以及预构血管通道联合血管束植入的成骨成血管化效果。

结果： HUVEC 在 Channeled scaffold 上比 Scaffold 增殖更多（$P < 0.001$）。各组支架在植入 2 周后即表现出一定的血管化，4 周时各组血管化进一步提升，Micro-CT 和组织学统计分析显示在成血管方面，Channeled scaffold+FVB > Channeled scaffold+LVB > Channeled scaffold > Scaffold。在通道结构中观察到了血管生长引导现象，由于血管化对成骨的促进作用，在成骨量上也表现为 Channeled scaffold+FVB > Channeled scaffold+LVB > Channeled scaffold > Scaffold。

结论：预构含仿生血管通道 TCP 支架具有较好的结构和力学性能，能满足骨组织工程支架材料的需要，HUVEC 在快速黏附在其上并能实现更快的增殖，联合血管束植入有助于提升 3D 打印 TCP 支架的血管化和成骨效果，其血管通道结构有助于引导血管从外向内、从内向外快速生长而实现整个支架的全面血管化，复合 rhBMP-2 后能异位成骨，为当前组织工程领域和颌骨再生领域解决大面积骨缺损修复提供一种思路。

【关键词】 3D 打印；仿生血管通道；血管束；血管化；成骨

A DNA-based Nanomedicine with Targeting and Enhanced Therapeutic Efficacy of Cancer Cells

战雨汐　四川大学华西口腔医院

【摘要】 Recently, a DNA tetrahedron has been reported to be a novel nanomedicine and a promising drug vector because of its compactness, biocompatibility, biosafety, and editability. Here, we modified the DNA tetrahedron with a DNA aptamer (AS1411) as a DNA-based delivery system, which could bind to nucleolin for its cancer cell selectivity. Nucleolin is a specific biomarker protein overexpressed on membranes of malignant cancer cells and its deregulation is implicated in cell proliferation. The antimetabolite drug 5-fluorouracil (5-FU) is an extensively used anticancer agent, however, its major limitation is the lack of target specificity. Cyanine 5 (Cy5), a fluorescent probe, can be used to label DNA tetrahedron and enhance photostability with minimal effects on its basic functions. In this study, we additionally attached 5-FU to the DNA-based delivery system as a new tumor-targeting nanomedicine (AS1411-T-5-FU) to enhance the therapeutic efficacy and targeting of breast cancer. We examined the difference of cellular uptake of AS1411-T-5-FU between breast cancer cells and normal breast cells and concluded that AS1411-T-5-FU had a better targeting ability to kill breast cancer cells than 5-FU. We further evaluated the expressions of cell apoptosis-related proteins and genes, which are associated with the mitochondrial apoptotic pathway. Ultimately, our results suggest the potential of DNA tetrahedron in cancer therapies and we develop a novel approach to endow 5-FU with targeting property.

【关键词】 5-FU; AS1411; DNA tetrahedron; cell apoptosis; breast cancer

GNPs/SF 定点耦合控释气凝胶在骨质疏松下的成骨效能评价

李帝泽　陈　陶　季　平　重庆医科大学附属口腔医院

【摘要】 目的：本研究将雷奈酸锶（SR）加载于明胶纳米球 (GNPs)/ 丝素蛋白 (SF) 复合气凝胶中，并通过酪氨酸酶（MT）/ 乙醇进行次序交联以形成具有微 - 纳米分级仿生的三维网络结构，并通过体内和体外实验评价其骨质疏松状态下的成骨效能。

材料与方法：GNPs 和 SF 混合后通过 MT 进行酶促次序交联。观察材料表面结构，检测定点交联效率和压缩强度，溶胀率，降解行为以及药物释放，并进行元素分析以及生物矿化行为观察。MC3T3-E1 和 SD 大鼠颅顶骨缺损模型用于体外和体内验证。

结果：茚三酮实验和同步荧光光谱证实 MT 定点耦合的高效性和稳定性；交联后材料表面新貌致密，压缩强度提升 缓释作用与体外模拟矿化加强。SEM 和 qRT-PCR 显示细胞粘附和成骨标志物表达的增强。OVX 大鼠在植入 8W 可以达到骨缺损面积 95% 的新骨覆盖率，Runx2 免疫荧光显示出载药缓释组对成骨的促进作用，TRAP 信号减弱。

结论：负载 SR 的 GNPs/SF 控释系统能够优化其释药行为，使力学性能大幅提升，并进一步提升药物缓释作用。该复合体系在体外和体内实验中均体现出良好的骨生成作用，是一种针对骨质疏松患者群体骨缺损的理想替代修复材料。

【关键词】 骨质疏松；骨生成；雷奈酸锶；次序交联；明胶纳米颗粒

实时响应血糖的壳聚糖载药体系应用于高糖环境下颌骨缺损治疗的研究

肖　宇　包崇云　四川大学华西口腔医院

【摘要】 引言：糖尿病患者的颌骨缺损修复一直是临床亟待解决的难题。本研究拟将血糖响应释药体系与骨组织工程支架相结合，为高血糖环境下颌骨缺损修复治疗提供一个新思路。

材料与方法：本研究首先利用同轴电纺技术制备出载 rhBMP2 的核 - 壳结构电纺纤维膜，随后通过化学接枝的方式将葡萄糖氧化酶固定在壳表面赋予其血糖响应的特性。接下来，本研究通过以下方法对其性质进行考察：a) 考察纤维在不同浓度的葡萄糖溶液中直径变化以及释药情况；b) 利用免疫荧光技术观察成骨相关基因 OCN 的表达并同时定量考察材料对于 OCN、OPN 以及 RUNX2 的表达情况 ;c) 成功构建出糖尿病大鼠颌骨缺损模型，并将材料植入缺损处，通过 X- 射线探测，组织学以及免疫组化等方法对其体内骨形成效果进行评价。

结果：1. 本研究首先成功得到一种核 - 壳结构交联电纺纤维；2. 该材料具备良好的实时响应血糖及控释药物的能力，同时，在高血糖环境下能够有效促进 BMSCs 向成骨细胞分化；3. 动物实验证实该材料能够提升糖尿病大鼠的颌骨缺损修复效果 ;

结论：该体系为高血糖环境下颌骨缺损修复的治疗提供了一种新思路。未来的研究将结合临床实际对材料的制备工艺进行不断优化，使其能够早日在临床上得到应用。

【关键词】 血糖敏感水凝胶，颌骨缺损修复， 药物控释，核 - 壳结构电纺纤维

口腔公共卫生

我国成年人口腔疾病卫生支出的公平性分析

程梦琳　首都医科大学附属北京友谊医院
司　燕　北京大学口腔医院

【摘要】 目的：了解我国成年人口腔疾病医疗支出筹资公平性，为成年人口腔疾病防治提供卫生经济学参考。方法：使用我国第三、四次全国口腔健康流行病学调查数据，根据家庭人均年收入五分类进行定性分析，应用 Kakwani 指数定量分析筹资累进性，使用泰尔指数分析地区因素上的公平及十年前后我国成年人口腔医疗支出的变化。结果：十年前后我国成年人口腔疾病医疗支出持续表现为个人现金支出的累退性，十年后老年人筹资累退更明显，对 35-44 岁青年人 Kakwani 指数从 -0.295 下降至 -0.301，对于 65-74 岁老年人则从 -0.274 下降至 -0.324；从随收入水平上升，累积口腔医疗支出占累积收入的比例越低，低收入人群面临更高经济风险。在地区因素上，两年龄组十年后总泰尔指数增加。对于青年人，不公平更多来源于区域内，对于老年人区域间不平衡对于筹资不公平的贡献上升。结论：我国成年人口腔医疗支出个人现金筹资途径累退性明显，地区因素造成的不公平性增加，可能与区域内、区域间的经济发展与资源配置不平衡相关。

【关键词】 成年人；口腔疾病医疗支出；公平性分析

口腔健康与全身健康

EZH2 在牙髓炎症中的表达及其对巨噬细胞趋化作用的影响

陈颖怡　刘　鹤　北京大学口腔医学院

【摘要】 目的：探讨表观遗传调控子 Enhancer of Zeste Homolog 2 (EZH2) 在牙髓炎症过程中的表达变化及其对单核巨噬细胞的趋化作用。

方法：以 10mg/ml 脂多糖（LPS）刺激大鼠牙髓，建立大鼠牙髓炎症模型。采用免疫组织化学的方法检测牙髓中 EZH2 的表达变化。利用 CCK-8 细胞增殖 - 毒性试剂盒检测不同浓度（1、10、20、40、100ng/ml）EZH2 重组蛋白对人牙髓细胞（hDPCs）及人单核细胞系 THP-1 细胞增殖的影响。采用 Transwell 迁移实验检测 EZH2 重组蛋白处理的 hDPCs 的上清液对 THP-1 细胞迁

移作用的影响。

结果：在 LPS 诱导牙髓炎症 8 小时内 EZH2 表达下降，但在刺激 1、3、7 天后，随着刺激时间的延长 EZH2 表达逐步上调。CCK-8 结果提示：EZH2 重组蛋白刺激 hDPCs 及 THP-1 细胞的适宜浓度为 20ng/ml。加入 EZH2 重组蛋白刺激 hDPCs 后的上清液与对照组上清液相比可以显著促进巨噬细胞趋化。

结论：EZH2 参与了牙髓炎症发展过程，并促进巨噬细胞的趋化，提示 EZH2 在牙髓炎症发展过程中有重要调控作用。

【关键词】 EZH2；牙髓炎；表观遗传；巨噬细胞

炎症微环境下 miR-140-5p 靶向作用 Smad3 影响软骨细胞生物学特性的机制研究

李伟豪　昆明医科大学附属口腔医院

李　松　昆明医科大学

【摘要】 颞下颌关节骨关节炎发病率高，对人体危害大，严重影响了患者的生活质量。其病因机制复杂且尚缺乏认识。以往的研究表明，miR-140-5p 在软骨细胞分化和软骨内稳态过程中发挥着重要的作用，miR-140-5p 基因敲除鼠会出现增龄性骨关节炎的症状。然而，有关 miR-140-5p 在 OA 不同阶段的表达作用仍存在争议。深入阐明是 miR-140-5p 在颞下颌关节骨关节炎中的作用机制，将为临床早期诊治奠定基础。

【关键词】 小 RNAs；转化生长因子 -β；颞下颌关节骨关节炎；软骨形成

三叉神经节内 P2Y14 受体对颌面部实验性炎症疼痛调控的研究

林　赳　沈颉飞　四川大学华西口腔医（学）院

【摘要】 目的：三叉神经节（TG）内神经元细胞（TGNs）和卫星胶质细胞（SGCs）之间的交互对话机制在口腔颌面部疼痛中发挥重要作用，P2 受体介导的促炎症因子在疼痛中的作用备受关注，研究表明 P2Y14 受体（P2Y14R）调节脊髓内小胶质细胞（Microglia）的活化，参与坐骨神经损伤性疼痛的发展。本课题旨在探究 P2Y 受体家族中 P2Y14R 在 TG 内调控口腔颌面部炎症性疼痛的作用，及其调控 SGCs 表达 IL-1β、CCL2 的机制研究。

方法：组织免疫荧光明确 P2Y14R 在 TG 内的定位。全弗式佐剂构建颌面部炎症模型，

Western Blot 检测 P2Y14R 和 SGCs 活化标志物 GFAP 蛋白表达；炎症模型大鼠 TG 内注射 PPTN 干预，Von Frey 法检测疼痛阈值变化，Western Blot 检测 TG 内 IL-1β、CCL2 表达。体外纯化培养 TG 内 SGCs，细胞免疫荧光研究 P2Y14R 在 SGCs 上的定位。应用药物作用于 SGCs（P2Y14R 特异性激活剂和阻滞剂，MAPK 通路阻滞剂），q-PCR 和 ELISA 检测 IL-1β、CCL2 表达，Western Blot 检测 GFAP 表达和 MAPK 通路中 ERK、P38、JNK 磷酸化水平。

结果：①免疫荧光证明 P2Y14R 定位在 TG 内 TGNs 和 SGCs。② 颌面部实验性炎症模型中，TG 内 P2Y14R、GFAP、IL-1β、CCL2 表达迅速显著升高，颌面部疼痛阈值显著降低。④ TG 内注射 PPTN，显著升高术后颌面部疼痛阈值，显著降低 GFAP、IL-1β、CCL2 表达。⑤ 纯化培养的 SGCs 细胞膜上表达 P2Y14R，该受体活化促进 IL-1β、CCL2 分泌，显著升高胞内 ERK、P38、JNK 磷酸化。⑥ P2Y14R、ERK、P38 参与 IL-1β、CCL2 分泌。

结论： P2Y14R 在 TG 内 TGNs 和 SGCs 上表达，参与调控颌面部炎症性疼痛发展，参与调控 TG 内促疼痛炎症因子表达、SGCs 活化。细胞实验证明 P2Y14R 通过 ERK 和 P38 通路调控 IL-1β、CCL2 表达。P2Y14R 有望成为三叉神经相关性疼痛的治疗靶点之一。

【关键词】 颌面部炎症；疼痛；三叉神经节；卫星胶质细胞；P2Y14 受体

Gas6 在 Pg-LPS 诱导内皮细胞诱导内皮 - 单核细胞黏附中的作用

刘颖君　王雪奎　安　娜　北京大学口腔医院

心血管疾病具有较高的患病率和致死率，动脉粥样硬化是其重要的病理基础，内皮功能紊乱被认为是动脉粥样硬化的始动因素，受损的内皮细胞表达多种黏附分子、趋化因子等，促进局部单核细胞浸润，由此开始动脉粥样硬化病变的发生。

牙周炎在我国成年人中患病率很高，多项大样本横断面及纵向流行病学研究显示，牙周炎症可能是动脉粥样硬化的相关危险因素。牙龈卟啉单胞菌（Porphyromonas gingivalis，Pg）是公认的牙周致病菌之一，有研究报道 Pg-LPS 刺激内皮细胞后可引起黏附分子及趋化因子高表达，提示 Pg-LPS 可能促进了动脉粥样硬化的形成。

Gas6 具有广泛的生物学效应，有研究显示 Gas6 及其受体 TAM 在树突状细胞、单核细胞中可以抑制 LPS 引起的炎性因子表达，在炎症消退中起关键作用，是先天免疫的多效抑制剂，但 Gas6 在内皮细胞受到 Pg-LPS 刺激的过程中类似的抑制作用未见报道。

本研究发现 Pg-LPS 刺激内皮细胞后 Gas6 及其受体 Axl、Mer 表达下调，Gas6 在 Pg-LPS 引起内皮细胞损伤过程中起到负向调控作用，抑制 P.g-LPS 诱导的 HUVECs 和 THP-1 细胞黏附，NF-κB 通路和 Akt 通路可能参与这一过程。Gas6 或许可以成为预防动脉粥样硬化的调控因子。

【关键词】 HUVEC；牙龈卟啉单胞菌 LPS；Gas6；内皮功能紊乱

Neuronal Death Related to Porphyromonas gingivalis and Stimulated Microglia: a vitro study

吕慧欣　周延民　于维先　吉林大学口腔医院

【摘要】 Abstract

Background Chronic bactierial systemic inflammation could play an important part in affecting nerve cells to cause inflammation and cell death. Chronic periodontitis related with Porphyromonas gingivalis could result in some types of systemic diseases such as diabetes etc. We aim to find the influence of Porphyromonas gingivalis and its LPS to nerve cells.

Methods We assumpted several influence factors that may have effect on neuron, including P.g(the ratio was 100:1), P.g LPS(the concentration were 1 μg/ml, 5 μg/ml, 10 μg/ml, 15 μg/m, 20 μg/ml), the conditioned medium from P.g-stimulated microglia(100:1) and that from P.g LPS-stimulated microglia(5 μg/ml, 10 μg/ml). We treated primary neuron with the above contents and their control medium for 24h, 48h and 72h, and then observed the changes of microglia and neuron. Levels of inflammatory factors from microglia were measured by Enzyme-Linked Immunosorbent Assay (ELISA), immunocytochemistry and NO assay kit. The number of neuron was measured with Cell Counting Kit-8(CCK-8) and flow cytometry(FC).

Results The number of neuron cells decreased after infected by P.g(100:1) at 24h and all conditioned medium from stimulated microglia at 48h. However, P.g LPS failed to damage neuron with all the concentrations in our study. Phosphorylated p38 MAPK in stimulated microglia was observed intracellularly at 48h. At the same time, we detected inflammatory cytokines, tumor necrosis factor-α (TNF-α), interleukin-6(IL-6), NO were up-regulated in the supernate from the medium of activated microglia,but interleukin-1β (IL-1β) was unchanged.

Conclusion These results suggested P.g itself, P.g-stimulated microglia and P.g LPS-stimulated microglia could cause neuronal death. However, LPS itself may be non-toxic to neuron.

【关键词】 Porphyromonas gingivalis; LPS; microglia; neuron; cell death

Improvement of the mechanical, tribological and antibacterial properties of glass ionomer cements by fluorinated graphene

孙　莉　兰州大学口腔医院

【摘要】 Objective. The aim of this study was to improve the mechanical properties, wear resistance and antibacterial properties of conventional glass ionomer cements (GICs) by fluorinated graphene (FG), under the premise of not influencing their solubility and fluoride ion releasing property.

Materials and methods. FG with bright white color was prepared using graphene oxide by a hydrothermal reaction. Experimental modified GICs was prepared by adding FG to the traditional GICs powder with four different weight ratios (0.5 wt%, 1 wt%, 2 wt% and 4 wt%) using mechanical blending. Compressive and flexural strength of each experimental and control group materials were investigated using a universal testing machine. The Vickers microhardness of all the specimens was measured by a Vicker microhardness tester. For tribological properties of the composites, specimens of each group were investigated by high-speed reciprocating friction tester. Fluoride ion releasing was measured by fluoride ion selective electrode methods. The antibacterial effect of GICs/FG composites on selected bacteria (Staphylococci aureus and Streptococcus mutans) was tested with pellicle sticking method.

Results. The prepared GICs/FG composites with white color were successfully fabricated. Increase of Vickers microhardness and compressive strength and decrease of friction coefficient of the GICs/FG composites were achieved compared to unreinforced materials. The colony count against S. aureus and S. mutans decreased with the increase of the content of FG. And the antibacterial rate of S. mutans can be up to 85.27% when the FG content was 4 wt%. Additionally, fluoride ion releasing property and solubility did not show significant differences between unreinforced and FG reinforced GICs.

Significance. Adding FG to traditional GICs could not only improve mechanical and tribological properties of the composites, but also improve their antibacterial properties. In addition, the GICs/FG composites had no negative effect on the color, solubility and fluoride ion releasing properties, which will open up new roads for the application of dental materials.

【关键词】 Fluorinated graphene; Glass ionomer cements; Mechanical strength; Antibacterial property

受损成牙本质细胞来源外泌体在抵御相邻细胞凋亡中的研究

王海胜　张　露　珞瑜路 237 号武汉大学口腔医学院

【摘要】 目的：龋病所致炎症刺激下，成牙本质细胞生存能力是牙髓良好预后的关键。本研究探讨了受损程度不同的成牙本质细胞之间，外泌体介导的细胞间通讯在抗凋亡中的作用。

材料与方法：①免疫组织化学（IHC）检测人牙髓健康组及龋病组标本中 TNF-α（炎症因子），CD63（外泌体标记物）及 Caspase-3（细胞凋亡）的表达；②利用梯度浓度脂多糖（LPS）刺激，构建体外成牙本质样细胞（矿化诱导 7 天后人牙乳头干细胞，M-hSCAP）差异化损伤（CCK-8 检测）模型，即 LPS 轻度影响成牙本质样细胞（MLM-hSCAP，1 μg/ml LPS 刺激 3 天），LPS 重度影响成牙本质样细胞（SLM-hSCAP，20 μg/ml LPS 刺激 3 天）；③超速离心法提取 SLM-hSCAP 上清外泌体（s-Exo），通过尺寸（粒径分析）、形态（扫描电镜）及表面标记物检测（CD9，CD63，CD81）鉴定；④ 10 μg/ml s-Exo 处理 M-hSCAP 及 MLM-hSCAP，检测抗凋亡能力（CCK-8，Casp-3 及 Survivin 表达）；⑤利用外泌体膜染料（PKH26）及外泌体摄取抑制剂（CPZ）研究外泌体摄取对其抗凋亡作用的影响。

结果：① IHC 显示牙髓炎症分布与龋病影响范围密切相关，近龋处炎症水平高，细胞凋亡明显，CD63 表达高；远龋处炎症水平低，细胞凋亡少，CD63 表达低；② s-Exo（5 μg/ml，10 μg/ml）不引起细胞活性降低及凋亡发生；③利用 s-Exo 与 MLM-hSCAP 共培养，显著降低 MLM-hSCAP 细胞凋亡；④荧光标记 s-Exo 后可见其被 MLM-hSCAP 摄取入胞，阻断摄取过程可抑制 s-Exo 在 MLM-hSCAP 中的抗凋亡作用。

结论：高浓度 LPS 刺激 M-hSCAP 所得外泌体可以通过其介导的细胞间相互作用，显著抑制低浓度 LPS 刺激 M-hSCAP 的细胞凋亡。

【关键词】 成牙本质细胞；外泌体；细胞凋亡；龋病；牙髓炎

关于牙周炎诱导软脑膜炎症反应的研究

王　鹞　于维先　周延民　吉林大学口腔医院

【摘要】 目的 探究慢性牙周炎对软脑膜炎症反应的上调及内在机制，并寻找潜在的治疗方法

材料与方法 我们使用牙周炎的主要致病菌 -- 牙龈卟啉单胞菌（ Porphyromonas Gingivalis PG）刺激小鼠巨噬细胞 RAW264.7。24 小时后用流式细胞术和 Elisa 试剂盒检测 TLR2、TNF-α以及 IL-6 水平。收集巨噬细胞上清滤液（SR）刺激软脑膜细胞，作为实验组。同时设立抑制剂组 -- 在用 SR 刺激前，使用 JAK2 抑制剂 AG490（50 μg/ml）孵育 12h。为排除残留在 SR 里的细菌代

谢产物对软脑膜细胞的影响，我们还设立了阴性对照组（将细菌放入无细胞培养基，24 小时后过滤除菌，以滤液孵育软脑膜细胞）。6 小时后，用 qRT-PCR 评价细胞炎性因子水平。最后 , 使用抑制天然植物提取物 -- 松柏醛（CA）在刺激软脑膜细胞前对细胞进行孵育，并通过 qRT-PCR 评测 CA 对软脑膜细胞炎性应答的影响。结果 流式细胞术和 Elisa 检测证明牙龈卟啉单胞菌能上调 RAW264.7 的炎性反应并促使其释放炎性因子，且 AG490 能抑制这种上调作用。qRT-PCR 证明活化后的巨噬细胞分泌物能介导软脑膜细胞炎性因子的上调，且 AG490 和 CA 均能抑制这种介导作用，且 CA 的抑制作用与其浓度呈现正相关。结论 通过体外实验我们证明，PG 可通过 JAK2 通路间接诱导软脑膜的炎性应答，且松柏醛对这种诱导作用有明显的抑制功效。

【关键词】 牙周炎；牙龈卟啉单胞菌；软脑膜；JAK2；松柏醛

Porphyromonas gingivalis induces depression via downregulating p75NTR-mediated BDNF maturation in astrocytes

王艺羲　中山大学附属口腔医院

【摘要】 Many cross-sectional epidemiological studies have shown the incidence of periodontitis is positive correlated with that of depression. However, their causal relationship and underlying mechanism are largely unknown. Porphyromonas gingivalis (Pg) is the main pathogen for periodontitis. Employing female mice treated with Pg every other day for 4 weeks, we found that Pg-mice showed obvious depression-like behavior, an increased number of activated astrocytes and decreased levels of mature brain derived neurotrophic factor (BDNF) and astrocytic p75NTR in the hippocampus. Both hippocampal injection of BDNF and overexpression of p75NTR in astrocytes alleviated Pg-induced depression-like behavior in mice. Moreover, Pg-lipopolysaccharides (LPS) generated similar phenotypes, which were reversed by the TLR-4 inhibitor TAK242. Our results suggest that Pg-LPS decreases the level of astrocytic p75NTR and then downregulates BDNF maturation, leading to depression-like behavior in mice. Our study provides the first evidence that Pg is a modifiable risk factor for depression and uncovers a novel therapeutic target for the treatment of depression.

【关键词】 Porphyromonas gingivalis; periodontitis; depression; astrocyte; p75NTR

复合树脂氧化锆填料与树脂基质结合的提高——纳米氢氧化锆的包裹和磷酸酯单体的调节

吴欣祎　陈　晨　江苏省口腔医院

【摘要】 目的：无机填料对复合树脂的机械性能有决定性作用，氧化锆填料目前尚缺乏适当的表面处理方法，限制了增强效果。本课题拟分析复合树脂氧化锆填料表面前期包裹碱性氢氧化锆和 / 或磷酸酯单体 MDP 处理对氧化锆填料与 Bis-GMA 树脂基质结合后相应牙科复合树脂的机械性能的增强效果并解释相关机理。方法：制备纳米氢氧化锆包裹的氧化锆填料通过透射电镜 (TEM), 红外光谱 (FTIR), 和 X 射线光电子能谱 (XPS) 观察和分析氧化锆表面的氢氧化锆包裹情况。制备含纳米氢氧化锆包裹的氧化锆填料并经 10-MDP 进行填料表面处理的复合树脂，通过测试三点抗弯强度和弹性模量以及 Weibull 分析评价复合树脂机械性能。结果：TEM，FTIR 和 XPS 分析证实了 Zr(OH)4 的包裹以及包裹后羟基的增加。XPS 分析发现 10-MDP 表面处理的 Zr(OH)4 包裹氧化锆填料中 Zr-O-P 键的含量最高。添加经 10-MDP 表面处理的表面包裹 Zr(OH)4 的氧化锆填料的复合树脂，可表现出较高的三点抗弯强度、弹性模量。结论：氧化锆填料表面进行磷酸酯单体调节，并结合前期包裹纳米氢氧化锆可以提高复合树脂的机械性能。

【关键词】 复合树脂；磷酸酯单体；氧化锆填料；机械性能

主穹隆蛋白（MVP）调控破骨细胞的作用机制研究

袁礼婵　赵　娜　南京医科大学附属口腔医院

【摘要】 目的：建立主穹隆蛋白（MVP）基因敲除的小鼠模型，探究 MVP 调控破骨细胞的作用机制。

材料方法：建立 MVP 全基因敲除小鼠（MVP-/-，KO）和 MVP 骨髓单核细胞系特异性敲除小鼠（MVPf/fLysM-Cre，f/f/ △），以同窝野生型（MVPf/f，WT）为对照组。Micro-CT、组织化学染色等观测体内骨组织形态的变化。细胞化学染色等观测体外破骨细胞细胞骨架、骨吸收功能的改变。RT-qPCR、Western Blot、基因测序、Co-IP 等探讨 MVP 调控破骨细胞的分子机制。

结果：MVP 在骨改建活跃的骨肉瘤、骨巨细胞瘤中高表达，提示 MVP 和破骨细胞间存在潜在联系。Micro-CT 示，KO 小鼠股骨骨量下降。骨组织三色染色、TRAP 染色、钙黄绿素 - 茜素红体内荧光标记等示 KO 组成骨细胞无明显变化，破骨细胞功能增强。由此推断 MVP 主要通过影响破骨细胞调控骨改建。采用 MVP 骨髓单核细胞系特异性敲除小鼠（CKO）深入探究。Micro-CT 及 HE 染色示，CKO 小鼠同样呈现骨质疏松的骨表型。体外破骨细胞染色示，CKO 组破骨细

胞体积大，细胞核数量多，肌动蛋白环更加完整，骨吸收功能更强，破骨细胞调节基因（c-Fos，NFATc1，Pu.1）和功能基因（Ctsk）的 RNA 及蛋白水平皆增高。Co-IP 及免疫荧光染色证明，MVP 通过调控 NFATc1 入核而影响破骨细胞的分化及功能。

结论：主穹隆蛋白（MVP）是破骨细胞生成中的关键负调控因子，在骨重塑中扮演重要角色。

【关键词】 骨重塑；主穹隆蛋白；破骨细胞；NFATc1

MicroRNA-1 affects the development of the neural crest and craniofacial skeleton via Bcl-2

赵　娜　Qin Wenhao　南京医科大学附属口腔医院

【摘要】 The neural crest (NC) is one of the key features of craniofacial development. MicroRNA-1 (miR-1), is one of the single-strand non-coding RNAs, which plays an important role in embryonic development. However, the function of miR-1 in neural crest cells (NCCs) is unknown. We reported for the first time that homozygous zebrafish lacking miR-1 exhibited developmental defects in craniofacial bone and heart. The defect may be caused by an increase of apoptosis of NCCs during migration and differentiation of embryo development. Meanwhile, the results in vitro demonstrates that this effect is modulated via Bcl-2 expression in mitochondrial apoptosis pathway. Furthermore, TargetScan analysis showed that Bcl-2 may be a target gene for miR-1. In conclusion, miR-1 can down-regulate the mitochondrial apoptosis pathway via Bcl-2. This suggests that miR-1 in NCCs is essential for craniofacial development.

【关键词】 miR-1；Bcl-2；neural crest；apoptosis, zebrafish.

牙周健康成年人上颌腭侧咀嚼粘膜厚度的 CBCT 测量分析

刘玲玲　烟台市口腔医院

【摘要】 目的：应用 CBCT 测量牙周健康成年人上颌腭侧咀嚼粘膜厚度 Thickness of Palatal Masticatory Mucosa (TPMM)，以丰富上颌腭侧咀嚼黏膜厚度解剖学数据库，为上皮下结缔组织移植术中供区选择提供理论依据。方法：在 CBCT 图像上，距离龈缘 2mm、5mm、8mm、12mm 水平处，分别测量上颌双侧尖牙区至磨牙区的咀嚼粘膜厚度。采用 SPSS 19.0 统计软件进行分析。结果：60 名牙周健康的成年人上颌腭侧咀嚼粘膜平均厚度是 3.5±1.1mm。腭侧咀嚼粘膜厚度在尖牙区、第一前磨牙区、第二前磨牙区、第一磨牙区、第二磨牙区分别是 3.29±0.84mm、3.58±0.79mm、3.55±0.95mm、3.38±0.88mm、3.57±1.49mm。多数牙位腭侧咀嚼粘膜厚度在不同腭穹窿形态之

间无统计学差异（p>0.05）。结论：尖牙至第二前磨牙区是软组织移植最合适的供区位置，但要注意避免损伤腭大神经血管束。

【关键词】 锥形束 CT；腭侧咀嚼粘膜；结缔组织移植

颌面重症间隙感染的规范化治疗

牛　强　空军军医大学口腔医院

【摘要】 口腔颌面部间隙感染 : 是发生于颜面、颌周、口咽部潜在筋膜间隙的化脓性炎症。其发病特点为：起病急、病情重、易反复，属于急重症。我科对于近 3 年间隙感染进行总结，制定了相关的治疗规范，使间隙感染的治疗流程化、精准化，显著提升了治疗质量。

【关键词】 间隙感染

肥胖及脂代谢相关基因对口腔鳞癌预后的影响研究

彭建敏　夏　娟　程　斌　中山大学附属口腔医院

【摘要】 目的：肥胖是多种肿瘤预后的危险因素，但它对口腔鳞状细胞癌（OSCC）的影响目前仍具争议。本研究旨在探究肥胖对 OSCC 患者预后的影响，以及脂代谢相关基因在 OSCC 中的表达及其预后意义。

方法：回顾性分析 576 例 T1/2N0M0 期 OSCC 患者，根据患者的 BMI 指数分组，采用单因素和多因素分析比较不同组间的无进展生存期（PFS）和疾病特异生存期（DSS）。其次，采用倾向性评分匹配（PSM）均衡组间混杂因素后，进一步比较患者预后。通过 GEO 及 TCGA 数据库探究脂代谢相关基因在 OSCC 中的表达及其预后意义。

结果：在单因素分析中，肥胖组和正常体重组患者的五年无进展生存率分别为 70.3% 和 78.5%，肥胖患者更容易发生疾病进展（P=0.023）；肥胖组和正常体重组的五年生存率分别为 60.3% 和 80.7%，肥胖患者的生存率显著更低（P=0.047）。多因素分析结果表明，肥胖是 OSCC 患者疾病进展（HR=2.016，P=0.023）及因肿瘤死亡（HR=2.022，P=0.038）的独立危险因素。在 PSM 队列中，结果进一步证实肥胖与 OSCC 患者的疾病进展（HR=4.612，P=0.008）及因肿瘤死亡（HR=3.848，P=0.036）显著相关。并且，脂代谢相关基因在 OSCC 中表达失调，其中，TGFB1、SPP1 和 SERPINE1 三个基因可以作为生物标志物用于提示患者预后。

结论：肥胖与早期 OSCC 患者的不良预后相关；脂代谢相关基因 TGFB1、SPP1 和 SERPINE1 可以作为生物标志物用于提示患者预后。

【关键词】 肥胖；口腔鳞癌；脂代谢相关基因；预后

Effects of type 2 diabetes mellitus and chronic periodontitis on Th1/Th2 and Th17/Treg paradigm

王 佳 晓涛陈 新疆维吾尔自治区人民医院

【摘要】 Objective: Recent studies have indicated that the chronic low‐grade inflammation induced by chronic periodontitis(CP) is related to type 2 diabetes mellitus(T2DM). The purpose of this study is to determine the main effects, and interactive effect, of T2DM and CP patients' Th1/Th2 and Th17/Treg paradigm.

Methods: A case-control design was employed and used a 2 × 2 factorial analysis of variance to determine the effects of T2DM and CP on Th1/Th2 and Th17/Treg paradigm. The study population comprised a total of 107 individuals, stratified into: 43 with type 2 diabetes and chronic periodontitis (T2DM + CP), 20 with chronic periodontitis (CP) , 23 with type 2 diabetes (T2DM) and 21 controls. We investigated the proportions of Th1/Th2/Th17/Treg cells and analyzed the main effects and interaction of T2DM and CP.

Results: There was a significant main effect of CP, but not T2DM, on patients’ Th1 cells in that those who were categorized as CP had significantly increased Th1 cells (F = 18.127; P = .000). Further, the main effect values of Th17/Treg for CP and T2DM were both significant (CP:F=7.920; P= .006; T2DM:F = 45.384; P = .000). Additionally, there was a significant ""T2DM x CP"" interaction effect on Th2,Th17,Treg and Th1/Th2 (Th2: F=6.251, P= .013; Th17: F=6.251, P= .013 ; Treg: F=6.251, P= .013.and Th1/Th2 : F=6.251, P= .013).

Conclusions: There is an interaction effect in the Th2, Th17, Treg and Th1/Th2 cells between T2DM and CP, which may contribute to the enhanced immune activation and inflammation, and subsequent development and progression of T2DM and CP. These findings may provide one new approach to the underlying mechanisms of the bidirectional relationship of T2DM and CP.

【关键词】 Diabetes mellitus; Chronic periodontitis; interaction; Th cell

Clinical analysis of patients with acute oral and maxillofacial infections

王　哲　Department of Oral Emergency, Peking University School and Hospital of Stomatology

【摘要】 ABSTRACT Objective: To analyze the composition、incidence and clinical characteristics of acute oral and maxillofacial infection in dental emergency. Methods: A comprehensive review of patients with acute oral and maxillofacial infection who visited the Department of Emergency in Peking University School and Hospital of Stomatology from January, 2016 to December, 2018 was performed based on the electronic medical record database. The basic information of the patients was collected. Through retrospective analysis, general characteristics such as disease composition、gender、age distribution and position of involved teeth were counted. RESULTS: A total of 8251 patients with acute oral and maxillofacial infection were finally analyzed, including 4364 male patients (52.8%) and 3887 female patients (47.1%), with a male to female ration of 1.67:1, showing statistical difference (P<0.01). The common diseases occurring in oral and maxillofacial regions were periodontal abscess (3792 cases, 46.0%)、alveolar abscess (3546 cases, 43.0%)、oral and maxillofacial space infection (739 cases, 9.0%)、sialadenitis (108 cases, 1.3%)、furuncle & carbuncle (56 cases, 0.7%) and osteomyelitis of jaws (10 cases, 0.1%). Different diseases were more likely to occur in different genders: male patients were more easily affected by periodontal abscess、space infection and furuncle& carbuncle than female patients with the gender ratios 1.24:1、1.26:1、2.5:1 individually, showing statistical differences (P<0.01) while the incidence of alveolar abscess and sialadenitis had no significant gender difference. Different diseases are prone to occur at different ages. The peak age of alveolar abscess was 5 to 9 years and 27 to 62 years, while the peak age of periodontal abscess was 45 to 64 years. Periodontal abscess usually occurred in permanent teeth, especially the molar teeth. Alveolar abscess may occur in both types (primary teeth and permanent teeth). In primary teeth, the most vulnerable tooth positions were primary molar teeth and maxillary central incisors while in permanent teeth the tooth positions were first molar teeth. CONCLUSION: Understanding the incidence of acute maxillofacial infection was conducive to the diagnosis and correct treatment of clinical diseases, as well as targeted education for patients of different ages and genders to prevent the occurrence of diseases.

【关键词】 Oral and Maxillofacial infections；Retrospective analysis

口腔流行病学

中国成年人小于 20 颗余留牙影响因素分析：基于中国 2015-2016 年第四次口腔健康流行病学调查

郭　静　班晶浩　王胜朝　空军军医大学第三附属医院

【摘要】 目的：本文的研究目的是探究中国不同年龄阶段成年人小于 20 颗牙齿余留牙的相关因素。

方法：论文的数据来源于中国第四次口腔健康流行病学横断面调查数据库，采用多阶段、分层、等容量、随机抽样的方法进行人群抽样，等比抽取中年人（35 ～ 44 岁）、中老年人（55 ～ 64 岁）和老年人（65 ～ 74 岁）共 13464 人，对牙齿缺失及修复情况进行描述分析，城乡及性别组间的率的比较采用卡方检测，均数比较采用非参数 Mann-Whitney U 检验。对余留牙数（是否小于 20 颗牙）进行趋势卡方分析及二元性 Logistic 回归分析。

结果：调查样本中余留牙数目小于 20 颗的人数为 1680 人（12.5%），其中余留牙数目小于 10 颗占 5.5%，余留牙数目为 11-19 颗占 6.9%。中国成年人中，居住于农村、居住地区位于中国西部地区、学历低于中专、低收入家庭（年收入低于 6 万元）、吸烟（包括已戒）、吸烟频率每天 6 支以上、每天刷牙少于一次、一年内未洗牙、口腔健康意识较低、得慢性病（中风、糖尿病、心脏病及慢阻肺）、有龋、有深牙周袋及附着丧失的人群小于 20 颗余留牙占比显著性高于大于等于 20 颗余留牙的人群占比。多变量的 logistic 回归分析显示：吸烟（OR=1.845，95%CI：1.545-2.203）是余留牙数少于 20 颗牙独立的相关危险因素（$P < 0.05$）。而无龋（DMFT=0）（OR=0.709，95%CI：0.693-0.716）、无深牙周袋（OR=0.461，95%CI：0.370-0.574）是余留牙数少于 20 颗牙独立的相关保护因素（$P < 0.05$）。

结论：中国成人余留牙数随经济发展不断增加。为了进一步提高中国成人（特别是老年人）的生活质量，可通过防龋、控制牙周病发展及控烟的方法，使更多老年人余留牙数达到 20 颗以上。

【关键词】 中国成年人；牙齿缺失；影响因素；logistic 回归分析；第四次全国口腔健康流行病学调查

AQP5 基因间交互作用与磨牙 - 切牙釉质发育不全的关联研究

庞亮月　林焕彩　中山大学附属口腔医院

【摘要】 目的：探索基因 - 基因的交互作用与 MIH 的关系并验证釉质形成基因和免疫相关基因与中国汉族青少年 MIH 的关系，为 MIH 的诊断和治疗提供分子水平的参考依据。

方法：从 1055 名 12-13 岁青少年中选取 86 名 MIH 青少年作为病例组，以年龄和性别为条件按照 1:4 进行配对的方法选取 344 名非 MIH 青少年作为对照组。从唾液样本中获取 DNA 信息，采用质谱法对 16 个 SNPs 位点测序分析。采用 Logistic 回归分析进行数据分析。

结果：rs13115627-AA 基因型携带者的 MIH 风险显著高于 GG 基因型（OR=4.942，95%CI 0.658-37.131），rs1784418-TT 基因型携带者也高于 CT 基因型（OR=2.203，95%CI 1.63-3.521）。rs1800972-CC 基因型携带者 MIH 风险远高于 GG，（OR=2.284，95%CI 1.267-4.115），rs1800972-C 等位基因的携带者也高于 G（OR=1.800，95%CI 1.106-2.929）。单独分析 AQP5 基因多态性，并未发现其与 MIH 相关。但在基因 - 基因交互作用分析时，我们发现 rs1996315 与 rs923911 存在交互作用（P=0.023）。与人群中携带 rs1996315-GG 和 rs923911-CC 基因型者相比，携带 rs1996315-AG 和 rs923911-AC 基因型者具有最高的 MIH 患病风险（OR=3.603，95%CI1.147-11.318）。

结论：AMBN 基因 rs13115627- GG 基因型 是 MIH 的保护因素。MMP20 基因 rs1784418-TT 基因型和 DEFB1 基因 rs1800972-C 等位基因以及 rs1800972-CC 基因型是 MIH 的危险因素。AQP5 基因的 rs1996315 和 rs923911 存在交互作用，人群中携带 rs1996315 - AG 和 rs92391-AC 基因型的人患 MIH 风险最大。

【关键词】 磨牙 - 切牙釉质发育不全，釉质形成基因，免疫相关基因，AQP5 基因，单核苷酸多态性

我国 12—15 岁年龄组口腔卫生服务利用及影响因素

吴慧竞　司　燕　北京大学口腔医院

【摘要】 研究背景：与第三次全国口腔流行病学调查结果相比，12—15 岁年龄段的口腔健康没有明显改善。同时世界范围内该年龄段卫生服务利用存在研究空白。

研究目的：为了解我国 12—15 岁年龄组卫生服务利用现状，并探究其影响因素。同时为该年龄段口腔疾病保健提供相关建议。

资料与方法：使用我国第四次全国口腔健康流行病学调查数据，采用卡方检验及二元 Logistic

回归进行数据分析。使用 Andersen 模型理论框架解释相关影响因素。

结果及结论：我国 12—15 岁年龄组口腔卫生服务利用仍处于较低水平，利用的主要目的仍为治疗。倾向性因素中的健康信念因素与需要因素为我国 12—15 岁年龄组口腔卫生服务利用的主要影响因素。加强面向学校的口腔健康教育，有望增加该年龄段对口腔保健知识的了解，提升保健意识与口腔卫生服务利用水平。

【关键词】 口腔，卫生服务利用，青少年，流行病学

我国中老年人口腔卫生服务利用的影响因素

许梦茹　司　燕　北京大学口腔医院

【摘要】 目的： 利用 Andersen 模型探究我国中老年人口腔卫生服务利用的影响因素 , 为口腔卫生资源分配和口腔卫生服务政策制定提供依据。 方法 利用全国第四次口腔流行病学调查数据，选择问卷完整的 7206 名成年人（35—44 岁年龄组：3669 人，65—74 岁年龄组：3537 人）。过去一年就诊率为结果变量。根据 Andersen 模型选取解释变量。利用单因素（卡方检验）和多因素（分层泊松回归）对成年人口腔卫生服务利用的影响因素进行分析。 结果 中年人组过去一年就诊率为 21.4%（95%CI:19.4%，23.7%），老年人组过去一年就诊率为 20.7%（95% CI:18.6%，22.9%）。分层泊松回归最终模型显示性别、口腔健康知识态度、自觉口腔卫生状况、DMFT 是中年人组过去一年是否就诊的主要影响因素。而在老年人组，性别、保险类型、受教育水平和收入水平、自觉卫生健康状况，是过去一年是否就诊的主要影响因素。结论 性别和自我口腔健康评价是影响中年人和老年人口腔卫生服务利用的共同因素。意外，教育水平、收入水平和保险也影响着老年人口腔就诊。扩大老年人的牙科就诊的保险覆盖范围，将会对提高老年人口腔服务利用有积极影响。通过口腔健康教育增加口腔保健知识、提高口腔卫生意识，可以促进我国中老年人的口腔卫生服务利用。

【关键词】 中老年人；口腔卫生服务利用

Clinical Analysis of First Visit Cases in Oral Emergency Department

杨　雪　北京大学口腔医院

【 摘 要 】 Objective: To analyze the clinical characteristics and classification of first visit dental emergency cases, providing guidance on rational and effective allocation of limited medical resources and more timely treatment of emergency patients.

Methods: To conduct a retrospective study on the intact data of the first visit emergency cases from January 2016 to December 2018 in the oral emergency department of a stomatology hospital, to analyze the distribution of the patients’ gender, age, visiting time and diagnostic classification.

Results: During the period, there were a total of 93,967 first visit patients in the oral emergency department. Patients’ ages ranged from 0 to 101 years old, and the male-female ratio was nearly 1:1. In the age group under 10 years old, the male-female ratio was 1.45:1, while dental trauma patients were the majority, accounting for 61.0% of the total number in this age group. In the age group between 20 and 39, the male-female ratio was 0.86:1, while 57.7% of this age group patients complained of pain. 66.2% of the patients who complained of pain were toothache. In these pain cases, pulpitis was the most common, followed by periapical periodontitis, pericoronitis. In the acute maxillofacial infection cases, there were 40.4% patients suffered apical abscess and 36.0% suffered periodontal abscess. 67.0% of the bleeding patients were bleeding after tooth extraction. non-emergency patients were 21.3%. The two peak times were 8:00-11:00 and 19:00-20:00.

Conclusion: There were various requirements for first visit dental emergency patients. Although mainly patients suffered acute oral diseases, there were still a large number of non-emergency patients, occupying some emergency medical resources. So it was necessary to establish a more complete triage system to improve the efficiency of diagnosis and treatment.

【关键词】 oral emergency, toothache, epidemiology

口腔美学

PRF+SVF+ 脂肪移植纠正颌面部凹陷的新策略：从基础到临床

刘富伟　孔　亮　李云鹏　空军军医大学第三附属医院

【摘要】自体脂肪移植术作为纠正颌面部畸形的新型治疗方法，具有来源丰富、手术操作微创、排斥反应小等优势，具有广泛应用前景。然而脂肪移植技术中仍存在一些不可控因素，如脂肪吸收、脂肪栓塞、脂肪变性坏死等，会导致远期效果不佳。为解决上述问题，基于组织工程理念，以基质血管成分（SVF）为干细胞来源，以富血小板纤维蛋白（PRF）为细胞因子来源，以自体脂肪颗粒（AG）作为支架，进行复合移植。在前期优化了提纯方法与配比的基础上，以新西兰大耳白兔耳皮下注射自体脂肪为对象，观察各组血管形成、脂肪吸收情况。再将最优方案应用于颜面畸形患者，以观察疗效。基础研究发现，脂肪移植术后 4 周、12 周、24 周通过血管透射、大体观察、HE 染色和超声检查可见，AG+PRF+SVF 组脂肪血管改建最好、存留率最高、吸收率最少，AG+PRF 组和 AG+SVF 组次之。临床研究发现，AG+PRF+SVF 联合分别植入患者唇、鼻、颞、

颜面等不同质地和张力的部位后，术后形态和丰满度均有明显改善，且术后 3-6 月复诊可见疗效稳定。至此，我们构建了一种基于 PRF、SVF 混合用于脂肪移植的新型技术，PRF 和 SVF 分别发挥着生长因子及种子细胞的作用；同时，生物实验证实，这一策略具有抗早期及晚期吸收的作用；并制定了其成熟的临床规范，在临床取得一定效果。

【关键词】 自体脂肪移植，富血小板纤维蛋白（PRF），基质血管成分（SVF），颌面软组织修复

一种新的牙龈微创美容缝合术 (MICST) 应用于美学牙冠延长术的疗效观察

张慧慧　武汉大学口腔医院

【摘要】 目的：前牙区牙冠延长术后需通过缝线进行龈瓣缝合以关闭手术创面、促进愈合。拆线前前牙区存在缝线与线结的暴露而影响美观；并且唇侧缝线的暴露也会加重菌斑的滞留，术后感染风险增加，影响愈合（图 1）。本研究拟提出一种新的牙龈微创美容缝合技术 (minimally invasive cosmetic suture technique, MICST)，并通过自身对照研究观察该缝合技术对前牙美学牙冠延长术术后美观及愈合状况的影响。方法：牙龈微创美容缝合技术通过唇侧龈乳头上皮下结缔组织内缝合及腭侧打结实现（图 2）。15 例由于被动萌出不足的“露龈笑”患者接受 #13-#23 牙位美学牙冠延长术并进行牙龈微创美容缝合。评估患者术前、术后即刻、术后 5 天、术后 1 个月、术后 3 个月的菌斑及牙龈状况、龈乳头充盈情况、患者美学满意度及术后 5 天切口愈合分级。结果：（1）术前至术后 3 个月菌斑指数均无明显变化，牙龈指数及出血指数于术后 5 天有所升高，术后 1 个月恢复至术前水平（表 1）；（2）术后 5 天，2 例患者出现龈乳头增生，至术后 1 个月时增生消退，3 个月时所有患者均未出现龈乳头增生及退缩（表 2）；（3）术后 5 天，所有患者手术切口均达到甲级愈合标准，未见软组织充血及感染、无瘢痕及压痕，术后 1 个月软组织完全愈合（图 4）；（4）术前患者美学满意度为 2.40±0.83；术后即刻，患者的满意度得到显著提高，达 7.93±1.16；术后 5 天、1 个月和 3 个月的美学满意度分别 9.07±0.70、9.42±0.52、9.40±0.51，较术前有显著性改善，较术后即刻也有轻度提高（图 3）。结论：牙龈微创美容缝合技术应用于前牙牙冠延长术，能够获得术后即刻的美观改善，避免缝线导致的菌斑滞留，减少术后的反应，加快组织的愈合。

【关键词】 美容缝合；牙龈；牙冠延长术；美学

口腔免疫学

Targeting CMTM6 suppresses stem cell-like properties and enhances anti-tumor immunity in head and neck squamous cell carcinoma

陈　磊　武汉大学口腔医院

【摘要】 CMTM6, a recently identified critical regulator of PD-L1 expression, is also thought to be involved in the modulation of tumor immunity. However, little is known about the biological function and underlying mechanism of CMTM6 in head and neck squamous cell carcinoma (HNSCC). In this study, we found that CMTM6 overexpression was a predictor for a poor prognosis for HNSCC patients by immunohistochemistry (IHC) analysis. Moreover, we discovered that CMTM6 was robustly correlated with the Wnt/β-catenin signaling pathway, which is essential for tumorigenesis and the maintenance of the cancer stem cell (CSC) and epithelial-to-mesenchymal transition (EMT) phenotypes in multiple cancers. Further experimental results confirmed the genetic deletion of CMTM6 via short hairpin RNAs (shRNAs), leading to nuclear β-catenin reduction, which resulted in the inhibition of stem-cell like properties, TGF-β-induced EMT and the proliferation of HNSCC cells. Consistent with these results, we observed a significant positive correlation between CMTM6 and EMT- and CSC-related genes in the public TCGA database. Interestingly, we found consistent positive correlations between CMTM6 and immune checkpoints at both the RNA and protein levels. More importantly, we found that CMTM6 silencing-induced PD-L1 downregulation delayed the growth of tumors due to SCC7 cells, increased the infiltration of both CD8+ and CD4+ T cells and enhanced T lymphocyte activation by increasing INF-γ, Granzyme B and TNF-α production. Overall, these findings demonstrate that CMTM6 plays a vital role in regulating stemness, EMT and T cell dysfunction; thus, CMTM6 may be a promising target for HNSCC.

【关键词】 CMTM6, PD-L1；Wnt/β-catenin；EMT；CSCs；immunotherapy

TIGIT/CD155 signaling blockade enhances anti-PDL1 immunotherapy in head and neck squamous cell carcinom

毛　亮　武汉大学口腔医院

【摘 要】 Anti-PDL1/PD1 therapy has recently been approved for head and neck squamous cell carcinoma (HNSCC). However, given large parts of HNSCC patients do not respond to PDL1/PD1 antibodies, combination strategies for elevating the response rate have raised great attention. Herein, the non-redundant role of CD155/TIGIT and PDL1/PD1 signaling was explored in HNSCC and the possibility of duel targeting CD155/TIGIT and PD1/PDL1 signaling was assessed. Multiplex flow cytometry analysis indicated that CD155 and PDL1 co-expressed myeloid cells were infiltrated in tumor microenvironment (TME) of HNSCC patients. High CD155 and PDL1 co-expression on monocytic myeloid-derived suppressor cells (M-MDSCs) in TME was associated with a lower density of infiltrating CD3 T cells and effector memory T-cell subset. In transgenic HNSCC mouse model, CD155 and PDL1 co-expressed myeloid cells were gradually infiltrated in the tumor microenvironment with the tumor progresses. Combined application of TIGIT and PDL1 monoclonal antibodies significantly decreased the tumor burden and enhanced the infiltration of CD3 T cell in the TME. Furthermore, the combination strategy prevented T cell exhaustion and promoted T cell tumor immunity. Above all, our results provide a potential strategy for improving the response of immunotherapy through co-targeting CD155/TIGIT and PDL1/PD1 signaling.

【关键词】 TIGIT；PDL1；MDSC；immunotherapy；HNSCC

Blockade of TIGIT/CD155 signaling reverses T cell exhaustion and enhances antitumor capability in head and neck squamous cell carcinoma

武　磊　Mao Liang　School and Hospital of Stomatology, Wuhan University

【摘要】 Immunosuppression is common in head and neck squamous cell carcinoma (HNSCC). In previous studies, TIGIT/CD155 pathway was identified as an immune checkpoint signaling pathway that contributes to the “exhaustion” state of infiltrating T cells. Here, we sought to explore the clinical significance of TIGIT/CD155 signaling in HNSCC and identify the therapeutic effect of TIGIT/

CD155 pathway in transgenic mouse model. TIGIT was overexpressed on tumor-infiltrating CD8+ and CD4+T cells in both HNSCC patients and mouse models, and was correlated with immune checkpoint molecules (PD-1, TIM-3, LAG-3). TIGIT was also expressed on murine regulatory T cells (Tregs) and correlated with immune suppression. Using a human HNSCC tissue microarray, we found that CD155 was expressed in tumor and tumor-infiltrating stromal cells, and also indicated poor overall survival. Multispectral immunohistochemistry indicated that CD155 was coexpressed with CD11b or CD11c in tumor-infiltrating stromal cells. Anti-TIGIT treatment significantly delayed tumor growth in transgenic HNSCC mouse models and enhanced antitumor immune responses by activating CD8+ T cell effector function and reducing the population of Tregs. In vitro coculture studies showed that anti-TIGIT treatment significantly abrogated the immunosuppressive capacity of MDSCs by decreasing Arg1 transcripts and Tregs by reducing TGF β 1 secretion, respectively. In vivo depletion studies showed that the therapeutic efficacy by anti-TIGIT mainly relies on CD8+ T cells and Tregs. Blocking PD-1/PD-L1 signaling increased the expression of TIGIT on Tregs. These results present a translatable method to improve antitumor immune responses by targeting TIGIT/CD155 signaling in HNSCC.

【关键词】 Immunosuppression; Head and neck squamous cell carcinoma; TIGIT; CD155; Immunotherapy

口腔黏膜病学

白细胞介素 -35 对口腔扁平苔藓患者外周血 Th17/Treg 平衡影响的初探

胡文芸　贵州医科大学口腔医学院

【摘要】 口腔扁平苔藓（oral lichen planus，OLP）是一种发生于口腔黏膜的自身免疫性疾病。现有研究表明：Treg 与 Th17 细胞平衡的异常参与了 OLP 的发病机制 [1,2]。IL-35 是一种主要由 Treg 细胞分泌的新型抑制性细胞因子，具有强效的免疫抑制作用。 它能增强 Treg 细胞的免疫抑制功能，抑制 Th17 细胞分化，阻止炎症对机体造成免疫损伤。IL-35 可能通过调节 Th17 细胞与 Treg 细胞之间平衡，实现其对 OLP 免疫调节及治疗作用。

【关键词】 口腔扁平苔藓；白细胞介素 35；Th17/Treg 平衡

口腔扁平苔藓患者外周血中滤泡辅助性 T 细胞相关细胞因子的表达及意义

靳大力　蔡　扬　贵州医科大学附属口腔医院牙周黏膜科
肖　琛　凯里市贵州医科大学第二附属医院口腔科

【摘要】 目的：了解口腔扁平苔藓（Oral lichen planus, OLP）患者外周血中趋化因子受体 CXCR5+（C-X-C chemokine receptor type 5，CXCR5）细胞比例及滤泡辅助性 T 细胞（T follicular helper cells，Tfh）相关细胞因子白细胞介素 -21（Interleukin-21，IL-21）、趋化因子 CXCL13（chemokine CXC ligand 13，CXCL13）的表达情况，探讨其在口腔扁平苔藓免疫发病机制中的作用和意义。方法 : 选择 OLP 患者 31 例（非糜烂型 14 例，糜烂型 17 例）和健康对照组 24 例。采用流式细胞术（Flow Cytometry, FCM）检测外周血中 CD3+、CD3+CD4+、CD3+CD8+、CD19+、CD16+56+[自然杀伤细胞（natural killer cell，NK）] 细胞的比例；使用散射比浊法检测血清中 IgG、IgA、IgM、补体 C3 和 C4 的水平；分析 OLP 患者的细胞免疫和体液免疫功能。应用酶联免疫吸附试验（Enzyme-linked immunosorbent assay, ELISA）检测 OLP 患者及健康对照组血清中 IL-21 和 CXCL13 的表达水平，并分析它们与免疫功能的相关性。采用流式细胞术（FCM）检测外周血中 CXCR5+ 细胞的比例，分析其与 IL-21、CXCL13 和免疫状况的关系。结果：OLP 患者外周血中 CD3+CD8+、NK 细胞比例、补体 C4 水平低于正常值（$P < 0.05$），CD19+ 细胞比例和 IgG、IgM 水平高于正常值（$P < 0.05$）。OLP 患者外周血血清中 IL-21 和 CXCL13 的表达低于正常对照组（$P < 0.05$），两者间呈正相关关系，IL-21 和 CXCL13 的表达与 NK 细胞均呈正相关关系。OLP 患者外周血中 CXCR5+ 细胞比例高于正常对照组（$P < 0.05$），且与 CD19+ 细胞亚群呈正相关关系。结论：OLP 患者存在细胞免疫功能低下，体液免疫功能亢进。升高的 CXCR5+ 细胞可能通过增强体液免疫参与 OLP 的发病过程。IL-21 和 CXCL13 可能通过负反馈参与 OLP 的免疫调节过程。

【关键词】 口腔扁平苔藓；滤泡辅助性 T 细胞；白细胞介素 21；CXCL13

抗单纯疱疹病毒核苷类似物的设计合成及活性初探

刘　江　赵　行　陈谦明　四川大学华西口腔医院

【摘要】 口腔黏膜病毒感染性疾病通常由单纯疱疹病毒、带状疱疹病毒等引起，具有发病率高、累及面广、潜伏性强、容易复发、可能癌变等特点。并且，由 HSV-1 感染导致的脑炎可能会危及生命，对人类的健康和经济的发展构成了严重的威胁。阿昔洛韦、更昔洛韦等核苷类药物虽然在治疗此

类疾病方面取得了巨大的成功，但是也存在作用靶点单一、生物利用度低、毒副作用大、易使病毒产生耐药性等缺点，远远不能满足人类健康的需求。因此，积极寻找开发高效低毒的广谱抗病毒新药对于国家战略储备和临床需求具有重要的意义。基于此，我们设计合成了 α 和 β 构型的 8-氮杂脱氧鸟苷，发现其具有一定抗 HSV-1 活性，并且与天然脱氧鸟苷相比，8- 氮杂脱氧鸟苷具有更强的碱基配对和碱基错配能力，可能通过与酶结合或者碱基错配发挥活性。8- 氮杂脱氧鸟苷由于具有荧光性质，还可作为示踪分子研究其在体内的代谢过程和碱基错配方式，为进一步研究其体内活性、活性机理奠定了基础。研究过程中，我们还发现一类嘧啶肟碱基中间产物，具有更好的抗 HSV-1 活性和选择性，部分化合物表现出广谱抗病毒性质，通过构效关系比较，筛选出 4 个先导化合物，具有潜在的应用价值。

【关键词】 8- 氮杂脱氧鸟苷；抗单纯疱疹病毒活性；DNA 性质；活性机理；构效关系

Porphyromonas gingivalis promotes colorectal carcinoma by modulating the tumor immune microenvironment

王　茜　Jia Yiqun　中山大学附属口腔医院

【摘要】 Objective Oral microbiome has been viewed as an important factor that affects gut microbiota homeostasis in recent years. Metagenomic analyses indicate that Porphyromonas gingivalis (P. gingivalis), a major periodontal pathogen is associated with colorectal carcinoma (CRC) but whether this is a causal link remains unclear. We investigated whether P. gingivalis contributes to CRC tumorigenesis or development.

Experimental Design We performed qPCR, immunohistochemistry, and fluorescence in situ hybridisation to confirm the existence of P. gingivalis in gut. Two cohorts were analyzed for evaluating the correlation of P. gingivalis infection and prognosis of CRC patients. Three mouse models were utilized to confirm the tumor promoting effects of P. gingivalis. Furthermore, we utilized flow cytometry to investigate the changes in tumor immune microenvironment and validated a P. gingivalis associated proinflammatory gene signature by RNA-sequencing and ELISA.

Results We found that P. gingivalis is enriched in human stool and tissue samples from CRC patients compared with those from colorectal adenoma patients or healthy subjects. Cohort studies demonstrated that P. gingivalis infection was associated with poor prognosis in CRC. Moreover, P. gingivalis increased the tumor counts in the ApcMin/+ mouse model of colorectal tumorigenesis and increased tumor growth in MC38 cell subcutaneous and orthotopic rectal carcinoma models. Furthermore, we observed a tumor-infiltrating myeloid cell recruitment proinflammatory signature in mice P. gingivalis-positive CRC by using an orthotopic MC38 rectal carcinoma model exposed to P. gingivalis.

Conclusions Collectively, these data suggest that P. gingivalis generates a proinflammatory microenvironment, which is conducive to colorectal neoplasia progression, by recruiting tumor-infiltrating immune cells.

【关键词】 Porphyromonas gingivalis；colorectal cancer；myeloid cell；immune

Oral lichen planus have a distinct metabolomic profile: A preliminary study using UHPLC-Q-Orbitrap HRMS

王晓霜　郑州大学第一附属医院

【摘要】 Objective: Oral lichen planus (OLP) is a T-cell-mediated chronic inflammatory disorder and potentially oral precancerous lesion. However, there are many flaws in the current way to diagnose OLP and metabolomics analysis may help to provide a new way, and we may know more about the disease.

Materials and methods: 115 OLP patients and 124 normal controls were assigned to either a training set (n=160) or a test set (n=79) randomly. The UHPLC-Q-Orbitrap HRMS was applied to identify the potential biomarkers and the serum metabolic changes were profiled and evaluated by multivariate analytical.

Results: Totally, 28 deferential metabolites were identified in the training set between OLP group and health group, whose dysregulations could affect 20 different pathways. We selected the three highest metabolites in ROC as a panel to predict the different groups in the test set, and the predictive value was 92.4%.

Conclusion: The study indicated that the metabolomic analysis of human serum may help us understand more about pathological processes of this disease, and put forward new ideas and new methods for the diagnosis of patients with OLP.

【关键词】 Oral lichen planus; Metabolomics analysis; Potential biomarkers; UHPLC-Q-Orbitrap HRMS

大鼠舌癌发生过程中 HIF-1α 与 VEGF 在外周血的表达及其关系

王薛藤　李爱迪　赖永先　西南医科大学附属口腔医院

【摘要】 目的：研究大鼠舌黏膜在癌变发展各阶段中 HIF-1α 与 VEGF 在外周血表达的变化，探索二者在癌变发展过程中表达的关系及其与大鼠病程发展的关系。方法 随机购买 90 只 6 周龄雄性 SPF 级 SD 大鼠，将其随机均分为 6 个组，每组 15 只，其中实验组 75 只，随机均分为 A、B、C、D、E 5 个亚组，对照组 15 只，实验组采用 4NQO 自主饮水法诱导大鼠舌黏膜癌变，对照组自主饮用 SPF 级动物专用灭菌纯净水。在实验过程中的第 10、14、18、22、24 处理 A、B、C、D、E 组，对照组与 E 组同一天处理，抽取大鼠外周血后切取舌黏膜组织做病理检查，按病理结果分组，ELISA 法检测各组大鼠 HIF-1α 与 VEGF 在外周血的表达，等级资料多个独立样本 Kruskal－Wallis 秩和检验分析病理分级差异； Pearson 相关、线性回归模型分析 HIF-1α 与 VEGF 在大鼠舌癌发生过程中表达的关系及其表达与大鼠病程的关系。结果 不同时期处理大鼠其病理检查结果不尽相同，共获得有效标本 77 例，其中 18 例正常舌黏膜，7 例上皮单纯增生，6 例轻度上皮异常增生，10 例中度上皮异常增生，11 例重度上皮异常增生，25 例舌鳞状细胞癌；VEGF 的表达与 HIF-1α 相关但未见明显线性关系；HIF-1α 与 VEGF 的表达均与病变程度相关，随着病变的加重，表达量增加。 结论 HIF-1α 与 VEGF 的表达与舌癌发展过程有关，VEGF 的表达与 HIF-1α 的表达有关系，可能有助于 TSCC 的早期诊断及治疗。

【关键词】 动物建模；HIF-1α；VEGF；舌鳞状细胞癌

利用诱导多能干细胞研究罕见遗传病白色海绵状斑痣病发病分子机制及相关药物筛选

蔡文萍　同济大学医学院，同济大学附属第十人民医院

【摘要】 罕见病白色海绵状斑痣病（WSN）是一种口腔黏膜常染色体显性遗传病。本研究通过收集两个 WSN 家系，采用电镜、HE 染色和免疫组化等手段确定白色海绵状斑痣病理特征。并且对 Keratin13（KRT13）基因进行突变分析。运用 ClustalW 软件对 23 个物种的 KRT13 蛋白序列同源比对分析。通过 qPCR 检测正常人和 WSN 患者 KRT13 的 RNA 转录水平差异。利用蛋白酶体抑制剂 MG132 处理正常人及 WSN 口腔上皮细胞后通过 Western 免疫印迹分析其对 KRT13 蛋白表达水平的影响。利用高通量 RNA 测序技术检测正常人和 WSN 患者差异表达基因，全面分析转

录组及信号通路差异。同时利用口腔组织活检获得正常人和WSN患者的口腔上皮细胞并体外培养，然后采用 Yamanaka 原理和方法将携带 Oct4、Sox2、c-Myc 和 Klf4 转录因子的 4 种逆转录病毒载体感染正常人和 WSN 患者口腔上皮细胞，并向口腔上皮细胞分化，同时进行相关药物筛选。通过分析确定 WSN 突变位点 , 为临床基因诊断提供参考。利用诱导多能干细胞（iPS）为研究 WSN 发病机制及相关药物筛选奠定基础。

【关键词】 白色海绵状斑痣病（WSN）；Keratin13（KRT13）；罕见病；发病分子机制；iPS

Ash1l 及其相关调控因子在口腔扁平苔藓病损组织中的表达及意义

汪　鹰　蔡　扬　贵州医科大学附属口腔医院

【摘要】 目的：探讨 Ash1l 及其相关调控因子在口腔扁平苔藓中的表达及意义。方法：1.OLP 病损组织 41 例（21 例非糜烂型，20 例糜烂型）和正常对照组 19 例。采用 RT-qPCR 法检测 OLP 病损组织中 Ash1l、A20、IL-6mRNA 的表达水平，采用免疫组织化学技术检测 OLP 病损组织中 Ash1l、A20、磷酸化 p38（p-p38）、IL-6 蛋白的表达与分布，分析上述因子与 OLP 临床及病理特征的关系。结果：1.OLP 病损组织中 Ash1lmRNA 的表达水平低于对照组（Z=-3.329，P=0.001），A20 及 IL-6mRNA 的表达水平均高于对照组（Z1=-3.107，P1=0.002；Z2=-3.345，P2=0.001）；糜烂型 OLP 组 A20mRNA 的表达水平高于非糜烂型 OLP。上述因子与 OLP 临床病理特征的相关性分析显示：Ash1lmRNA 的表达与淋巴细胞浸润程度呈负相关（r=-0.344，P=0.028）；IL-6mRNA 的表达与淋巴细胞浸润程度呈正相关（r=0.368，P=0.018）。2.OLP 病损上皮层中 Ash1l 蛋白的阳性表达率为 24%（10/41）低于正常对照组 79%（15/19），A20、p-p38、IL-6 蛋白的阳性表达率分别为 46%（19/41）、73%（30/41）、78%（32/41）均高于正常对照组；OLP 固有层中 Ash1l、A20、p-p38 和 IL-6 蛋白的阳性表达率分别为 29%（12/41）、44%（18/41）、71%（29/41）和 73%（30/41）均高于正常对照组（P ＜ 0.05）；糜烂型 OLP 病损固有层中 Ash1l 及 A20 蛋白阳性表达率高于非糜烂型 OLP（(12=4.822，P1=0.028；(22=7.276，P2=0.007）；OLP 固有层中 IL-6 蛋白的阳性表达率在淋巴细胞浸润程度及基底细胞液化变性程度高分组均高于低分组（P ＜ 0.05）。相关性分析显示 OLP 上皮层中 Ash1l 蛋白分别与 IL-6 及 p-p38 的表达呈负相关（r1=-0.522，P1 ＜ 0.001；r2=-0.553，P1 ＜ 0.001）；IL-6 与 p-p38 的表达呈正相关（r=0.610，P ＜ 0.001）。OLP 固有层 Ash1l 与 A20 的表达呈正相关（r=0.403，P=0.009）；IL-6 与 p-p38 的表达呈正相关（r=0.336，P=0.032）。结论：Ash1l 及相关调控因子在 OLP 病损中存在表达异常且与临床类型及病理特征有关，提示 Ash1l 及其调控因子的异常表达可能参与了 OLP 的病损形成及发展。

【关键词】 口腔扁平苔藓（OLP）；Ash1l；A20；磷酸化 p38（p-p38）；IL-6

口腔全科

Prompt facial nerve regeneration induced by aligned fibrin nanofiber hydrogel and dental pulp stem cells

母晓丹　哈尔滨医科大学附属口腔医学院

【摘要】 Objective To study the application of aligned fibrin hydrogel and dental pulp stem cells in facial nerve repair. Methods Dental pulp stem cells (DPSCs) of rabbit were isolated and cultured. DPSCs were induced to differentiate into neuron-like cells, which were verified by immunofluorescence (IF) and Western blot (WB). DPSCs on fibrin were stained with phalloidin. aligned fibrin hydrogel (AFG) was prepared by electrospinning and its arrangement was examined by scanning electron microscopy (SEM). The buccal branches of rabbit facial nerve were repaired in vivo. The histological evaluation was performed by immunohistochemistry (IHC), toluidine blue (TB) and transmission electron microscopy (TEM). Results SEM showed that AFG was arranged in parallel, while random fibrin hydrogel (RFG) was disorderly. DPSCs grew in orientation on AFG,and after successfully expressed NF and Nestin protein after induction. TB results showed the number of regenerated nerve fibers in DPSCs group and DDPSCs group was less than that in Autograft group, and more than that in AFG and RFG group; TEM showed that the thickness and quantity of myelin sheath in DDPSCs group was second only to that in Autograft group, and more than that in DPSCs group. There was no significant difference in thickness between RFG group and Hollow group. Conclusion Aligned fibrin nanofiber hydrogel promoted facial nerve regeneration. And carried with dental pulp stem cells or differentiated dental pulp stem cells respectively, the aligned fibrin nanofiber hydrogel further promoted facial nerve regeneration.

【关键词】 facial nerve regeneration；aligned fibrin nanofiber hydrogel；dental pulp stem cells

非生理 pH 激活内源性生长因子对牙复合组织再生的作用

王赛楠　北京大学口腔医院

【摘要】 目的：机体多种组织均储存有非活性状态的转化生长因子 β1 (transforming growth factor β1，TGFβ1)，激活后对组织损伤修复再生具有重要作用。本课题旨在研发新型可注射明

胶微球材料调节局部碱性微环境，激活牙本质中的内源性 TGFβ1，诱导再生牙软硬复合组织。

方法：通过液滴微流控芯片技术制备大小形态可控的明胶微球，经碱性处理后，与 Nb 和 Tr 功能基团改性的明胶水凝胶复合，形成可注射的碱性明胶微球体系；检测并调节明胶微球材料的碱性强弱、凝胶时间、孔隙率、弹性模量、降解性能；检测碱性明胶微球材料对牙本质释放 TGFβ1 的激活作用，及其对骨髓间充质干细胞趋化、增殖、成牙本质向分化及相关信号通路的作用；通过小型猪年轻恒牙牙髓损伤模型观察可注射碱性明胶材料对牙髓牙本质再生、牙根发育及牙根机械性能改变的作用。

结果：研发了非生理碱性条件下可以成胶、且凝胶时间可控的新型可注射明胶微球体系，在调节局部微环境 pH 的同时可作为良好的支架材料，在短时间内激活牙本质中的 TGFβ1，显著趋化内源性干细胞，并能通过调节 SMAD 信号通路参与细胞分化，促进组织修复；使用该碱性明胶微球体系，在牙髓损伤的小型猪模型内，成功诱导再生出富含血管、神经的牙髓组织及牙髓牙本质复合体结构；此外，短时弱酸或弱碱处理能够激活血清中的非活性 TGFβ1，在多种组织修复中具有应用潜力。

结论：通过可注射明胶材料调节局部微环境 pH，从而激活内源性生长因子可能作为一种简单和有效的促进组织修复再生的方法。

【关键词】 TGFβ1；牙髓再生；明胶支架

炎症微环境下 AKT 在成骨细胞中的表达研究

吴赛璇　史东梅　徐慧君　张　咪　　董明　牛卫东　大连医科大学口腔医学院附属口腔医院牙体牙髓科

【摘要】

目的：革兰氏阴性细菌脂多糖（LPS）作用的炎症环境下，研究 AKT 在成骨细胞中表达水平，从而为临床慢性根尖周炎的治疗提供一定的实验依据。

方法：采用实时荧光定量 PCR 检测 LPS 作用于成骨细胞 24h 后 AKT、 BMP2、Runx2 基因的表达情况。蛋白免疫印迹法 Western Blot 检测 LPS 作用于成骨细胞 24h 后 AKT、 BMP2、Runx2 蛋白水平的表达情况。

结果：实时荧光定量 PCR 结果显示 LPS 刺激后成骨细胞中 AKT、 BMP2、Runx2 的表达量明显低于对照组 ($P < 0.05$)，具有统计学意义。蛋白免疫印迹 Western Blot 结果发现 LPS 刺激后成骨细胞中 AKT、 BMP2、Runx2 的表达量明显低于对照组 ($P < 0.05$)，具有统计学意义。

结论：在 LPS 作用的炎症微环境下，AKT 在成骨细胞中的表达降低。

AKT；成骨细胞；根尖周炎；实时荧光定量 PCR；蛋白免疫印迹法

【关键词】 AKT；成骨细胞；根尖周炎；实时荧光定量 PCR；蛋白免疫印迹法

布鲁顿酪氨酸激酶在难治性根尖周炎中的表达研究

张　咪　大连医科大学口腔医学院

【摘要】 目的：研究布鲁顿酪氨酸激酶（BTK）在难治性根尖周炎模型中的表达，以进一步研究 BTK 与难治性根尖周炎骨破坏的关系。

方法 构建粪肠球菌感染难治性根尖周炎动物模型，对实验动物组织样本进行显微 CT 断层扫描，分析根尖骨破坏情况；采用苏木精 - 伊红染色观察粪肠球菌作用后根尖周组织的变化。采用免疫组织化学染色分析 BTK 在粪肠球菌感染动物模型中的蛋白表达水平。采用实时荧光定量 PCR 分析 BTK 在粪肠球菌感染动物模型中的基因表达水平。

结果 micro-CT 及 HE 结果显示：粪肠球菌感染难治性根尖周炎动物模型构建成功，粪肠球菌感染根管后，炎症细胞在根尖聚集并形成骨破坏；IHC 结果显示，BTK 在粪肠球菌感染动物模型中的蛋白表达趋势呈倒 V 型，BTK 在粪肠球菌感染 2w 后达到高峰（$p<0.05$）；PCR 结果显示，在粪肠球菌感染后，BTK 的基因表达水平在 2w 时的 mRNA 表达水平达到高峰（$P<0.05$），且与 CTSK 的基因表达水平具有相同趋势。

结论 BTK 在难治性根尖周炎模型中有表达，暗示其参与了难治性根尖周炎的发展过程，具体机制有待进一步探究。

【关键词】 布鲁顿酪氨酸激酶；粪肠球菌；难治性根尖周炎；免疫组织化学染色

口腔外科黏膜

颞下颌关节不可复性盘前移位致髁突骨吸收关键细胞因子的筛选及验证

冯诗阳　雷　杰　傅开元　北京大学口腔医院

【摘要】 目的：颞下颌关节不可复性盘前移位（Disc displacement without reduction, DDw/oR）常伴有口面部疼痛、下颌运动受限等症状，部分患者可能发生髁突骨吸收甚至牙颌面畸形的改变。然而，目前尚不清楚 DDw/oR 致髁突骨吸收的分子机制。因此，本研究的目的是筛选 DDw/oR 致髁突骨吸收组与对照组关节液中差异表达的关键因子，并探讨差异表达的细胞因子 MIP-1β 和 RANTES 在髁突骨吸收中的生物学作用。

材料和方法：本研究纳入健康志愿者 6 人，不可复性盘前移位患者 25 人，其中不伴骨吸收

者 12 人，伴有骨吸收者 13 人。使用人 27 因子试剂盒及高灵敏度的免疫分析方法筛选并验证不可复性盘前移位致骨吸收的关键细胞因子。细胞实验选用小鼠巨噬细胞系 RAW264.7 细胞，通过 CCK-8 法、Transwell 小室、TRAP 染色、蚀骨实验观察 MIP-1β 和 RANTES 对巨噬细胞增殖、迁移、破骨分化的影响。

结果：MIP-1β 在不可复性盘前移位不伴骨吸收的患者关节液中含量显著升高；RANTES 在不可复性盘前移位伴骨吸收的患者关节液中显著升高；MIP-1β 和 RANTES 均具有募集巨噬细胞的作用；RANTES 可促进经 RANKL 介导的破骨细胞形成。

结论：本研究发现 RANTES 可能是参与颞下颌关节不可复性盘前移位致髁突骨吸收的关键细胞因子之一。

【关键词】 颞下颌关节；不可复性盘前移位；骨吸收；RANTES；MIP-1β

Decorin、EGFR、C-myc 和 P21 在 OSCC 中的表达及相关性分析

赖永先　Nie Min-Hai　Liu Xu-Qian　西南医科大学附属口腔医院

【摘要】 目的：探讨饰胶蛋白聚糖（Decorin）、表皮生长因子受体（epidermal growth factor receptor,EGFR）、致癌基因 C-myc 和细胞周期蛋白依赖性激酶抑制剂（P21）四种蛋白在口腔鳞状 细胞癌（oral squamous cell carcinoma,OSCC）和正常牙龈组织中的表达、相互关系及其临床意义。 方法：分别收集 72 例 OSCC 患者的癌组织和 16 例志愿者正常牙龈组织，采用免疫组织化学法检 测上述四种蛋白的表达情况并进行相关性分析。结果：从正常牙龈至高、中、低分化 OSCC 的过 程中，Decorin 蛋白和 P21 蛋白的阳性表达率逐渐降低，EGFR 蛋白和 C-myc 蛋白的阳性表达率逐 渐升高，其差异性具有统计学意义（P<0.05）；Decorin 与 EGFR（rs=-0.79）、Decorin 与 C-my（c rs=-0.98）、EGFR 与 P21（rs=-0.94）、C-myc 与 P21（rs=-0.91）等蛋白的阳性表达率呈负相关关系。结论：Decorin 和 P21 可能抑制 OSCC 的发生发展；而 EGFR 和 C-myc 可能促进 OSCC 的发生发展；Decorin 可 能抑制 EGFR 与 C-myc 的表达，进而促进 P21 的表达，最终抑制 OSCC 的发生发展。

【关键词】 鳞状细胞癌；饰胶蛋白聚糖；表皮生长因子受体；致癌基因； 细胞周期蛋白依赖性激酶抑制剂

β2-AR 阻滞剂抑制 CD133+ 口腔鳞癌细胞相关特性的研究

张　翀　马　振　麦华明　广西医科大学附属口腔医院

【摘要】 本研究旨在研究 β2 肾上腺素能受体在 CD133+ 口腔鳞癌细胞中的表达情况以及阻滞 β2 受体后口腔鳞癌细胞的相应的细胞功能的变化以及探索相关差异表达基因。利用 Rqt-PCR 及 Western blot 检测发现 CD133+ 细胞中 β2 受体呈现过表达，我们随即将 β2 受体特异性阻滞剂 ICI118-551 作用于该细胞，CCK-8、划痕及 transwell 侵袭实验均发现随药物浓度的增加 CD133+ 细胞增殖、迁移及侵袭的能力均受到抑制。同时高通量测序发现经 ICI118-551 作用后 MAPK 及 PI3K-Akt 两通路中的差异基因数量最多，变化最明显。我们得出结论，β2 受体可能是口腔鳞癌治疗中的一个潜在靶点。并且 β2 受体可能通过 MAPK 和 PI3K/Akt 等信号通路以参与口腔鳞癌的发生与发展。

【关键词】 β2 肾上腺素能受体；CD133+ 口腔鳞癌细胞；阻滞；细胞功能；差异表达基因

Metabolic reprogramming of normal oral fbroblasts correlated with increased glycolytic metabolism of oral squamous cell carcinoma

张卓远　四川大学华西口腔医院

【摘要】 Cancers show a metabolic shift towards aerobic glycolysis. By “corrupting” their micr-oenvironment, carcinoma cells are able to obtain energy substrates to “fuel” their mitochondrial metabolism and cell growth in an autophagy-associated, paracrine manner. However, the metabolic changes and role of normal fbroblasts in this process remain unclear. We devised a novel, indirect co-culture system to elucidate the mechanisms of metabolic coupling between stromal cells and oral squamous cell carcinoma (OSCC) cells. Here, we showed that normal oral fbroblasts (NOFs) and OSCC become metabolically coupled through several processes before acquiring an activated phenotype and without inducing senescence. We observed, for the

frst time, that NOFs export mitochondria towards OSCCs through both direct contact and via indirect mechanisms. NOFs are activated and are able to acquire a cancer-associated fbroblasts metabolic phenotype when co cultivation with OSSC cells, by undergoing aerobic glycolysis, secreting more reactive oxygen species (ROS), high l-lactate and overexpressing lactate exporter MCT-4, leading

to mitochondrial permeability transition pore (mPTP) opening, hypoxia, and mitophagy. On the other hand, Cav-1-low NOFs generate l-lactate to “fuel” mitochondrial metabolism and anabolic growth of OSCC. Most interestingly, the decrease in AMPK activity and PGC-1α expression might involve in regulation of ROS that functions to maintain fnal energy and metabolic homeostasis. This indicated, for the frst time, the existence of ATP and ROS homeostasis during carcinogenesis. Our study suggests that an efcient therapeutical approach has to target the multiple

mechanisms used by them to corrupt the normal surrounding stroma and metabolic homeostasis.

【关键词】 Metabolic reprogramming；ROS；Mitochondrial transfer；l-Lactate；autophagy

下颌前突及后缩病人 SSRO 手术前后髁突稳定性与颞下颌关节匹配度之间相关性的回顾性研究

尹　晴　四川大学华西口腔医院

【摘要】 【研究目的】比较下颌前突和下颌后缩患者在双侧下颌支矢状劈开术（SSRO）后髁突位置稳定性的区别以及分析手术后髁突位置改变和颞下颌关节匹配度之间的相关性。【研究方法】选取 30 例于 2014-2017 年就诊于华西口腔医院的患者（下颌前突 19 例，下颌后缩 11 例，所有患者均仅行单颌双侧 SSRO，利用患者螺旋 CT 资料进行三维重建，分别比较患者术前、术后一周、术后长期的髁突位置，并测量患者髁突及相应关节窝体积，计算关节匹配度。最后利用统计学方法比较下颌前突及下颌后缩患者之间髁突位置变化的差异，以及髁突位置变化与关节匹配度之间的相关性。【研究结果】下颌后缩患者的髁突位置变化在术后短期大于下颌前突患者，两类患者的术后长期髁突位置变化相较于术后短期无明显统计学差异。相关性分析结果表明髁突位置变化与关节匹配度之间呈现负相关的关系，即关节匹配度越高，髁突位置变化越小。【结论】对于关节匹配度较小的病人，例如大部分下颌后缩患者，维持 SSRO 术后关节稳定性就显得更为重要，术中对于髁突位置的把控以及术后正确咬合位置的维持也许是使颞下颌关节术后保持稳定的关键之一。

【关键词】 颞下颌关节；髁突稳定性；下颌前突；下颌后缩；SSRO

口腔修复学

Chondrogenesis of BMSCs for maxillofacial rehabilitaion

巴睿恺　Yimin Zhao　第四军医大学口腔医院修复科

【摘要】 Little capacity of cartilage’s self-regeneration after degeneration for its avascular nature leads to clinical treatment starving for functional tissue engineering strategies. Induction of MSCs chondrogenesis by co-culture with chondrocytes has drawn more and more attention as it can relieve the shortage of donors’ chondrocytes and construct larger quantity of cartilage tissue engineering. In this work, we use cell bricks(fragmented chondrocyte macroaggregates) and PRP(platelet-rich plasma) to achieve a novel injectable niche for chondrogenesis of bone mesenchymal stem cells(BMSCs) as well as preventing its ossification to realize maxillofacial rehabilitaion.

【关键词】 Extracellular matrix；BMSCs；Chondrocyte bricks；PRP；Cartilage regeneration

MiR-137 knockdown promotes the osteogenic differentiation of human adipose-derived stem cells via the LSD1/BMP2/SMAD4 signaling network

范　聪　Peking University School and Hospital of Stomatology

【摘要】 MicroRNAs are a group of endogenous regulators that participate in several cellular physiological processes. However, the role of miR-137 in the osteogenic differentiation of human adipose-derived stem cells (hASCs) has not been reported. This study verified a general downward trend in miR-137 expression during the osteogenic differentiation of hASCs. MiR-137 knockdown promoted the osteogenesis of hASCs in vitro and in vivo. Mechanistically, inhibition of miR-137 activated the bone morphogenetic protein 2 (BMP2)-mothers against decapentaplegic homolog 4 (SMAD4) pathway, while repressed lysine-specific histone demethylase 1 (LSD1), which was confirmed as a negative regulator of osteogenesis in our previous studies. Furthermore, LSD1 knockdown enhanced the expression of BMP2 and SMAD4, suggesting the coordination of LSD1 in the osteogenic regulation of miR-137. This study indicated that miR-137 negatively regulated the osteogenic differentiation of

hASCs via the LSD1/BMP2/SMAD4 signaling network, revealing a new potential therapeutic target of hASC-based bone tissue engineering.

【关键词】 microRNA; human adipose-derived stem cells; LSD1; osteogenic differentiation; signaling

3D 打印与注塑技术制作的内部网格及表面酸蚀微孔促进 peek 植入物与软组织结合的应用研究

冯晓珂　豪　于　空军军医大学第三附属医院

【摘要】 聚醚醚酮 (peek) 是骨科负重器械中最常用的材料之一，具有良好的耐辐射性能和力学性能。然而，目前表面光滑的 peek 植入物可以导致纤维囊的形成。为解决这一问题，本研究采用三维打印和注塑技术制作了具有良好内交联结构 (大孔径 1.0-2.0mm) 的 peek 试样，并采用浓硫酸酸蚀得到了微孔表面。实验在体外比较了光滑 peek 表面和酸蚀后微孔 peek 表面细胞粘附及增值情况，在体内采用新西兰大白兔背部皮下移植的动物模型比较了不同尺寸内网状结构的光滑多孔聚醚醚酮 (peek）在体内的软组织反应。酸蚀微孔表面促进人皮肤成纤维细胞粘附，内部交联结构提高 peek 试样与软组织形成机械结合的能力。具有内交联结构和外酸蚀微孔表面的 peek 标本能有效促进软组织紧密融合，防止纤维囊的形成，具有临床应用于外科修复的潜力。

【关键词】 聚醚醚酮；3D 打印；注塑

泛素特异性酶 34 通过 BMP 信号调控骨髓间充质干细胞成骨分化和小鼠种植体骨结合

郭雨晨　薛寒骁　袁　泉　四川大学华西口腔医院

【摘要】 研究背景：间充质干细胞成骨分化是形成种植体稳定骨结合的关键。以往研究证实，泛素 - 蛋白酶体系统在间充质干细胞成骨分化的调控中起重要作用。本研究首次以去泛素化酶为研究对象，探究泛素特异性酶 34 调控骨髓间充质干细胞成骨分化和小鼠颌骨种植体骨结合的作用机理。

研究方法：使用 siRNA 敲降 hBMSCs 中 USP34 表达，在体外成骨诱导培养环境中检测 USP34 敲降对 hBMSCs 体外成骨分化的影响。下一步，利用 CRISPR/Cas9 技术构建 Usp34 flox 小鼠，并利用 Prx1-Cre 介导同源重组，在小鼠体内特异性敲除 Usp34，观察 Usp34 缺乏对小鼠骨改建的影响。同时，在 Usp34 特异性敲除小鼠上颌骨植入钛种植体，观察 Usp34 缺乏对钛种植体骨结合的影响。最后，结合 RNA-seq 和 co-IP 技术进行机理研究，找到 USP34 调控上述表型的信号通路。

研究结果：USP34 敲降抑制 hMBSCs 体外成骨分化。Usp34 特异性敲除致小鼠股骨骨量降低，骨生成速率下降。同时，Usp34 特异性敲除抑制种植体骨结合的形成。最后，通过机理研究证明 USP34 通过 BMP 信号通路调控 BMSC 成骨分化。

研究结论：USP34 正向调节 BMP 信号通路，调控 BMSC 成骨分化和种植体骨结合。

【关键词】 USP34；种植体骨结合；间充质干细胞；成骨分化；BMP 信号通路

Mitochondria transfer enhances BMSC osteogenic, migration, invasion abilities in vitro, and bone defect repair in vivo

郭雨思　迟晓培　北京大学口腔医院

【摘要】 Mitochondria plays an important role in self-renewal, differentiation, and cell metabolism of stem cells. Mitochondria have been discovered to have the capacity to transfer from cell to cell spontaneously in vivo. Thus, we aimed to investigate the potential benefit of mitochondria transfer from donor rat bone marrow mesenchymal stem cells (BMSCs) to recipient BMSCs in vitro and in vivo. Here, we show that compared with normal BMSC, BMSCs transferred with mitochondria showed a stronger promotion on bone formation and on increasing bone mass when transplanted into the bone defect area in a rat cranial 5mm critical-sized model (n=3). After osteogenic induction for 14 days, BMSCs with transferred mitochondria showed a greater osteogenic differentiation capability ($p<0.05$), revealed by Alizarin red staining, PCR and Western Blot. BMSC migration and invasion abilities were also improved by mitochondria transfer detected by transwell test. Therefore, we conclude that mitochondria transfer has the ability to enhances osteogenesis, migration and invasion of BMSC in vitro, and transplantation of BMSCs with transferred mitochondria promoted bone defect healing process in vivo.

【关键词】 Mitochondria transfer; BMSC; osteogenesis; bone defect repair

The unique regulation of implant surface nanostructure on macrophages M1 polarization

何奕德　Zhang YuMei　Song Wen　空军军医大学口腔医院

【摘要】 The inflammatory response is the first and inevitable event after implant surgery in vivo, in which the macrophages M1 polarization is mediated. Numerous publications indicate that the

physical properties of implant surface nanostructure can influence macrophages M1 polarization status, whereas the regulation mechanisms have not been elucidated yet. Unlike the conventional biochemical factors that can directly bind to the cellular surface receptors or be transported into cytoplasm, the physical information of implant surface nanostructure can only be sensed by direct contact with cells. Therefore, we infer that the implant surface nanostructure may have unique regulation mechanisms. In this study, we compared the influences of the titanium implant surface coated with titania nanotubes on the surface (~100 nm diameter, NT-100) and the standard IFN-γ/LPS stimulation on the macrophages M1 polarization. Both the NT-100 surface and IFN-γ/LPS stimulation could induce macrophages M1 polarization, indicated by significant upregulation of M1-specific molecules including CD86, iNOS, CCR7 and IL-1β, without affecting the M2-specific molecules including CD206, Arg1 and IL-10. However, we found that the IFN-γ/LPS induced macrophages M1 polarization was mediated by the RBP-J-IRF8 pathway, whereas the NT-100 surface was related to the MAPK pathway, e.g. the JNK and Erk1/2 signaling. Our study demonstrated that the implant surface nanostructure has great potential to trigger the host inflammatory response through distinct pathways from conventional biochemical factors, which may remind us to re-consider the unique regulation mechanisms of nano surface on cell functions. Our finding offers a theoretical basis for titanium implant modification to benefit tissue integration.

【关键词】 Inflammatory response; surface nanostructure; macrophages polarization; RBP-J; MAPK

The Mechanism of Setd7 Regulating Chondrocyte Apoptosis in High Oxygen Partial Pressure.

贾筱诗　李茂泉　中山大学附属口腔医院
王记位　广州医科大学附属口腔医院

【摘要】 目的：炎症状态下，软骨组织易发生进行性降解及软骨细胞凋亡。有研究表明在骨关节炎的软骨组织中，氧分压较正常状态偏高，然而氧分压升高的机制及其对软骨细胞的作用尚未明确。我们前期发现氧分压升高后 Setd7 表达升高，本研究旨在阐明 Setd7 在调控炎性状态下软骨内氧分压升高及其诱导软骨细胞凋亡的机制，以探索预防软骨细胞凋亡的分子靶点。

方法：首先，用 TNF-α 刺激软骨细胞后提取上清诱导内皮细胞迁移，并检测软骨细胞趋化因子的表达改变。免疫组化检测衰老及 OA 小鼠关节软骨内 CD31 表达。在不同氧分压下，进行软骨细胞 RNA-seq，筛选出 Setd7 表达升高最明显。干扰 Setd7 表达后，western 验证 JAK/STAT 通路活化情况、HIF-1α 及糖代谢相关酶表达表达改变，检测软骨细胞凋亡情况。TNF-α 刺激软骨细胞后提取上清诱导内皮细胞迁移

结果：①衰老及 OA 小鼠关节软骨内 CD31 表达升高，TNF-α 刺激软骨细胞后，NF-kB 通

路激活，趋化因子表达升高，上清促进内皮细胞迁移；②氧分压升高后，JAK/STAT 通路激活，Setd7 表达升高；③沉默 Setd7 后，软骨细胞上清诱导内皮细胞迁移能力减弱，软骨细胞凋亡减少，HIF-1α 蛋白增加，无氧糖酵解相关酶表达升高。

结论：在炎症因子刺激下，软骨细胞能够诱导内皮细胞迁移，导致软骨氧分压升高，后者通过 JAK/STAT 通路促进 Setd7 表达，Setd7 一方面形成回路进一步调控氧分压，另一方面诱导软骨细胞凋亡。

【关键词】 氧分压；Setd7；软骨细胞凋亡；糖代谢

BMP4、BMP2 基因突变在先天性缺牙和骨异常患者中的检测和功能分析

刘　洋　王　皓　冯海兰　北京大学口腔医院修复科

【摘要】目的：在先天性缺牙患者中检测 BMP4、BMP2 基因突变，并探索突变携带者骨质情况。

方法：收集 120 名单纯型多数牙先天缺失患者或综合征型先天性缺牙患者，采集血液样本提取 DNA，对其中 18 名患者进行全外显子测序，47 名患者进行扩增子测序，筛查与先天性缺牙相关的 35 个基因，55 名患者进行 BMP4 基因常规 Sanger 测序。根据致病性预测筛选错义突变，Sanger 测序验证突变及家族共分离分析。体外转染野生型和突变质粒，Western Blot 试验检测 BMP 通路下游调节分子 SMAD1/5/9 蛋白磷酸化水平。对突变携带者进行骨密度检测及影像学检查测量。

结果：筛查到 3 个 BMP4 新突变：c.58G>A（p.Gly20Ser），c.614T>C（p.Val205Ala），c.326G>T（p.Arg109Leu）和 1 个以往检出过的变异：c.751C>T（p.His251Ty）。致病性预测 c.614T>C 和 c.751C>T 可能有功能影响。功能实验证实这两个突变型 BMP4 蛋白导致 BMP 通路下游调节分子 SMAD1/5/9 蛋白磷酸化水平低于野生型。携带者腰椎、髋部骨密度减低。

全外显子测序在 18 名先天性缺牙患者中检出 BMP2 错义突变 c.393A>T（p.Arg131Ser）。功能实验证实突变型 BMP2 蛋白导致 BMP 通路下游调节分子 SMAD1/5/9 蛋白磷酸化水平低于野生型。患者上颌骨发育不足、腭部形态异常，腰椎、髋部骨密度减低。

结论：具有功能影响的 BMP4 突变在先天性缺牙患者中检出率为 3.3%（4/120）。BMP4 及 BMP2 突变可能导致先天性缺牙及骨密度减低。

【关键词】 先天性缺牙；骨异常；基因变异；骨形态发生蛋白

17β-estradiol Enhances Occlusal Interference-induced Masseter Muscle Hyperalgesia via Upregulating Trigeminal Ganglion TRPV1 in OVX Rats

刘　云　谢秋菲　北京大学口腔医院

【摘要】 Objective: To investigate whether 17β-estradiol (E2) could enhance occlusal interference-induced masseter muscle hyperalgesia in rats, and whether this involved TRPV1 expression.

Methods: In the first part, four groups of adult rats (male-control, female-control, male-occlusal interference, female-occlusal interference, n=4) were prepared to compare the sex difference of masticatory muscle hyperalgesia following 0.4-mm-thick metal crowns insertion. In the second part, 30 female rats were randomly divided into 5 groups (n=6): a group of sham-ovariectomized rats and 4 groups of ovariectomized rats that treated with E2 by subcutaneously injections at doses of 0μg, 20μg, 80μg, and 200μg respectively for 10 days. All rats received occlusal interference on the last day. Head withdrawal thresholds (HWT) were examined using a modified electronic von-Frey anesthesiometer. Expression of TRPV1 in trigeminal ganglion (TG) was detected using western blotting. Immunofluorescence staining was used to reveal locations of estrogen receptors (ER-α, ER-β, and GPR30) and TRPV1 in TG. All differences between groups were examined by ANOVA.

Results: Both male and female rats exhibited decreasing HWT in temporal muscles and masseter muscles on both sides following occlusal interference insertion. The mechanical hyperalgesia peaked from 5d to 7d, with females more sensitive than males ($P<0.05$). E2 decreased HWT in masseter muscle and exacerbated occlusal interference-induced nociceptive response in ovariectomized rats in a dose-dependent manner as compared with 0μg group ($P<0.05$). Western blotting indicated that TRPV1 expression was up-regulated in TG with increasing dosage of E2. In addition, ER-α, ER-β and GPR30 were co-localized with TRPV1 in intact female rats TG neurons.

Conclusion: Our study suggests the high levels of E2 may be a risk factor for occlusal interference-induced masseter muscle hyperalgesia in rats, and the up-regulation of TRPV1 in TG related to E2 may explain the great masseter muscle hyperalgesia in female rats.

【关键词】 Estradiol；Orofacial pain；Nociception；Trigeminal ganglion；TRPV1

Improving the wear performance of feldspathic veneering porcelain by ion-exchange strengthening

蒙　萌　空军军医大学口腔医院修复科

【摘要】 Objectives: The present study examined the improvement of wear performance of feldspathic veneering porcelain caused by ion-exchange.

Methods: Bar (N=90, n=10) and disk (N=30, n=6) specimens were prepared using IPS classic as feldspathic veneering porcelain. After ion-exchanged by melt KNO3 at two temperature with different time, the bars were tested for three-point flexural strength, hardness and fracture toughness. The disks paired with zirconia antagonist were tested by a pin-on-disk tribometer with 10N up to 5.4　105 wear cycles in artificial saliva. Wear analysis of porcelain and zirconia was performed using 3D profilometer and analyzed with one-way analysis of variance and Tukey’s post-hoc pairwise comparison procedures. Worn surfaces were examined with scanning electron microscopy.

Results: The lower exchange temperature (380℃) exhibited a better mechanical properties, specifically, it showed an obvious advantage with prolonging the exchange time. The time-dependent wear behavior of the porcelain showed running-in and steady wear stage with characteristic microstructure of worn surfaces, and the 380℃/64h group which is with a thick better ion-exchange layer presented the best wear performance.

Conclusion: The feldspathic veneering porcelain with low temperature and longtime ion-exchange may be an effective way to resist wear.

【关键词】 Feldspathic veneering porcelain; Ion-exchange; Mechanical properties; Wear performance

两种后牙贴面预备釉质超微结构观察与有限元分析

沈冬妮　傅柏平　浙江大学医学院附属口腔医院

贴面是一种覆盖后牙咬合面的无固位形修复体，Mange 等认为是超嵌体的一种特殊类型。在微创修复理念越来越得到重视的当下，贴面能减少对牙体组织的预备量，成为后牙保存性修复的有效替代方案，尤其是对于严重磨损或酸蚀的病变。然而，贴面的临床应用难点包括有效的粘接固位效果、修复体的抗折性能等。本实验探究两种边缘预备方式下釉质微观形貌及贴面应力分布，为寻求一种减少应力集中，增加釉质粘接效果的贴面边缘预备设计提供参考。实验组采用贴面边缘浅凹形预备，对照组为边缘对接式预备，(1) 扫描电镜（SEM）分别观察牙备后

釉质超微结构。(2) 三维有限元分析（Finite element analysis,FEA) 采用 Micro-CT 扫描法构建上颌前磨牙三维模型，用 Rhino 软件设计𬌗贴面预备。在有限元分析软件 Abaqus 中分析两组𬌗贴面设计的应力分布情况。结果显示𬌗贴面边缘浅凹形预备相比于对接式预备能增加垂直向釉柱暴露量，同时减少修复体与预备牙的应力集中。

【关键词】 𬌗贴面，釉质形貌，三维有限元分析

钛种植体表面自组装缓释系统的构建及其增强骨结合的研究

邢鹤琳　邹石泉　江青松　首都医科大学附属北京口腔医院

【摘要】 目的：制备新型靶向缓释 CTSK-siRNA 的种植体，促进骨质疏松条件下的骨结合，为改善骨质疏松患者种植体修复提供新策略。

方法：结合种植体表面改性和相关基因药物的研究基础，利用层层自组装技术将 CTSK-siRNA 纳米金颗粒装载于种植体表面；系统分析此新型种植体的表征；结合细胞学和动物实验观察此新型种植体缓释 CTSK-siRNA 的作用及在骨质疏松条件下的骨结合能力。

结果：层层自组装技术可将 CTSK-siRNA 纳米金颗粒成功装载于钛片及纯钛种植体表面，实现种植体的改性；体外实验揭示改性后的钛片能够缓释 CTSK-siRNA，进而抑制接种于钛表面的破骨前体细胞血小板源性生长因子 BB（PDGF-BB）的合成和分泌，进而影响骨髓间充质干细胞的成骨分化和内皮前体细胞的成血管作用。体内动物实验揭示靶向缓释 CTSK-siRNA 种植体能够促进骨质疏松条件下种植体骨结合。

结论：层层自组装技术创建的新型靶向缓释 CTSK-siRNA 种植体具有促进骨质疏松条件下种植体骨结合能力。

【关键词】 金纳米颗粒；骨结合；基因治疗；CTSK

Epithelial Wnt10a is essential for tooth root furcation morphogenesis

余　淼　冯海兰　韩　冬　北京大学口腔医院

【摘 要】 WNT10A plays a crucial role in tooth development, both bi-allelic WNT10A mutation patients and Wnt10a-/- mice show taurodontism. However, whether epithelial or mesenchymal WNT10A controls the initiation of root furcation formation, and the functional significance of

WNT10A in regulating tooth root morphogenesis remain unclear. In this study, we investigated how Wnt10a affected tooth root development by generating different tissue-specific Wnt10a

conditional knockout mice. Wnt10a-knockout in whole tissue (EIIa-Cre;Wnt10aflox/flox) and dental epithelium (K14-Cre;Wnt10aflox/flox) both developed an absence or apical position of root furcation in mandibular molars, a phenotype that resembled taurodontism. Immunofluorescent staining of E-Cadherin and EdU revealed a decreased epithelial cell proliferation at the cervical region of first mandibular molar in K14-Cre;Wnt10aflox/flox mice at post-natal day 0 (PN0), right before the initiation of root morphogenesis. Interestingly, we found an increased mesenchymal cell proliferation in the pulp of putative root furcation region of first mandibular molar in K14-Cre;Wnt10aflox/flox mice at PN4 and PN7. RNA-seq indicated that among the Wnt ligands with high endogenous expression level in tooth germ at PN4, Wnt4 was increased after epithelial knockout of Wnt10a. By immunofluorescent staining, we confirmed mesenchymal expression of Wnt4 and active-β-catenin in the putative root furcation region, where the overgrowth of dental pulp took place, was significantly increased in K14-Cre;Wnt10aflox/flox molars. Furthermore, after suppressing the elevated Wnt4 level in K14-Cre;Wnt10aflox/flox molars by Wnt4 shRNA adenovirus and kidney capsule graft, the root furcation defect was partially rescued. Taken together, our study provides the first in vivo evidence that epithelial Wnt10a guides the root furcation formation, and demonstrates that epithelial Wnt10a plays a crucial role in controlling the organized proliferation of adjacent mesenchymal cells by regulating the proper Wnt4 expression during root furcation morphogenesis.

【关键词】 Wnt10a; taurodontism; proliferation; root furcation; tooth root development

SGCs 中 MAPKs 通路在 SP 调控的口颌面炎性疼痛中的作用

张艳艳　四川大学华西口腔医（学）院

沈颉飞　四川大学华西口腔医院

【摘要】 背景：神经元和胶质细胞之间通过一系列信号分子及其受体形成交互对话信号网络，影响神经功能。三叉神经节（TG）神经元（TGNs）与卫星胶质细胞（SGCs）之间的交互对话及 SGCs 功能活化在 TG 的外周致敏中扮演重要角色。P 物质（SP）作为调控疼痛的重要神经递质和神经调质，广泛分布在外周神经系统中。炎性条件下，TGNs 合成和分泌 SP 增加，但其对 SGCs 的作用尚未完全阐明。结合相关领域研究最新进展，本课题提出：SP 可能通过调控 SGCs 活化、MAPKs 信号通路激活、细胞因子产生及核内基因表达等途径参与炎性口颌面炎性疼痛的调控。

方法：通过在 SD 大鼠腮胡区注射 CFA 用于诱导炎性疼痛模型。急性分离 TG，用免疫荧光技术及 Western Blot 检测 TG 中 GFAP、MAPKs 的分布及表达。在 SD 大鼠 TG 内注射 NK-1 拮抗剂、MAPKs 抑制剂检测 TG 内 IL-1β、TNF-α 的表达及行为学变化。同时进行体外验证。

结果：（1）CFA 诱发 SD 大鼠口颌面疼痛异常且持续至术后 5 天；（2）SP 促进 SGCs 中 GFAP、p-MAPKs、NK-1、IL-1β 及 TNF-α 合成分泌及表达（P<0.05）；（3）L703,606、

U0126、SB203580 可抑制炎性条件下 SP 诱导的 NK-1、IL-1β、TNF-α 上调及口颌面疼痛异常（P ＜ 0.05）。

结论： SP 通过结合 SGCs 膜上的 NK-1R 激活胞内 ERK1/2 和 p38 途径活化 SGCs，一方面促进 SGCs 内 IL-1β、TNF-α 的合成分泌，另一方面促进 SGCs 中形成 SP-NK-1R 正反馈环，参与口颌面炎性疼痛的调节。

【关键词】 三叉神经节；卫星胶质细胞；P 物质；炎性疼痛 ; 神经激肽受体 -1；丝裂原活化蛋白激酶；

种植体表面掺锶抑制成脂并促进老年大鼠骨整合的研究

周　川　浙江大学医学院附属口腔医院

【摘要】 研究背景

增龄性骨质疏松患者骨髓间充质干细胞（BMSCs）数量和成骨活性下降，骨髓脂肪增加，牙种植修复普遍存在初期稳定性差、骨愈合延迟和种植失败率高等问题。锶在临床用于治疗骨质疏松症，具有促进成骨、抑制成脂的作用，但其具体机制尚不明确。将锶引入种植体表面改性有利于其在局部发挥促成骨作用。

研究内容

本研究采用喷砂酸蚀结合水热法合成法在纯钛表面构建掺锶微纳米多孔钛表面（Sr-SLA），以喷砂酸蚀后蒸馏水中保存 4 周的 modSLA 钛表面作为对照。通过细胞实验检测 Sr-SLA 表面对衰老 BMSCs 内氧压力和成脂分化的影响；通过老年大鼠胫骨种植体植入模型观察 Sr-SLA 种植体对骨髓脂肪细胞形成的影响和种植体早期骨整合效果。

研究结果

1. Sr-SLA 具有微纳米多孔仿生形貌，并能持续释放锶离子。

2. Sr-SLA 能抑制其表面衰老 BMSCs 内活性氧（ROS）和氧自由基水平，提升谷胱甘肽过氧化物酶（GSH-Px）含量，从而平衡细胞内氧化还原状态。

4. Sr-SLA 能抑制其表面衰老 BMSCs 内成脂分化转录因子和标记物表达。

3. Sr-SLA 能促进老龄大鼠种植体骨整合形成（2 周和 8 周），并对骨髓脂肪形成具有一定抑制作用。

结论：MNT-Sr 对衰老的干细胞具有抗氧化和抑制成脂分化的作用，能促进骨整合早期形成，在老年患者牙种植治疗中具有良好的应用前景。

【关键词】 锶；种植体；骨整合；成脂分化；间充质干细胞

大气压冷等离子体提高龋影响牙本质粘接性能的研究

齐　璇　北京大学口腔医学院
朱晓鸣　北京大学口腔医院第二门诊部

【摘要】 目的：研究大气压冷等离子体处理对人工龋影响牙本质粘接强度的影响。方法：收集新鲜拔除的、无龋坏的、完整的第三磨牙，垂直于牙长轴去除合面釉质、暴露中层牙本质，一部分未经 pH 循环处理的样本为健康牙本质对照组 (SD)，另一部分样本经过 14 天的 pH 循环制备得到人工龋影响牙本质，随机分为龋影响牙本质对照组 (CAD)、实验组 (CAD-P) 两组。SD 组及 CAD 组无处理，CAD-P 组采用介质阻挡放电大气压冷等离子体处理 30s。采用场发射扫描电镜（FESEM）观察大气压冷等离子体处理对龋影响牙本质表面形貌的影响。采用微拉伸实验测定即刻粘接强度。结果：（1）扫描电镜观察显示，SD 组和 CAD 组表面覆盖玷污层，牙本质小管大部分关闭，横断面可见 CAD 组部分牙本质小管内部矿化栓堵塞。大气压冷等离子体处理后大部分牙本质小管开放，表面更加清洁，横断面可见对牙本质小管内部矿化栓作用不明显。（2）牙本质 - 树脂即刻微拉伸强度结果显示，SD 组为（50.1±0.94）MPa,CAD 组为（35.5±1.00）MPa，CAD-P 组分别为（49.2±0.70）MPa，CAD 组显著低于 SD 组和 CAD-P 组，SD 组和 CAD-P 组间无统计学差异（$P < 0.05$）。结论：大气压冷等离子体处理对龋影响牙本质表面玷污层具有清洁作用，可以有效提高龋影响牙本质 - 树脂的即刻粘接性能。

【关键词】 大气压冷等离子体；龋影响牙本质；牙本质粘接

大块充填树脂修复磨牙 MOD 缺损的边缘渗漏及牙尖形变研究

杨　洋　北京大学口腔医学院

【摘要】 目的：评价大块充填树脂在直接修复磨牙 MOD 缺损后边缘渗漏和牙尖形变的情况，并与普通复合树脂直接充填和可切削复合树脂间接修复进行对比。方法：选择离体磨牙制备 MOD 缺损（4mm*4mm），分为三组：BF 组（Sonicfill2 大块树脂整块充填），CR 组（Herculite 通用型复合树脂分层充填），CA 组（润瓷可切削复合树脂 CAD/CAM 嵌体修复）。冷热循环老化后进行染色切片，体视显微镜下测量各组合面、邻面边缘渗漏深度。3D 轮廓测量仪测量各组充填 / 修复前后牙冠颊舌宽度差值为牙尖形变量，并在牙体预备后、充填即刻及冷热循环老化后三次观察轴面釉质裂纹，计算新增釉质裂纹比例。结果：BF 组合面平均渗漏深度为 524.5±196.3 μm，与 CA 组无显著性差异，邻面渗漏深度 825.1±335.6 μm，大于 CA 组；CR 组合面及邻面渗漏深度均最大（$p<0.05$）。BF 组充填前后牙冠宽度差值为 0.510±0.086mm，与 CA 组无显著性差异

（p=0.08），明显小于 CR 组（p ＜ 0.05）。BF 组充填后即刻釉质裂纹增加 20%，老化后裂纹增加 40%，CR 组分别增加 55% 及 75%，CA 组分别增加 10% 及 25%。结论：采用大块充填树脂直接法修复磨牙 MOD 缺损具有较小的边缘渗漏和牙尖形变，明显优于普通复合树脂，与间接法树脂修复在合面边缘渗漏和牙尖形变方面具有一定可比性。

【关键词】 大块树脂；牙体缺损；边缘渗漏；牙尖形变

Glass-ceramic resin-bonded fixed partial dentures for replacing a single premolar tooth: A prospective investigation with a 4-year follow-up

张新艳　山东大学口腔医学院

【摘要】 Statement of problem. Resin-bonded fixed partial dentures (RBFPDs) are a reliable treatment option for the replacement of a single missing tooth. Glass-ceramic may be a promising material for the fabrication of RBFPDs, but clinical verification has been lacking.

Purpose. The purpose of this prospective clinical study was to evaluate the outcomes of glass-ceramic RBFPDs on participants with a single missing premolar.

Material and methods. Twenty participants were treated with 2-retainer RBFPDs. These RBFPDs were made of lithium disilicate glass-ceramic (IPS e.max Press; Ivoclar Vivadent AG) and designed with improved C-shaped retention. These prostheses were evaluated at 6 months, 12 months, and annually thereafter, and were classified as survival or failure. Analysis was performed with the Kaplan-Meier analysis (95% confidence interval). Modified United States Public Health Service (USPHS) criteria were used to rate the clinical performance. Parameters assessed were fracture, marginal integrity, marginal discoloration, color of restoration, secondary caries, and abutment looseness mobility.

Results. Twenty RBFPDs were provided, 9 in the maxilla and 11 in the mandible. The mean observation time was 49.2 months. Nineteen RBFPDs were evaluated as having survived during the observation period with some acceptable marginal discoloration, 1 RBFPD had to be replaced because of fracture and secondary caries and was evaluated as a failure. The Kaplan-Meier analysis revealed a survival rate of 95% after a 4-year observation.

Conclusions. The glass-ceramic RBFPDs in this study displayed a good survival rate and clinical performance, indicating that glass-ceramic RBFPDs might be a promising approach for the short-term replacement of a single premolar. However, further investigations are needed to determine the long-term outcome.

【关键词】 glass-ceramic; resin-bonded fixed partial dentures; premolar loss; dentition defect; minimally invasive dentistry

口 腔 预 防

生物钟调控干细胞稳态影响骨发育

周　鑫　陈莉莉　华中科技大学同济医学院附属协和医院

【摘要】 目的：干细胞具有自我更新、复制和多向分化的能力，在青少年生长发育期，由于成骨量发生明显变化，骨髓间充质干细胞（BMSCs）分化异常可导致多种临床疾病，如成骨不全、骨龄异常、骨性错颌畸形等。生物钟调控多项生命活动，最新的研究表明：生物钟基因在成体干细胞中表达，但是生物钟如何调控 BMSCs 的稳态及命运，目前阐述得不是很清楚。

方法：干细胞同步化后，通过 PCR 实验，检测原代 BMSCs 不同时间点生物钟基因的表达；将核心生物钟基因 BMAL1 敲除后，利用碱性磷酸酶染色和茜素红染色检测干细胞成骨分化能力的差异；利用 PCR 及 Western Blot 检测成骨相关分子 BMP2、OCN 的表达；通过番红 - 固绿染色检测 BMAL1 对 BMSCs 成软骨分化的影响；β - 半乳糖苷酶染色检测 BMAL1 缺失对 BMSCs 衰老的影响；免疫荧光染色检测衰老相关标志分子 P16 的表达。

结果：将 BMSCs 同步化后，检测不同时间点生物钟基因的表达，显示钟基因 Bmal1，Per3，Rev – erbα 的 mRNA 具有节律性表达。将核心生物钟基因 BMAL1 敲除后，BMSCs 成骨分化能力降低；成骨相关分子 BMP2、OCN 的表达降低。并且 BMAL1 敲除后，BMSCs 成软骨分化能力也降低。同时，BMAL1 敲除后，BMSCs 增殖能力下降，衰老加速，免疫荧光结果显示：衰老相关标志分子 P16 的表达较高。

结论：骨髓间充质干细胞不仅表达生物钟基因，而且生物钟在干细胞稳态维持中起重要作用，我们的研究为骨组织发育性疾病的防治提供了新的防治思路。

【关键词】 生物钟；骨发育；干细胞稳态

口腔正畸学

Force-induced hydrogen sulfide activates M1 macrophages to promote orthodontic tooth movement via STAT-1

何丹青　北京大学口腔
刘福良　赛德阳光口腔诊所
周彦恒　北京大学口腔医院

【摘要】 Background: In this study, we investigated the regulatory role of force-induced H2S on macrophage polarization and its contributions to OTM.

Materials and Methods: C57 mice were divided into four groups, control group, Force group, Force+HA, and Force+GYY4137. Mechanical force was applied for 7 days; HA or GYY4137 was administered every other day since one day before force application. Each group comprised 5-6 mice. After 7 days, the maxilla was harvested to observe the distance of tooth movement. Immunofluorescence staining was used to observe the changes of macrophages in the periodontal ligament. The supernatant of force-loaded periodontal ligament stem cell (PDLSCs) with or without HA was added to macrophages to observe the changes of macrophages. In addition, the supernatant of force-loaded PDLSCs with or without STAT-1 inhibitor was added to macrophages to detect the mechanism.

Results: Mechanical force application promoted the expression of cystathionine-β-synthase (CBS), which is one of the H2S-generating enzymes. It also increased the number of M1 macrophages which stained positive for CD68 and nitric oxide (NO) in the compression side of the periodontal ligament. Injection of CBS inhibitor or H2S donor could further repress or increase the number and cytokine expression of M1 macrophages, and the distance of OTM. Mechanistically, force-loaded periodontal ligament stem cells (PDLSCs) enhanced H2S production, which increased the expression of M1-associated cytokines in macrophages. These effects could be blocked by the administration of CBS inhibitor HA. Moreover, force-induced H2S steered M1 macrophage polarization via the STAT-1 signaling pathway in vitro and in vivo.

Conclusion: These data suggest that force-stimulated PDLSCs produce H2S to polarize macrophages towards the M1 phenotype via the STAT-1 signaling pathway, which contributes to the OTM process.

【关键词】 hydrogen sulfide；macrophage polarization；orthodontic tooth movement；mechanical force

长链非编码 RNA MIR31HG 在间充质干细胞定向分化中的作用机制及应用研究

黄一平　郑云飞　李巍然　北京大学口腔医院

【摘要】 目的：探索长链非编码 RNA（lncRNA）MIR31HG 对间充质干细胞定向分化的作用及其机制，并探索以 MIR31HG 为靶点改性钛材料表面增强干细胞成骨分化运用于骨组织工程学。

方法：通过 FISH 检测 MIR31HG 定位。通过 qRT-PCR 检测干细胞成骨成脂分化过程中 MIR31HG 表达量变化。通过慢病毒建立稳定敲低及过表达 MIR31HG 的干细胞，并进行定向诱导，通过 ALP、茜素红、油红 O 染色及成骨成脂标志物检测干细胞定向分化能力的变化。通过蛋白印迹、染色质免疫共沉淀等实验方法研究 MIR31HG 的分子作用机制。通过将壳聚糖 /siRNA 复合物负载到材料表面制备 siMIR31HG 改性的钛材料。对材料进行表征和活性测定。通过裸鼠体内实验，检测 siMIR31HG 改性的钛材料在体内异位成骨能力。

结果：MIR31HG 在细胞质和细胞核中均有分布。干细胞成骨分化过程中 MIR31HG 表达量逐步下调，而在成脂分化过程中表达量上调。敲低 MIR31HG 促进干细胞成骨分化、抑制成脂分化，过表达 MIR31HG 抑制干细胞成骨分化、促进成脂分化。机制上，MIR31HG 直接与 IkBa 相结合参与 NF-kB 的激活介导炎症下的成骨抑制。另一方面，敲低 MIR31HG 后， FABP4 的启动子区组蛋白 H3K4 三甲基化及 H3 乙酰化水平下降，FABP4 转录抑制，成脂分化受到抑制。将敲低 MIR31HG 的 siRNA 负载到钛材料表面。siRNA 负载效率接近 70%，siRNA 在第一天释放 80% 左右，第 7 天几乎达到 100%。siMIR31HG 改性的钛种植体没有明显的细胞毒性，同时明显增强间充质干细胞的成骨活性。

结论：敲低 MIR31HG 促进干细胞成骨分化，抑制成脂分化。siMIR31HG 生物功能化钛种植体可用于临床上以获得更好骨整合。

【关键词】 长链非编码 RNA；MIR31HG；干细胞定向分化；钛材料表面改性

Bidirectional regulation of Interleukin-17 on osteogenesis and osteoclastogenesis

廖崇珊　华咏梅　同济大学附属口腔医院

杨雁琪　香港大学

【摘要】 Bone remodelling is a strictly regulated dynamic process of bone formation and resorp-

tion. The cytokine interleukin (IL)-17 critically orchestrates the activation and differentiation of both osteoblasts and osteoclasts. Osteocytes, which are the most abundant cells in bone, have long been thought to orchestrate bone remodelling in response to the flow of extracellular fluid by detecting and coordinating the function of osteoblasts and osteoclasts. However, the contribution of IL-17 to osteocyte-related bone resorption and/or formation remains unclear.

To investigate the role of IL-17 in osteoclastogenesis, we tested the osteocyte-like MLO-Y4 cell line and bone marrow macrophages (BMMs). It was found that IL-17 activated osteoclastic differentiation in the co-culture system of MLO-Y4 and BMMs, and this differentiation was attenuated by shear stress. Additionally, the extracellular signal-regulated kinase (ERK)1/2 and the signal transducer and activator of transcription (STAT)3 pathways in osteocytes were suppressed by IL-17 but activated by shear stress. The intercellular EphA2-ephrinA2 and EphB4-ephrinB2 signalling pathways played important roles in the IL-17-dependent osteoclastic differentiation.

To study the role of IL-17 in osteogenesis, we tested mesenchymal stem cells (MSCs), MC3T3-E1 pre-osteoblasts, MLO-A5 post-osteoblasts and MLO-Y4 osteocytes. It was found that IL-17 induced the osteogenesis of the MSCs and was further promoted when co-cultured with osteocytes. The inflammatory factors IL-6 and IL-1β played important roles in the IL-17-dependent differentiation by activating the phosphorylation of signalling pathways AKT, STAT3 and ERK1/2 in the MSC niche.

Our results indicate that IL-17 plays various roles in the different stages of osteogenesis and osteoclastogenesis, and osteocytes pivotally regulated the IL-17-dependent differentiation. These findings provide important insights into the mechanisms underlying osteoclastic and osteoblastic differentiation. IL-17 modulation-based approaches could be developed as novel therapeutic strategies for enhancing bone remodelling efficiency and stability.

【关键词】 IL-17；Osteocytes；Bone remodeling；Osteogenesis；Osteoclastogenesis

外源性 TGF-β1 与 PDGF-BB 联合应用对正畸牙压力侧 Pyk2 蛋白和基因的影响

梅　梅　遵义医科大学附属口腔医院

【摘要】 目的：探讨外源性生长因子 -β1 与外源性血小板衍生生长因子 -BB 联合应用对牙周组织破骨细胞内 Pyk2 的表达影响。方法：160 只 SD 大鼠随机分为 2 组，建立正畸牙移动模型。A 组注射含 rhTGF-β1 与 rhPDGF-BB 的混合液 0.1 mL，B 组注射相同容量的 PBS。加力后 1、4、7、10、14 d 分别处死每大组的 1 小组大鼠。测量牙移动距离变化，TRAP 染色行破骨细胞计数，Pyk2 蛋白和基因水平分别用免疫组织化学染色法和 RT-PCR 检测。采用 SPSS19.0 软件包对数据进行统计学分析。结果：2 组牙移动距离在第 4、7、10、14 天均具有统计学差异（P<0.05）；

A 组压力侧破骨细胞计数明显高于 B 组，除第 14 天外，其余各时间点均具有差异 (P<0.05)；A 组 Pyk2 蛋白和基因表达均比 B 组高，2 组均在第 7 天达到最高峰，除第 1 天外，其余时间点 Pyk2 蛋白表达均具有统计学差异（P<0.05）；第 4、7 天，2 组 Pyk2 基因表达均具有统计学差异（P<0.05）。结论：外源性 TGF-β1 与 PDGF-BB 联合应用从蛋白和分子水平上调了正畸牙牙周组织压力侧 Pyk2 的表达，这可能是加速正畸牙移动速率的原因之一。

【关键词】 rhTGF-β1；rhPDGF-BB；正畸牙；破骨细胞；Pyk2

Three-Dimensional Mechanical Microenvironment Enhanced Osteogenesis Potential of Mesenchymal Stem Cell-Derived Exosomes

苏晓霞　四川大学华西口腔医院

【摘要】 Objective: Exosomes secreted by Mesenchymal stem cells (MSCs) emerge as significant media of cellular communication and key components in cell-free therapy in regenerative medicine. As mechanical sensitive cells, MSCs respond to the mechanical microenvironment to orchestrate their function and behavior. But whether biomechanical cues affect the exosomes of MSCs remains unknown. Thus, this study aims to explore the functional change of exosomes secreted by MSCs in periodontium in response to mechanical environment.

Methods: PDLSCs were cultured in a 3D strain microenvironment model engineered with microscale magnetically stretched collagen hydrogels. The morphology, particle distribution, marker protein expression of exosomes secreted by PDLSCs cultured in different mechanical environment were analyzed. The pro-osteogenesis property of exosomes on human bone marrow mesenchymal stem cells (HBMSCs) was evaluated through cell viability, cell proliferation, cell migration and cell differentiation assay. Next, exosomes were locally injected into alveolar bone defect in SD rat models to evaluate their function in osteogenesis in vivo. To explore the mechanism of the effect of biomechanics on exosomes, miRNA expression in exosomes were analyzed by high-throughput miRNA Sequencing.

Results: Detailed characterization revealed that exosomes secreted by PDLSCs in different mechanical microenvironment were with similar morphology, particle distribution and surface markers. Exosomes secreted by PDLSCs under mechanical stimulation were more prone to be endocytosed by hBMSCs and more potent in inducing proliferation and migration of hBMSCs, when comparing with PDLSCs under non-stress environment. Alizarin red staining and molecular analysis confirmed that treatment of exosomes secreted by PDLSCs under mechanical stimulation lead to a significant increase in osteogenic differentiation of hBMSCs in vitro. MicroRNA sequencing revealed significant

differences in miRNA expression between exosomes secreted by PDLSCs with or without mechanical stimulation.

Conclusion: Exosomes secreted by PDLSCs in a mechanical microenvironment are more potent in promoting bone formation. Our findings reveal biomechanical cues profoundly affect the bio-activity of exosomes secreted by PDLSCs, which providing a foundation for using mechanical microenvironment to control the characteristics and enhance the osteo-inductive functions of exosomes in cell-free therapy for bone regeneration.

【关键词】 exosomes；mechanical microenvironment；MSCs；osteogenesis

不恰当的矫治力导致牙根吸收的作用机制研究

谢炎伶　唐清明　陈莉莉　华中科技大学同济医学院附属协和医院

【摘要】 目的：正畸诱导的炎症性牙根吸收（OIIRR）是常见的正畸临床并发症，与牙周膜细胞等效应细胞的作用及其产生的炎症因子密切相关。不同强度的力可导致不同程度的牙根吸收，其机制尚未完全阐明。生物钟系统是几乎所有生理活动的主要调节因子，其破坏可对健康产生严重后果，例如炎症。研究机械力，生物钟与 OIIRR 之间的关系，从新的角度阐明 OIIRR 的机制具有重要的临床意义。

方法：用轻力（30g）和重力（100g）牵拉大鼠上颌第一磨牙，收集标本检测牙根吸收。使用 Flexcell FX-5000T™ 分别对人牙周膜细胞施加轻力（5%）和重力（20%），检测炎症因子的表达量。检测轻力和重力下生物钟基因在体内和体外的表达变化，并探索机械力、生物钟与 OIIRR 之间的机制。

结果：重力下大鼠的牙根吸收比轻力下更严重。重力处理的细胞中的炎症因子水平高于轻力处理的细胞。在不同强度的力下，牙槽骨组织和牙周膜细胞的生物钟基因表达均产生了变化，这些变化与炎症反应密切相关。机械力导致钟基因表达变化的机制与 ERK 信号通路相关。

结论：机械力、生物钟基因与 OIIRR 密切相关，机械力影响生物钟基因的表达，进而影响炎症反应与 OIIRR。

【关键词】 机械力；生物钟；正畸诱导的炎症性牙根吸收（OIIRR）

Signal Transducer and Activator of Transcription 3 is critical for osteoclast differentiation and bone remodeling

杨屹羚　Dai Qinggang　Jiang Lingyong　上海交通大学医学院附属第九人民医院

【摘要】 The remodeling of alveolar bone is the basis of orthodontic treatment, periodontal treatment, and dental implantation. Signal Transducer and Activator of Transcription 3 (STAT3) plays a central role in cell survival and function. STAT3 has been demonstrated to participate in maintenance of bone homeostasis in osteoblasts, but its role in osteoclasts in vivo remains undefined. Here we generated a conditional knockout mouse model in which Stat3 was deleted in osteoclasts by Cathepsin K-Cre (Ctsk-Cre). In this model, osteoclast-specific Stat3 deficiency caused increased bone mass in mice, which was attributed to impaired bone catabolism by osteoclasts. Stat3-deficient bone marrow macrophages (BMMs) showed decreased expression of nuclear factor of activated T cells, cytoplasmic 1 (NFATc1) and reduced osteoclast differentiation, determined by decreases in osteoclast number, TRAP activity and expression of osteoclast marker genes. Enforced expression of NFATc1 in Stat3-deficient BMMs rescued the impaired osteoclast differentiation. Mechanistically, we revealed the novel cooperation of STAT3 and c-Fos to drive the expression of NFATc1. Furthermore, pharmacological inhibition of STAT3 by AG490 also impaired osteoclast differentiation and formation in a similar way to gene deletion of Stat3. In summary, our data provided the first evidence that Stat3 was significant in osteoclast differentiation and bone homeostasis in vivo, and may be identified as a potential pharmacological target for the treatment of bone metabolic diseases.

【关键词】 alveolar bone remodeling; Osteoclasts; STAT3; transgenic mice

舌侧支抗

胡　波　宋锦璘　重庆医科大学附属口腔医院

【摘要】 支抗在口腔正畸学是一个很重要的概念，是正畸医师移动错位牙齿的“基石”。通常希望矫治牙按设计要求的方向及程度移动，而支抗牙不发生移动或者有控制的移动，因此支抗控制至关重要。大多数正畸矫治装置或技术的发明与革新都与支抗控制有关。传统 Nance 弓、舌弓、横腭杆（transpalatal arch，TPA）等中度支抗装置在临床中使用较为广泛。其主要采用成品带环焊接而成，缺乏个性化、体积大、与磨牙形态难以匹配，这给正畸医生和患者带来了一系列潜在的不利影响。为解决这些潜在问题，笔者应用 3D 打印技术研发设计出一种舌侧支抗装置，并获批

实用新型专利两项。该新型支抗装置能有效减轻医生临床工作量和患者痛苦，提高正畸矫治效率，利于清洁卫生，为临床提供了新思路，值得进一步推广应用。

【关键词】 支抗；传统支抗；3D 打印；舌侧支抗；专利

上颌腭部结构重叠的准确性和可重复性验证

潘一琛　许天民　陈　贵　北京大学口腔医学院

【摘要】 目的：本研究旨在验证腭部区域结构重叠的稳定性，并与 CBCT 前颅底结构体素重叠进行对比验证其准确性和可重复性。

方法：研究纳入 20 名成年患者治疗前后 CBCT(C1，C2) 和模型 (M1，M2)。分别采用 CBCT 体素重叠和腭部结构重叠两种方法进行重叠。在 Dolphin 中，将 C1 和 C2 进行前颅底区域体素重叠，导出在新位置上的治疗后 CBCT 为 C2’。建立 C1 和 C2’的硬组织结构建立表面模型（要求清晰显示上颌牙冠结构），并导出为 STL 格式。将 M1 和 M2，分别与 C1 和 C2’进行重叠。再导入一个新的治疗后模型记为 M2’，将 M2’ 与 M1 进行腭部结构重叠。在模型上标记分别标记两侧上颌第一磨牙的近中颊尖和两侧上颌中切牙的切缘中点，分别作为对应牙的标记点。测量 M2 和 M2’模型上标志点在 x、y、z 轴上的偏差。随机选择 10 名患者，由第二个测量者重复模型与 CBCT 重叠及腭部结构重叠，分别计算各个测量值两个步骤的 ICC。

结果：M2、M2’模型上所有标记点的平均偏差小于 0.3mm，与 0 没有统计学差异。在模型和 CBCT 重叠中，所有 ICC 都大于 0.99。在腭部结构重叠中，测量者间 ICC 在 0.85-0.99 之间，测量者内 ICC 在 0.88—0.99 之间。

结论：在成人，对数字化模型利用上颌腭部结构重叠可以得到与 CBCT 体素重叠几乎相同的重叠结果。方法准确性和重复性高。

【关键词】 牙骀数字模型；腭部重叠；CBCT；体素重叠

下前牙内收过程中的牙槽骨改建及其与牙移动的比率研究

徐静晨　四川大学华西口腔医学院

陈　嵩　四川大学华西口腔医院

【摘要】目的：研究倾斜或控根内收下前牙后，患者下前牙区牙槽骨厚度，以及牙根颈部、中部、根尖部唇舌侧骨皮质改建状况；研究不同垂直骨面型患者牙槽骨改建与牙齿移动比率。

方法：纳入拔除下颌第一前磨牙解除下前牙唇倾的病例 103 例，根据牙齿内收方式分为倾斜内收组（57 例）与控根内收组（46 例），选取其正畸治疗前后的头颅侧位片，以下颌平面（mandibular

plane, MP）及过下颌角点与 MP 平面垂直的平面为参考平面，分别测量下前牙切缘、颈部、根尖部在矢状向上内收前后的移动距离，下颌前牙区牙根颈 1/3、中 1/3、尖 1/3 处唇舌侧牙槽骨厚度以及相应层面唇舌侧牙槽骨骨皮质点改建量。根据治疗前患者下颌平面与眶耳平面的夹角（MP-FH）将患者分为高角组、均角组、低角组，分别计算三组患者牙槽骨皮质点改建量与牙齿内收移动的比率（B/T）。利用 SPSS 20.0 对数据进行统计分析。

结果：倾斜内收及控根内收组均实现了下前牙的内收和直立，两组治疗后三个层面的牙槽骨总厚度、牙根颈部和中部唇侧牙槽骨厚度，及牙根颈部舌侧牙槽骨厚度均有显著减小（$P < 0.05$）。倾斜内收组治疗后牙根颈部唇舌侧骨皮质点向舌侧改建，而牙根中部及根尖骨皮质点向唇侧改建（$P < 0.001$）；控根内收组治疗后三个层面唇舌侧骨皮质点均向舌侧改建（$P < 0.001$）。倾斜内收组高角、均角、低角患者的 B/T 依次为 77.98%，80.30%，82.74%；控根内收组高角、均角、低角患者的 B/T 依次为 79.16%，82.74%，84.98%。

结论：下前牙内收后，牙槽骨改建以吸收为主，前牙区牙槽骨总厚度减小。牙槽骨皮质改建方向与牙齿移动方向相同，但其改建量小于牙齿移动量。高角患者牙槽骨改建与牙移动比率较均角和低角患者小，临床中应尽量控制其前牙整体移动，以减小骨开裂和骨开窗的风险。

【关键词】 牙槽骨塑建；倾斜内收；控根内收；垂直骨面型；骨改建与牙移动比率

口腔治疗和重建

胶原与类胶原基质用于构建成骨材料的初步研究

李　元　空军军医大学第三附属医院

【摘要】 探索胶原作为有机成分改善磷酸钙材料成骨生物活性并构建人工支架材料的可行方法，并利用自组装类胶原多肽 RAD16-I 及 SP 构建基质环境并接种 hUCMSCs 进行体外立体培养，观察复合体向类骨胶原转化的表现。

【关键词】 胶原；类胶原；成骨

小鼠上颌第一磨牙拔除后愈合过程的观察性研究

张武阳　空军军医大学第三附属医院

【摘要】 研究背景：拔牙创动物模型的构建对于影响拔牙创愈合因素的研究至关重要，目前大部分研究选择大鼠、兔子或者犬等大型动物为载体构建拔牙创模型，近年来通过拔除小鼠第一

磨牙构建拔牙创动物模型的研究逐渐增多，但是关于小鼠第一磨牙拔牙创愈合过程的详细研究报道少见。

研究方法：选取 40 只 8w 龄 C57BL/6 雌性小鼠为研究对象，全麻状态下拔除小鼠上颌第一磨牙，在拔牙后的第 3、5、7、10、14、21、28、35 天分别处死各组小鼠，然后利用体式显微镜、Micro-CT 及 HE 染色、TRAP 等观察并记录拔牙后不同时间点软组织及骨组织的愈合变化情况。

研究结果：1. 拔牙后第 5 天拔牙窝底部出现新生骨质，第 14 天新生骨质充满牙槽窝，软组织连续性恢复，继而新生骨质继续改建，骨密度显著增加，35 天时改建基本完成；2. 三个拔牙窝的愈合速度存在差异，近中牙槽窝愈合较快；3. 拔牙创愈合的早期（14 天内）在牙根间隔顶端（拔牙时牙挺着力部位）可发现空骨陷窝的存在，随着骨质的愈合改建逐渐消失，提示牙挺的使用会对牙槽骨造成一定程度的损伤。

研究结论：小鼠上颌第一磨牙拔牙窝在术后 14 天时充满新生骨质，35 天左右完成骨重塑改建，本研究为临床工作及其他以 C57BL/6 为载体构建拔牙创模型的基础研究提供了一定的理论参考依据。

【关键词】 C57BL/6 小鼠；上颌第一磨牙；拔牙创愈合

牙槽窝加深法解决下颌阻生第三磨牙自体移植后骨缺损问题的病例总结

侯　锐　空军军医大学第三附属医院

【摘要】 下颌近中或水平阻生第三磨牙造成第二磨牙病变以及牙槽骨吸收的情况是临床常见现象。常规治疗方法是将二者全部拔除后种植或活动义齿修复。若采用第三磨牙自体移植替代第二磨牙，我们前期常用人工骨填充材料来修复颊侧及远中较大的骨缺损，但是术后反应较重，治疗效果欠佳。为此，近三年我们改用牙槽窝加深法来解决上述问题。

【关键词】 牙槽窝加深法，阻生第三磨牙，自体移植，骨缺损

后牙区短植体修复后 3—7 年的临床效果及影像学研究

汤祎熳　邱立新　北京大学口腔医院第四门诊部

【摘要】 目的：通过对后牙区 Thommen 短植体修复后 3—7 年的回顾性研究，评估短种植体的中长期临床效果并探究冠根比等修复因素、植体因素、患者特异性因素对短植体边缘骨吸收的影响。

方法：本实验共纳入 130 例牙列缺损患者，植入 180 枚 Thommen 短种植体（6.5mm 及

8mm），术后 3—6 个月完成冠修复，术后 36-82 个月（平均 50.6 个月）进行随访观察，包括临床和影像学检查。评价指标包括植体成功率、边缘骨吸收、植体周相关参数、冠种植体比（crown-implant ratio，C/I）、生物及机械并发症等。

结果：短植体存留率为 100%；近、远中边缘骨吸收分别为（－ 1.08±1.00）、（－ 0.79±0.88）mm；临床 C/I 为（1.16±0.36），按临床 C/I ＜ 1、1 ≤ C/I ＜ 2 和 C/I ≥ 2 将植体分为 3 组，各组间边缘骨吸收有统计学差异；单因素相关分析结果显示临床 C/I 与边缘骨吸收之间为负相关（r ＝－ 0.25；P ＝ 0.001）；单冠或联冠修复在边缘骨吸收、生物及机械并发症发生率方面无统计学差异。

结论：在严格控制适应证的情况下，Thommen 短植体 3-7 年存留率高 , 生物学及机械并发症少，修复后使用良好 , 在后牙区垂直骨高度不足时具有良好的临床应用价值。

【关键词】 短植体；边缘骨吸收；临床冠根比

口腔种植学

低剂量唑来膦酸对去势大鼠下颌骨的影响

程余婷　健　廖　贵州医科大学附属口腔医院

【摘要】 背景：目前双膦酸盐（Bisphosphonate，BP）虽能有效地预防绝经后妇女的骨丢失，但其对下颌骨影响及其机制尚不十分清楚 。

目的：研究去势大鼠下颌骨经低剂量唑来膦酸（Zoledronic acid，ZA）作用后，观察大鼠的下颌骨组织形态病理学改变，探讨 RANKL/RANK/OPG 信号系统在唑来膦酸抑制骨吸收过程中的调控效应与机制。

方法：取 36 只 250-300g 成年雌性 SD 大鼠行两侧卵巢切除术或假手术，建立骨质疏松模型。术后 12 周随机分为对照组及低剂量唑来膦酸治疗组：（1）假手术对照组；（2）去卵巢模型组；（4）皮下一次性注射 20ug/kg 唑来膦酸组；对照组和模型组皮下注射相应剂量的盐水。用药一周后对所有分组的大鼠拔除左侧下颌磨牙，于 4 周后处死动物，分离并取出下颌骨进行检测。通过影像学 X 射线大致观察大鼠拔牙窝剩余牙槽嵴状况，苏木精 - 伊红 (Hematoxylin-eosin，HE) 染色检测下颌骨皮质和骨松质的病理结构改变，TUNEL 凋亡实验检测凋亡的成骨细胞数量，利用免疫组织化学技术检测下颌牙槽骨内细胞核因子 κB 受体活化因子配基（RANKL）、骨保护素（OPG）、细胞核转录因子（NF-κB）的表达情况。

结果与结论：①唑来膦酸皮下注射低剂量 20ug/kg 时，能有效抑制破骨细胞；②成骨细胞的凋亡在用药后均有减少，与正常对照组没有明显的差异；③用药后，RANKL/OPG 比例均有下降，NF-κB 下调。

【关键词】 唑来膦酸；去势大鼠；破骨细胞骨吸收；成骨细胞凋亡；核因子 κB 信号通路

氨磷汀调节放射对已形成种植体骨结合界面的研究

黄　波　宫　苹　华成舸　四川大学华西口腔医学院

【摘要】 头颈部恶性肿瘤约占全身肿瘤的 5%，治疗方式为放化疗结合手术治疗。临床报道患者因接受肿瘤接受放疗后，种植体处颌骨发生病理性骨折；由于种植体是高密度金属影像，放射时，种植体周围的骨组织射线比正常高 25%。 那么放射对已经正常行使功能的种植牙在细微结构上有何影响，缺乏相关的基础报道。

细胞保护剂是用来预防或减少肿瘤放化疗产生毒、副作用的。氨磷汀是唯一可以用于临床的泛细胞保护剂。氨磷汀能在放射条件下提高牵张成骨的骨质和骨量，但其能否减轻放射对已经形成种植体骨结合的种植体的影响。

围绕上述核心问题，本课题采用 SD 大鼠，观察放射对已经形成种植体骨结合的影响。通过探讨氨磷汀在放射条件下对骨髓间充质干细胞的作用机制和其在体内对放射情况下种植体骨结合界面的影响。

研究结果显示：

1）放射能够对已经形成种植体骨结合的种植体产生影响。种植体的最大拉出力明显降低。

2）放射会降低骨髓间充质干细胞的成骨分化能力，增强其成脂分化能力；导致细胞 DNA 损伤、促进细胞凋亡、升高细胞内氧自由基含量等。而氨磷汀能够降低放射对骨髓间充质干细胞的这些影响。

3）动物实验证实在放射条件下，氨磷汀能够提高种植体骨结合率，提高种植体的最大拉出力。

【关键词】 氨磷汀；放射；种植体骨结合；骨髓间充质干细胞；

Effects of Programmed Local Delivery from a Micro/Nano-Hierarchical Surface on Titanium Implant on Infection Clearance and Osteogenic Induction in an Infected Bone Defect

李一涵　陈　陶　重医附属口腔医院

【摘要】 The two major causes for implant failure are postoperative infection and poor osteogenesis. Initial period of osteointegration is regulated by immunocytes and osteogenic-related cells

resulting in inflammatory response and tissue healing. The healing phase can be influenced by various environmental factors and biological cascade effect. To synthetically orchestrate bone-promoting factors on biomaterial surface, built is a dual delivery system coated on a titanium surface (abbreviated as AH-Sr-AgNPs). The results show that this programmed delivery system can release Ag+ and Sr2+ in a temporal-spatial manner to clear pathogens and activate preosteoblast differentiation partially through manipulating the polarization of macrophages. Both in vitro and in vivo assays show that AH-Sr-AgNPs-modified surface renders a microenvironment adverse for bacterial survival and favorable for macrophage polarization (M2), which further promotes the differentiation of preosteoblasts. Infected New Zealand rabbit femoral metaphysis defect model is used to confirm the osteogenic property of AH-Sr-AgNPs implants through micro-CT, histological, and histomorphometric analyses. These findings demonstrate that the programmed surface with dual delivery of Sr2+ and Ag+ has the potential of achieving an enhanced osteogenic outcome through favorable immunoregulation.

【关键词】 antibacterial; macrophage polarization; multifunctional coating; osteogenesis; surface modification

基于 CBCT 的颏孔前部种植相关解剖结构的测量分析

尚　将　朱祥奎　烟台市口腔医院

【摘要】 目的：研究下颌颏孔前部种植相关解剖结构，及各解剖结构的出现率与形态特征，为该区域的种植、牙周、根尖外科手术安全提供指导。材料与方法：根据纳入标准，选择 32 例下颌骨标本，对标本进行相关解剖结构的实体测量。拍摄 32 例标本的 CBCT，利用 NNT-Viewer 三维软件进行扫描与重建并测量。测量项目及观测指标包括：颏孔、副颏孔、正中舌侧孔的出现频率、直径、孔下缘到下颌骨下缘的距离以及孔上缘到牙槽嵴顶的距离。结果： 32 例标本中总计包含正中舌孔 59 个，出现机率为 100％。副颏孔的发生率为 12.5%（4/32）。除正中舌孔与牙槽嵴顶距离外（ICC=0.658），两种方法测量其他变量的的结果呈现出高度一致性。结论：采用 CBCT 的测量方法和大体标本实际测量所得的测量结果具有高度一致性，可以在颏孔前区域手术前采用本方法利用 CBCT 对颌骨相关解剖结构进行分析。在没有 CBCT 的条件下，建议在颏孔前区域行种植手术时，种植体长度不超过 12mm。

【关键词】 下颌骨；颏孔；舌孔；口腔种植

Graphdiyne Sensitized TiO2 Nanofibers (TiO2/GDY) with enhanced Photocatalytic Antibacterial and Persistent Osteoinductive Activity for Implants Infection

时缪斯　张玉峰　武汉大学口腔医院

【摘要】 For decades, titanium implants have been widely used in bone tissue engineering. However, orthopaedic implants associated infections increase the risk of implant failure and even lead to amputation in severe cases even. Though TiO2 has the photocatalytic activity to produce reactive oxygen species (ROS), the recombination of generated electrons and holes limit its antibacterial ability. Here we described a graphdiyne (GDY) composite TiO2 nanofiber to combat implant infections through the enhanced catalysis effect and prolonged antibacterial ability. In addition, GDY modified TiO2 nanofibers exerted a superior biocompatibility and osteoinduction ability for cells adhesion and differentiation, thus contribute to the bone tissue regeneration process in drug-resistant bacteria induced implant infection.

【关键词】 Ti；implant infection; TiO2/graphdiyne; photocatalysis; antibacterial

浓缩生长因子对人上颌窦粘膜细胞增殖迁移影响的实验研究

王　菲　同济大学附属口腔医院

【摘要】 目的：探讨浓缩生长因子提取液（concentrated growth factors extract, CGFe）对上颌窦粘膜细胞增殖、迁移的影响。方法：体外培养人上颌窦粘膜细胞，实验组采用含 CGFe 的 α-MEM 完全培养基，对照组采用不含 CGFe 的 α-MEM 完全培养基培养。通过 CCK-8 法（cell counting kit-8, CCK-8）、细胞周期检测法评估细胞增殖速率变化，划痕实验评估细胞迁移速率，免疫荧光、实时荧光定量 PCR 法 (real-time PCR,RT-PCR)，检测上颌窦粘膜细胞表达增殖相关的基因的变化。结果：实验组的细胞增殖、迁移速率及增殖相关标记物的表达均高于对照组。结论：浓缩生长因子提取液能有效促进上颌窦粘膜细胞的增殖、迁移。

【关键词】 上颌窦粘膜细胞；浓缩生长因子；组织修复

Bio-HPP 作为种植修复固定桥支架性能的初步研究

王文雪　滕敏华　青岛大学附属医院
金杭颖　青岛大学

【摘要】 目的：比较 Bio-HPP（改性聚醚醚酮）和钛合金作为种植修复固定桥支架的性能。

方法：1. 将瓷化树脂粘接于两种圆柱形支架材料上，每组 25 个：Bi 组（Bio-HPP）和 Ti 组（钛合金）。24h 湿贮存后经冷热循环、疲劳加载后使用万能试验机测定剪切结合强度。2. 制备由 Bio-HPP 和钛合金制成的 CAD/CAM 3 单位桥支架各 25 个。通过扫描电镜观察桥支架与复合基台之间的边缘密合性，测量记录两者之间的垂直距离。3. 支架经瓷化树脂饰面，经冷热循环、疲劳加载后使用万能试验机测定其抗压性能。对数据结果进行统计分析。

结果：1）剪切结合强度 Bi 组 (30.99±3.25) MPa，Ti 组（20.80±1.71）MPa，两者有统计学差异（$p < 0.001$）。2）平均边缘间隙 Bi 组 (19.84 ±4.56) μm，Ti 组 (19.27±5.06) μm，两者无统计学差异（$p > 0.05$）。3）加载负荷后，Bi 组在平均负荷（1535±109）N 时支架断裂，断裂前未发生瓷化树脂崩裂。Ti 组在平均负荷（2020±207）N 时瓷化树脂崩裂，未发生支架断裂。

结论：CAD/CAM 制作的 Bio-HPP 支架与瓷化树脂有良好的结合强度，饰面后有较强的抗断裂性能，与种植体有良好的边缘适合性，可以考虑将其作为种植修复支架配合瓷化树脂饰面进行临床使用。

【关键词】 Bio-HPP；支架；瓷化树脂；强度；种植修复

The Effects of Air Cold Atmospheric Plasma on Cellular Early Attachment, Proliferation and Migration on Pure Titanium Surfaces

谢艳婷　河南大学赛思口腔医院

Cold plasma has been studied for several fields of medicine, for example, pathogen inactivation and implant functionalization. Previous studies have provided evidence that plasma treatment promotes the adhesion of osteoblasts and is becoming a popular method for modifying the characteristics of substrate surfaces. However, its clinical application is limited as the effects of plasma treatment cannot be maintained for a long time. Air cold atmospheric plasma (CAP) is cost-efficient and convenient for clinical application compared to other work gas atmospheric plasma. In this study, the behavior of

MC3T3-E1 cells on titanium discs was analyzed after treatment with air CAP. The characteristics of the titanium surfaces before and after the air CAP treatment were analyzed by a field emission scanning electron microscope (SEM), atomic force microscope (AFM), X-ray photoemission spectroscopy (XPS) and contact angle measurements. The morphologies of cells attached to the titanium surfaces were observed by SEM and fluorescence microscope at 2, 8 and 24 h after seeding. The gene expression levels of integrin β1, α2 and α5 were examined by RT-PCR after incubating 2, 8 and 24 h, respectively. The abilities of cell proliferation and migration were studied by MTT assay and migration assay, respectively. The roughness of titanium surfaces with and without air CAP were 30.6 ± 9.00 nm and 27.66 ± 3.68 nm, respectively. There was no obvious difference ($p>0.05$). The air CAP made the titanium surfaces more hydrophilic. The MC3T3-E1 cells adhered to the untreated surface were fusiform, whereas the cells covered a larger surface area on the air CAP-treated surface at 2 h. The gene expression levels of integrin β1, α2, and α5 in cells on the surfaces treated by air CAP were upregulated at 2 and 8 h compared to those untreated. And the air CAP-treated titanium surfaces enhanced cell proliferation and migration with more developed cellular network. In conclusion, air CAP treatment is a potential surface modifying method that can enhance the initial cellular attachment, proliferation and migration. Since the effects of plasma treatment cannot be maintained for a long time, it is expected that implants treated by air CAP immediately before implantation could improve the successful rate of implants.

【关键词】 air atmospheric plasma；attachment；proliferation；migration；integrin

骨髓间充质干细胞来源外泌体对牙槽骨吸收影响的实验研究

许舒宇　王佐林　同济大学附属口腔医院

【摘要】 患者失牙区骨量不足是牙种植手术中的常见问题。雌激素减少（OVX）、 机械应力下降（牙缺失）等可导致牙槽骨吸收。本研究发现，卵巢切除及牙缺失可以通过单纯或协同作用导致牙槽骨骨量丢失，破骨样细胞 (Trap+MNCs) 增加。在体外及体内，BMMSC-exos 均可以被破骨细胞摄取 ; 骨吸收大鼠的 BMMSC-exos 可促进破骨细胞的分化。对外泌体成分进行分析，骨丢失大鼠部分 miRNAs 可通过破骨功能相关通路调节靶细胞的生物学功能。其中具有炎症负反馈性调节作用的 miR-146a 显著上调。并且在炎性环境下，miR-146a 过表达的破骨前体细胞所诱导形成的破骨细胞数量显著减少。本研究表明，在骨质疏松及骨吸收的炎症微环境下，BMMSCs 外泌体中的 miR-146a 上调并负反馈抑制破骨细胞分化， miR-146a 可作为治疗骨质疏松的新靶点，为如何预防骨质疏松症患者牙槽骨丢失提供了潜在的治疗方案。

【关键词】 外泌体；破骨；miR-146a

种植体周围黏膜炎和牙龈炎的微生物群落研究

于晓琳　中山大学光华口腔医学院·附属口腔医院
陈裕琪　香港大学

种植体周围黏膜炎与牙龈炎均是由菌斑引起的软组织炎症。然而，系统研究两者微生物菌落差异的文献甚少，且忽略了个体间的菌群差异。 因此，本研究通过宏基因组测序结合生物信息学方法，比较同一患者种植体周围黏膜炎与牙龈炎位点微生物群落的差异。在同一患者中（n=22），共 4 组临床样本被采集： i) 牙龈炎位点龈上菌斑（TP）； ii) 牙龈炎位点龈下菌斑（TB）； iii) 种植体周围黏膜炎位点黏膜上菌斑（IP）; iv) 种植体周围黏膜炎位点黏膜下菌斑（IB ）。共发现 11 种不同菌门。在龈上菌斑 / 粘膜上菌斑中，Chloroflexi 和 Proteobacteria 在种植体黏膜炎粘膜上菌斑的丰度显著高于牙龈炎龈上菌斑，而 Actinobacteria 在种植体黏膜炎粘膜上菌斑的丰度低于牙龈炎龈上菌斑。相较于牙龈炎龈下菌斑，种植体周围黏膜炎粘膜下菌斑中 Synergistetes 丰度增加，Actinobacteria 丰度减低。13/118 个菌属的丰度在 PT 组和 PI 组存在显著差异，27/118 个菌属的丰度在 BI 组和 BT 组存在统计学差异。基于 UniFrac 距离矩阵的 nMDS Ordination 显示 TP、TB、IP 和 IB 组菌群结构具有显著差异，个体间菌群结构差异显著。 种植体周围黏膜炎和牙龈炎的致病菌是高度复杂和多变的。种植体周围黏膜炎和牙龈炎生态位具有相似的核心微生物菌落，但是两者菌群结构具有显著差异。个体间的口腔微生物群落差异显著。

【关键词】 种植体周围黏膜炎；牙龈炎；口腔微生物群落

唑来膦酸通过调节 NF-κB 和 JNK 信号通路抑制破骨细胞的分化及功能

周　倩　黄晓林　廖　健　贵州医科大学附属口腔医学院 / 附属口腔医院

【摘要】 目的：通过将唑来膦酸（zoledronic acid, ZOL）作用于核因子 κB 受体活化因子配体（receptor activator of nuclear kappa-B ligand,RANKL）诱导的向破骨细胞分化的前体 RAW264.7 细胞，探讨 ZOL 对 RANKL 诱导破骨细胞形成的影响并进一步探索相关的信号分子机制。方法 : 通过 CCK8 实验分别检测有无 RANKL 共同作用下不同浓度 ZOL（0、0.1、1,5、15、30、50 μM）对小鼠单核巨噬细胞系 RAW264.7 细胞的细胞活力，排除毒性浓度范围；经 RANKL 将 RAW264.7 细胞诱导为破骨细胞，倒置相差显微镜下观察其形态变化并通过罗丹明标记的鬼笔环肽染色、DAPI 染色鉴定破骨细胞；抗酒石酸酸性磷酸酶 (tartrate-resistant acid phosphatase,TRAP)

染色评估不同浓度 ZOL 在破骨细胞分化的不同阶段对破骨细胞形成的影响，计算 TRAP 阳性细胞数目和面积百分比；此后通过骨吸收陷窝实验检测破骨细胞骨吸收功能并且同样分析骨吸收陷窝的数目和面积百分比；最后实时定量荧光 PCR（Real-Time quantitative PCR，RT-qPCR）检测破骨细胞形成相关基因的表达，包括降钙素受体 (calcitonin receptor, CTR)、核因子 κ B 受体活化因子（receptor activator of NF-κB, RANK）、TRAP、树突状细胞特异性跨膜蛋白 (dendritic cell-specific transmembrane protein, DC-STAMP)、活化 T 细胞核因子 (Nuclear Factor of Activated T cells c1， NFATc1) 和 c-fos，最后通过蛋白质印记法，即 Western blotting 分别检测破骨细胞相关蛋白（IκBα、P65、P38、JNK 及、ERK）的表达。结果： RAW264.7 细胞在 RANKL 的刺激下，可成功诱导出多核且有完整肌动蛋白结构的破骨细胞；在有无 RANKL 共同作用情况下，浓度大于 15 μM 的 ZOL 作用于 RAW264.7 细胞 48 h 后都有毒性，且浓度越高，作用时间越长，则毒性越大。相比对照组，低于该浓度的 ZOL 以时间和浓度依赖性方式抑制破骨细胞分化，同时还抑制肌动蛋白结构的形成和细胞核的聚集。此外，ZOL 处理后骨吸收陷窝数目和面积也都明显减少。分子水平上，RANKL 极大促进以上破骨细胞标志基因的表达；此外，它还迅速诱导 IκBα、P65、P38、JNK 和 ERK 磷酸化，激活对应的通路。然而，ZOL 抑制破骨细胞相关基因的表达，并且抑制 RANKL 诱导的 IκBα、P65 和 JNK 磷酸化，其它蛋白磷酸化未见明显改变。结论：ZOL 在体外可能通过抑制 NF-κB 和 JNK 信号通路来抑制破骨细胞形成和骨吸收功能，是治疗如骨质疏松症类的破骨细胞相关疾病的潜在药物。

【关键词】 破骨细胞；ZOL；RANKL；骨吸收；信号通路

Accessary canals of the canalis sinuosus: a prevalent but often overlooked anatomical variation in the anterior maxilla

单钿钿　曲　杨　古丽莎　中山大学附属口腔医院

【摘 要】 Accessary boney canals (ACs) communicating with the canalis sinuosus (CS), a boney canal carrying the anterior superior alveolar nerve and vessels, can often be present but overlooked in the anterior maxilla. This anatomic variation has been considered as a hidden threat to neurovascular complications resulting from implant placement in this region. Injuries to the ACs can cause haemorrhage, temporary or permanent paresthesia as well as non-integration of dental implants. The objective of this study was to verify the characteristic parameters of the ACs and their relationship to the terminal CS, anterior maxilla and anthropometric parameters. Radiographic measurements were taken on 1007 cone-beam computed tomography scans from Mongolian subjects. Identified in 372 scans, a total of 463 ACs were registered in this study. Prevalence of the ACs was 36.9%, positively correlated with the volume of anterior maxilla (OR 1.414, $p < 0.001$) and negatively correlated with distance from the terminal CS to the buccal alveolar crest (OR 0.431, $p < 0.05$). Diameter of the ACs

was 1.11±0.13mm, which was significantly higher in males ($p < 0.05$), positively correlated with the diameter of the ipsilateral CS (rs =0.163, $p < 0.05$) and distance from the palatine foramen of the ACs to the palatal alveolar crest (rs = 0.192, $p < 0.001$). All ACs in our study crossed the alveolar process in a straightforward way from the buccal side to the palatal side. Bifurcation site of the CS, which was the outset of the AC, was 19.29±2.74mm away from the buccal alveolar crest and mostly distributed in the middle third region relative to the nasal cavity. Palatine foramen of the AC was 5.72±2.39mm away from the palatal alveolar crest and located predominantly between the central incisor and the lateral incisor. In conclusion, as anatomic variations of the CS, ACs have high prevalence in the anterior maxilla. However, given the small size, they are usually invisible on plain radiographs and overlooked in clinical procedures. It is necessary to identify and locate this anatomic variation meticulously in presurgical radiological examinations, especially for the patients with large anterior maxillary volume but short maxillary height, to decrease possible neurovascular complications and achieve better prognosis.

【关键词】 accessary boney canal；canalis sinuosus；anterior superior alveolar nerve；anatomic variation

Linear measurements of sinus floor elevation based on voxel-based superimposition of cone beam CT images

黄　洁　wang zuolin　ye ying　同济大学附属口腔医院

【摘要】 Background

Postsurgical evaluation of sinus floor elevation regularly involves linear measurements of the elevated volumes in the cone beam computed tomography (CBCT) images. The accuracy of measurements could be compromised due to ill-defined sinus floor outline if implants are placed simultaneously.

Purpose

The aim was to examine a CBCT superimposition method to improve the measurement accuracy.

Materials and Methods

Twenty patients who received transalveolar sinus floor elevation with immediate implantation were enrolled. CBCTs before and after surgery were transformed into DICOM format and imported into the Dolphin Imaging software. Voxel-based superimposition was automated to merge the files. In the superimposed image, parameters including alveolar bone height, protruded implant length, and total elevated height were measured. The superimposition and measurements were performed independently by two examiners and in two timepoints with one-week time interval. We used intraclass correlation

coefficient (ICC) to analyze the interexaminer and intraexaminer agreements.

Results

Of measured parameters, the mean of difference between two timepoints ranged from 0.18 to 0.26 mm by examiner 1, and from 0.16 to 0.20 mm by examiner 2. ICCs were equal or greater than 0.98, indicating perfect intraexaminer agreement. For interexaminer reliability, the largest mean of difference was 0.27 mm in measuring alveolar bone height between two examiners. ICCs were greater than 0.98, showing perfect interexaminer agreement.

Conclusions

The voxel-based superimposition of pre- and post- surgical CBCT images with Dolphin Imaging is an effective and reliable way for linear measurements so as to assess the surgical outcome. There is minimal effect on reproducibility of measured data by different timepoints or performers.

【关键词】 Keywords: sinus floor elevation; implantation; CBCT; voxel-based superimposition; Dolphin.

自体牙片移植用于前牙区牙槽嵴水平骨增量的临床观察

王文雪　姜雅萍　滕敏华　青岛大学附属医院

【摘要】 目的：对比自体牙片和自体骨块移植用于牙槽嵴水平骨增量的有效性、安全性。

方法：选取 2018 年 1 月至 2018 年 10 月就诊于我科进行种植治疗的患者 21 例，缺牙区垂直骨高度≥ 9mm，水平骨宽度≤ 4mm，分为自体牙片组和自体骨块组，测量术前、术后即刻、术后半年 CBCT 在距离牙槽嵴顶 0、3、6mm 处的水平骨量，记为 W1、W2、W3，对比两组患者牙槽嵴宽度及其差值。术后 1 周、1 月、3 月记录手术安全性，是否发生软组织开裂、感染等，并在术后 1 周对患者进行疼痛评分。

结果：21 例患者共 45 个骨增量位点，术后半年在 34 个种植体植入位点均成功植入一定型号的种植体。各测量位点的骨量：（1）术后半年水平骨量：牙片组：W1（4.96±0.96）mm、W2（7.31±1.72）mm、W3（8.52±2.13）mm，骨块组： W1（4.78±1.03）mm、W2（7.31±1.35）mm、W3（8.34±1.58）mm。（2）术后半年骨增量：牙片组：W1（2.35±0.90）mm、W2（3.69±1.21）mm、W3（4.40±1.60）mm，骨块组：W1（2.20±0.93）mm、W2（4.16±1.08）mm、W3（4.23±1.33）mm。（3）术后半年骨吸收量：牙片组：W1（0.69±0.33）mm、W2（0.62±0.45）mm、W3（0.47±0.50）mm，骨块组：W1（0.55±0.41）mm、W2（0.53±0.61）mm、W3（0.71±0.49）mm。两组在各测量位点的水平骨量均无显著差异（p 大于 0.05）。两组患者软组织愈合均良好，无软组织开裂、感染等症状。两组疼痛评分比较 P=0.010，两者有显著差异。

结论：自体牙片移植用于牙槽嵴水平骨增量，短期效果良好，安全有效，手术创伤小，术后反应轻，能满足延期种植骨量需求，可以考虑作为自体骨块移植的替代疗法进行临床推广使用。

【关键词】 牙片；骨增量；引导骨再生；骨块移植

数字化导板与动态导航的牙种植精度对比研究

周　卉　周　苗　广州医科大学附属口腔医院

【摘要】 目的：采用体外实验比较数字化种植导板与动态导航的牙种植精度。

材料与方法：

①数字化导板组：对三维打印的下颌牙列缺损树脂模型进行 CBCT 扫描、光学扫描，在 Guidemia 种植设计软件中模拟种植体植入，设计制作全程种植导板。在导板辅助下，在 10 个下颌 3DP 模型植入 40 枚种植体。

②动态导航组：在同样的树脂模型缺牙区安装 U 型管进行 CBCT 扫描，在易植美口腔种植导航系统软件中模拟种植体植入，在导航系统辅助下，在 10 个下颌 3DP 模型上植入 40 枚种植体。

③精度检测：术后两组模型再次进行 CBCT 扫描，分别导入相应的软件中，测量种植体设计位置与实际位置的差异（颈部偏差、根尖偏差、角度偏差）。在 SPSS 18.0 软件中对测量结果分别使用描述性统计进行分析。

结果：

数字化导板组种植体颈部偏差为 1.15±0.34mm、根尖偏差为 1.37±0.38mm，角度偏差为 2.6±1.11°，而动态导航组种植体的颈部偏差为 0.40±0.41mm、根尖偏差为 0.34±0.33mm，角度偏差为 0.97±1.21°。动态导航组的种植偏差，随着种植次数的增加，逐渐减小，并在 19 次种植之后明显减小并趋于稳定。数字化全程导板组的种植偏差与种植次数的关联并不大，趋向于围绕一定的偏差值上下波动。

结论：在体外模型中，数字化动态导航和导板引导下牙种植均有较好的精度，前者的种植精度要高于后者；数字化导板牙种植的根部偏差比颈部大。

【关键词】 牙种植；导板；动态导航；精度；三维打印

老年口腔医学

增龄性炎症微环境对骨髓间充质干细胞的影响

彭　欣　周　鑫　华中科技大学同济医学院附属协和医院

【摘要】 目的：探讨增龄条件下的炎性微环境对骨髓间充质干细胞（BMSCs）的生物学影响，

以期为增龄性骨质疏松的临床治疗提供新思路。

方法 : 采用全骨髓培养法提取 BMSCs, 培养至第 3 代（年轻组）和第 8 代 (衰老组)，分别收取 P3 和 P8 代细胞上清。用收取的细胞上清分别培养 BMSCs, β - 半乳糖苷酶染色检测不同上清对干细胞衰老的影响；通过 cck8、EDU 染色检测对干细胞增殖能力的影响 ,TUNEL 染色检测是否影响干细胞凋亡；成骨成脂诱导后分别通过茜素红、油红 O 染色，RT-PCR，Western Blot 检测对细胞分化能力的影响。进一步验证不同上清处理后对 BMSCs 干性的影响。ELISA 检测 P3 及 P8 代细胞上清液中以及不同年龄组 C57BL/6 小鼠血清中炎症因子的水平。

结果：本研究证明了相较于 P3（年轻组），P8（衰老组）细胞上清中炎症因子的表达水平较高，动物血清检测也验证了随着年龄的增长，产生了增龄性的炎症微环境。经过 P8（衰老组）细胞上清处理后的 BMSCs 增殖能力下降，成骨成脂分化能力也降低；而这种增殖分化能力的下降是由于增龄性的炎症微环境对细胞干性影响导致。

结论：随着年龄增长，骨质疏松个体的骨髓间充质干细胞生物学功能发生了改变，通过体外实验探究这种增龄性的炎症微环境对 BMSCs 的生物学功能的影响，为改善骨质疏松状态提供靶点和理论依据。

【关键词】 炎症微环境；增龄性；骨髓间充质干细胞

流　行　病

颞下颌关节紊乱病的流行病学调查与锁𬌗的相关研究

贾梦莹　新疆医科大学第一附属医院

【摘要】 目的：探讨后牙锁𬌗与颞下颌关节紊乱病的相关性，并分析单侧后牙正锁𬌗者的咀嚼肌表面肌电特征，评价伴后牙锁𬌗的翼外肌痉挛患者封闭治疗的效果。方法：抽取新疆医科大学大学生 700 例行颞下颌关节专科检查及问卷调查，计算患病率，使用 SPSS20.0 软件，采用多因素逻辑回归分析，分析后牙锁𬌗与颞下颌关节紊乱病的相关性；选取上述大学生中单侧单颗后牙正锁𬌗 40 例，个别正常𬌗 40 例为研究对象，对其进行颞肌及咬肌的肌电检测，使用 one-way ANOVA 方差分析；分析 27 例伴单侧后牙锁𬌗的翼外肌痉挛患者封闭治疗前后的 Fricton 颞下颌关节功能指数。结论：后牙锁𬌗是颞下颌关节紊乱病的相关危险因素，锁𬌗是导致咀嚼肌表面肌电变化的主要原因，封闭注射术能有效缓解锁𬌗导致的翼外肌痉挛。

【关键词】 锁𬌗；颞下颌关节紊乱病；肌电；翼外肌痉挛

免　疫

Tet 介导的 DNA 去甲基化对牙周膜干细胞免疫调节功能的影响及其机制研究

余婷婷　北京大学口腔医院正畸科

【摘要】目的：通过研究在 DNA 去甲基化及促进基因转录过程中起关键作用的 TET（Ten-eleven translocation）蛋白家族及其催化氧化产生的 5- 羟甲基胞嘧啶（5-hydroxymethylcytosine，5hmC）在牙周膜干细胞（Stem cells derived from periodontal ligament，PDLSCs）中的功能调节作用，以明确 TET 介导的 DNA 去甲基化是否参与调控 PDLSCs 的免疫调节能力及其机制，以促进干细胞治疗免疫相关疾病疗效，并且将有助于提供全新的干细胞临床应用思路以及理论支持。

方法：利用 siRNA 在体外调节 PDLSCs 中 TET 的表达水平，检测 PDLSCs 对 T 细胞诱导凋亡及 T 细胞分化能力的影响；建立小鼠炎症性肠炎疾病模型，并对其进行系统性干细胞治疗，进一步在体内明确 TET 对 PDLSCs 免疫调节能力的作用；利用 RNA-seq 筛选出 TET 介导的去甲基化调控干细胞免疫调节功能相关目的基因，并研究其下游信号通路，以促进 PDLSCs 治疗免疫系统疾病疗效。

结果：低表达 TET1，2 后 PDLSCs 在体外共培养中诱导 T 细胞凋亡能力增强，且促使其向 Treg 细胞分化。将低表达 TET1，2 的 PDLSCs 经尾静脉系统回输入炎症性肠炎小鼠体内，结果分析显示其治疗疗效较对照组 PDLSCs 更好。机制上，敲低 TET1，2 后，分析显示 PDLSCs 中 DKK-1 启动子区域 DNA 甲基化水平升高，DKK-1 表达水平降低，WNT 通路上调，进而影响细胞凋亡信号通路 FasL 上调，最终导致 PDLSCs 杀伤体细胞能力增强，具有更强的免疫调节能力。

结论：TET 介导的 DNA 去甲基化参与调节 PDLSCs 免疫调节功能。

【关键词】间充质干细胞；TET；DNA 去甲基化；免疫调节

龋 病 学

Plasticity of the pyruvate node modulates hydrogen peroxide production and acid tolerance in multiple oral streptococci

程兴群 齐 偲 徐 欣 四川大学华西口腔医院

【摘要】 Commensal Streptococcus sanguinis and Streptococcus gordonii are pioneer oral biofilm colonizers. Characteristic for both is the SpxB-dependent production of H2O2, which is crucial for inhibiting competing biofilm members, especially the cariogenic species Streptococcus mutans. H2O2 production is strongly impacted by environmental conditions, yet few mechanisms are known. Dental plaque pH is one of the key parameters dictating dental plaque ecology, and ultimately oral health status. Therefore, the objective of the current study was to characterize the effect of environmental pH upon H2O2 production by S. sanguinis and S. gordonii. S. sanguinis H2O2 production was not found to be affected by moderate changes in environmental pH, whereas S. gordonii H2O2 production declined markedly in response to lower pH. Further investigation into the pyruvate node, the central metabolic switch modulating H2O2 or lactic acid production, revealed increased lactic acid levels from S. gordonii at pH6. Accordingly, a Δldh mutant of S. gordonii produced significantly more H2O2. The bias for lactic acid production at pH6 resulted in a concomitant improvement in the survival of S. gordonii at low pH and seems to comprise part of its acid tolerance response. Additionally, the differential response to pH similarly affects other oral streptococcal species suggesting that the observed results are part of a larger phenomenon linking environmental pH, central metabolism, and the capacity to produce antagonistic amounts of H2O2.

【关键词】 Oral biofilm; Pyruvate oxidase; Hydrogen peroxide; Environmental pH

Beloved Enemy-The Thin Line between Mutualism and Competition in Oral Mixed-Species-Biofilms

程兴群 徐 欣 周学东 四川大学华西口腔医院

【摘要】 Introduction: Caries and periodontal diseases are recognized as polymicrobial infections

caused by a shift in the oral microbial composition. This shift is driven by synergistic and antagonistic interactions among the microbial species. Streptococci as early colonizers of the dental surface not only provide attachment sites for other species in the early phase of multi-species-biofilm formation. Pyruvate oxidase (SpxB) dependent H2O2 release of Streptococcus sanguinis SK36 (SK36) and Streptococcus gordonii DL1 (DL1) is known to inhibit the growth of competing bacteria like Streptococcus mutans (Sm), a major contributor of initial enamel caries.

Objectives: SpxB expression is known to be under control of carbon catabolite protein A (CcpA). As a consequence, when CcpA is depleted in SK36 and DL1, spxB expression and thus H2O2 release are increased. However, the ability to inhibit the growth of competing bacteria surprisingly decreased. Thus, in this study, we aim to investigate the cause and ecological meaning of such contradictory findings.

Methods: We investigated ccpA mutants and generated spxB deletion as well as ccpA/spxB double mutants of SK36 and DL1. H2O2 release was detected and quantified by a chromogenic assay. Growth inhibition assays as well as H2O2-inhibition and H2O2-protection assays (disc diffusion) were performed by co-culturing SK36 or DL1 derivatives with Sm or other streptococcal / staphylococcal isolates.

Results: H2O2-dependent growth inhibition of both SK36 and DL1 was observed. Remarkably, a protective effect against H2O2-mediated killing of both SK36 and DL1 spxB mutants was found when H2O2 was added to co-cultured species. In addition, both SK36 and DL1 ccpA/spxB double mutants showed a substantial enhanced protection compared to their corresponding single mutants ($p < 0.001$). Because of the observed long range effect (agar diffusion > 5 mm), the protective activity was attributed to extracellular components being produced by the SK36 and DL1 mutant strains. The components have been characterized. So far, besides their ability to diffuse through the agar, they were heat-stable (100° C, 30 minutes), suggesting that they are unlikely to be proteins. Moreover, the protective phenotype could only be found when growing bacterial cells on solid media. No effect could be detected in supernatant of liquid cultures.

Conclusion: Our findings uncovered the presence of a so far unknown phenotype of SK36 and DL1. The release of components protecting against H2O2-mediated killing provide a new aspect in bacterial mutualism in oral mixed-species-biofilms.

【关键词】 Oral biofilm; Pyruvate oxidase; Hydrogen peroxide; Carbon catabolite protein A; Bacterial interactions

THE ROLE OF YAP/TAZ AND ACTIN TENSION IN THE INCISOR STEM CELL NICHE

杜 玮 杜 文 周学东 四川大学华西口腔医院

【摘要】 Tissue homeostasis and injury repair depend on the correct regulation of stem cell self-renewal and differentiation. The mouse incisor is an ideal system to study these processes as it maintains a group of dental epithelial stem cells that continuously give rise to enamel-secreting ameloblasts. The key factors of Hippo pathway, Yes associated protein (YAP) and Transcriptional co-activator with PDZ-binding motif (TAZ) (YAP/TAZ) has been shown recently to be involved in the regulation of cellular self-renewal, proliferation and differentiation during organgenesis. Here we show that nuclear YAP is associated with proliferating transit-amplifying cells prior to their differentiation. Conditional deletion of YAP and its homolog TAZ shows that they have overlapping functions in promoting cell proliferation and survival, and inhibiting differentiation. Meanwhile, the defect was observed in labial cervical loop of Yap/Taz deficient mice, some of which may not be able to form the labial cervical loop. Surprisingly, actomyosin tension negatively regulates nuclear YAP accumulation in the dental epithelial stem cells. Profilin2, an actin monomer-binding protein which is tightly connected with actin skeleton tension, is enriched in the DESCs region. Other experiments are currently underway to further investigate how tissue tension and actin dynamics signaling may influence dental epithelial stem cells through YAP/TAZ activity.

【关键词】 dental epithelial stem cells；YAP/TAZ；actin

Intelligent Anti-bacterial Resin Adhesives to Defend Secondary Caries and Maintain the Balance of Oral Microecology

梁静鸥 邹 静 程 磊 四川大学华西口腔医学院

【摘要】 Introduction:Very few considered about intelligent anti-caries materials that could response to oral environment and help keep oral eubiosis. Here, we report novel non-leaching intelligent dental adhesives modified by tertiary amine which had long-term reversible pH-responsive anti-bacterial properties.

Materials & Methods: Tertiary amines (TAs) DMAEM and HMAEM were synthesized. MIC and MBC against Streptococcus mutans (S. mutans) of TAs in acid and neutral medium were tested. 5% (w/w) TAs were then incorporated into adhesive resin and light-cured repectively, yeilding adhesive resin modified by TAs (TA@RAs). The micro-tensile strength, surface roughness and cytotoxicity of eluents were measured. 48 h S. mutans biofilms were cultured on TA@RAs disks. The broth was with or without neutral buffer systems (PIPES+/PIPES-) to regulate the pH of incubation. The MTT test, acid production measurement and biofilm staining were conducted to evaluate the intelligent anti-biofilm effect. Moreover microbial ageing model was conducted to investigate the long-term effect. Saliva-derived biofilms was incubated on the specimens and the microbial diversity was analysized by 16S rRNA gene sequencing. Finally, the anti-caries effect was investigsted in vivo secondary models.

Results & Discussion: MIC and MBC greartly decreased in acid medium, which showed that TAs had acid-activated anti-bacterial effect. What’s more, addition of TAs into the adhesive had no side effect on microtensile bond strength, surface roughness and cytotoxicity of eluents of the adhesives. Anti-biofilm test showed TA@RAs had antibacterial effect only in the PIPES- medium where the pH kept below 5.5, the critical pH value of de-/re-mineralization balance due to the protonation of TAs. The viability, acid production and EPS production was significantly reduced. However, in PIPES+ medium, with pH keeping above 5.5, the effect greatly decreased. Furthermore, the effect changed accordingly with the exchange of the medium during the incubation, which verified the revesibility of the effect. Long-term effect was confirmed as TA@RAs still showed anti-bacterial effect after 30 d saliva-derived biofilms ageing. 16S rRNA gene sequencing results showed that the novel adhesives could increase the diversity of the saliva-derived biofilms. The shannon index was much higher in TA@Ras groups, which inferred that TA@RAs could help regulate the microbial community. The secondary caries rat models showed that the TA@RAshad caries-preventing effect since the lesion depth and mineral loss was significantly reduced in the TA@RAs groups.

Conclusions:In conclusion, TA@Ras were reversible pH-responsive and non-leaching dental materials which had long-term anti-biofilm effect and also helped maintain the oral microecological balance. Therefore, they have great research and application potential in the furture.

【关键词】 pH-responsive；non-leaching；anti-bacterial；anti-caries；oral microecology

基于儿童唾液蛋白质组防龋功能多肽的构建及其促矿化作用研究

王　琨　张凌琳　四川大学华西口腔医学院

【摘要】 龋病是儿童最常见的慢性感染性疾病之一，因龋病导致的牙齿问题是困扰儿童健康的重要原因。如何促进脱矿牙齿的再矿化也一直是口腔材料研究领域的关注热点和重要内容。唾

液作为与牙体硬组织紧密接触的口腔微环境，被认为是龋病病因中能够调控龋病进展过程中最重要的宿主因素之一。大量研究发现唾液蛋白在保持牙面完整性、促进脱矿牙齿的再矿化方面具有重要作用。近年来，蛋白质组学技术的进步为发现更多唾液蛋白成分提供了技术支撑。本课题通过采用同位素标记的相对和绝对定量蛋白质组技术和质谱多反应监测技术对来自不同龋病易感性的儿童唾液样本进行分析，经筛选鉴定获得防龋相关蛋白质组，并基于研究结果设计合成了具有潜在促矿化作用的功能多肽 DE-11。通过对该功能多肽的结构稳定性、细胞毒性作用和体外再矿化作用进行检测，进一步证实了 DE-11 具有良好的脱矿牙釉质吸附能力和促早期釉质龋再矿化作用，为儿童龋病的早期防治提供了新的思路和方法。

【关键词】 唾液蛋白质组；儿童龋病；防龋功能多肽；再矿化；早期釉质龋

抗菌肽 GH12 综合防龋作用及其机制研究

王雨霏　张凌琳　四川大学华西口腔医院

【摘要】 目的：抗菌肽具有快速杀菌能力、多模式杀菌机制及多重生物活性，自主研发的抗菌肽 GH12 具有快速杀伤变异链球菌（Streptococcus mutans）及清除 S. mutans 生物膜的作用，并且有良好的稳定性及安全性。本研究围绕 GH12 对 S. mutans 致龋毒力因子，对多菌种生物膜及对龋病动物模型的影响，评估其作为防龋药物的潜能和作用机制。

方法与结果：通过产酸、耐酸实验，激光共聚焦显微镜观察及 RT-qPCR 等，发现 GH12 显著抑制了 S. mutans 的产酸量、酸性条件下的存活率及胞外多糖合成量，并且下调了相关基因的表达；构建体外致龋三菌种生物膜模型，通过荧光原位杂交技术及实时荧光定量聚合酶链式反应，发现 GH12 可以显著改变致龋三菌种生物膜的微生物组构成，增加格氏链球菌和血链球菌的占比；大鼠龋病动物模型发现每天 3 次使用 5 min 的 GH12 在体内降低了龋病的发生率和严重程度。

结论：课题组自主研发的抗菌肽 GH12 在杀菌浓度 8mg/L 时，可抑制 S. mutans 生长。当 GH12 被消耗至亚抑菌浓度时，GH12 可抑制其产酸和产糖能力的同时又可以降低 S. mutans 对环境和其他菌种的耐受和抵抗能力，因此口内生物膜更易于被清除，同时降低残留生物膜的酸性和完整性。GH12 的这些抑菌效应减少了牙釉质暴露于酸性生物膜的机会，从而抑制了牙体硬组织脱矿，抑制了大鼠体内龋病的发生和发展。

【关键词】 抗菌肽；变异链球菌；格氏链球菌；生物膜；大鼠

DNA 框架核酸递送多重靶向的反义寡核苷酸以抑制生物膜的形成

张雨欣　四川大学华西口腔医学院

生物膜的形成导致许多慢性感染并且成为严重的健康问题。细菌和细胞外多糖的生长使生物膜具有粘附性和毒性，并且对抗生素产生抗性，因此难以根除。抑制细菌合成胞外多糖可以抑制细菌生物膜的形成，降低其稳定性并促进去除。本研究开发了具有四面体构型的框架核酸递送系统，它可以自由进入细菌细胞并通过将反义寡核苷酸运输到特定基因发挥其功能。我们基于变异链球菌中 VicK 蛋白结合的保守区设计了具有多个靶点的反义寡核苷酸序列，并使用框架核酸递送。我们观察到 EPS 的合成显著降低且生物膜厚度显著降低。递送系统同时降低了所有靶向基因的表达，证明了其高效性。本研究展示了一种新型核酸纳米材料在抑制生物膜形成中的作用，对治疗由生物膜引起的慢性感染有巨大潜力

【关键词】 生物膜；反义治疗；框架核酸；胞外多糖

Differences in plaque microorganism in Baikuyao children versus Han children in Guangxi

周恺燕　曾晓娟　广西医科大学附属口腔医院

【摘要】 Objective The objective of this study was to further characterize and contrast the plaque microorganism in Baikuyao children versus Han children in Guangxi. Methods A total of 32 Baikuyao and Han 12-year-old children were selected（16 caries-active and 16 caries-free）,and the 16S rRNA gene sequence analysis was used to compare the microbiomes of supragingival plaque samples from 32 Baikuyao and Han 12-year-old children. Results 1. The Observed Species, Chao1, and ACE indexes of Baikuyao children were significantly higher than those in Han ($P < 0.05$). 2. At the genus level,Capnocytophaga, Treponema, Ottowia, SR1_genera_incertae_sedis and Catonella in Baikuyao was higher than that in Han ($P < 0.05$), while the abundance of Veillonella and Lachnoanaerobaculum in Baikuyao was lower than that of the Han ($P < 0.05$). 3.Haemophilus in Han caries-active group was higher than that in Han caries-free; the abundance of Prevotella and Campylobacter in Baikuyao caries-active group was higher than that in Baikuyao caries-free, while the Cardiobacterium in Baikuyao caries-active group was lower than that in Baikuyao caries-free. Conclusion The results confirmed significant differences in the plaque microbiomes of the two ethnic groups and identified several taxa relevant to these differences,suggesting that ethnic and caries status may both affect the composition of

oral microorganisms.

【关键词】 Baikuyao; caries; supragingival plaque; microorganism

龋病预防

Experimental study on the effect of Sophora flavescens Ait extract on the main cariogenic bacteria in oral cavity

从兆霞　新疆医科大学第一附属医院（附属口腔医院）牙体牙髓科

【摘要】 Abstract:Objective To observe the effects of Sophora flavescens Ait extract on the growth,adhesion,acid production and sugar production of the main cariogenic bacteria and their biofilms,and to explore its anti-caries mechanism.Methods The minimum inhibitory concentration of the extract of Sophora flavescens Ait was determined by double gradient dilution method,0.5g/L chlorhexidine was used as the positive control,and the drug-free group was used as the negative control group;the bacterial adhesion was determined by ultraviolet spectrophotometer;Biofilm inhibition concentration and biofilm removal concentration were determined by membrane crystal violet staining;bacterial acid production and synthetic water insoluble extracellular polysaccharide were determined by ΔpH method and phenol-sulfuric acid method,respectively.Results The minimum inhibitory concentration of Sophora flavescens Ait extract on the main cariogenic bacteria was 4g/L;At 4g/L,the adhesion inhibition rates for Streptococcus mutans,Streptococcus sobrinus,Streptococcus sanguis,Actinomyces viscosus and Aetinomyces naeslundii were (77.6%±1.2%),(66.7%±1.8%),(60.68%± 2.9%),(79.8%± 1.2%) and (85.1%±1.3%),respectively.2g/L could significantly inhibit the ability of planktonic bacteria to produce acid and synthesize water-insoluble extracellular polysaccharides.The inhibition rate of biofilm formation against Streptococcus mutans,Streptococcus sobrinus,Streptococcus sanguis,Actinomyces viscosus,Aetinomyces naeslundii and Lactobacillus acidophilus at 4g/L was (87.5%±1.3%),(85.4%±0.5%),(89.0%±0.3%),(77.2%±0.7%),(87.4%±1.1%) and (80.4%±1.3%),respectively;The minimum biofilm eradication concentrations of the above bacterial biofilms were 16g/L,16g/L,16g/L,16g/L,8g/L and 8g/L,respectively.At 50% minimum biofilm eradication concentration,the inhibition rates of Sophora flavescens Ait extracts on acid production and synthetic water-insoluble extracellular polysaccharides in single biofilms were 67.5% to 94.1% and 42.3% to 60.0%,respectively.Conclusion Sophora flavescens Ait extract could inhibit the growth,adhesion,acid production and sugar production of the main cariogenic bacteria in the planktonic and biofilm state,which may become a dental caries prevention preparation.

【关键词】 Sophora flavescens；cariogenic bacteria；biofilm；virulence factors

The Structure and Composition of Lipoteichoic Acid in Streptococcus mutans Isolated from Caries-Active and Caries-Free Adults

黄　珊　吴敏婧　黄晓晶　福建医科大学附属口腔医院

【摘要】 Objective:To investigate the structure and composition of lipoteichoic acid(LTA) in Streptococcus mutans clinical isolates that have been verified their difference in cariogenicity.

Methods:The LTA of Sm 593(isolated from caries-active individual),Sm 18(isolated from caries-free individual) and Sm ATCC 25175(reference strain) were extracted from disrupted bacterial cells with n-butanol/water, followed by hydrophobic interaction chromatography.The samples were confirmed by comparison with standard LTA using FT-IR.The chain length is determined by detecting the molar of phosphorus.The molar ratio of D-alanine to phosphorus were also analysed.QRT-PCR was used to detect dltABCD mRNA level in these three strains.

Results:The chain length of S.m 593 is shorter than S.m25175 and S.m 18.While the length in S.m 18 is shortest.The molar ratio of D-alanine to phosphorus in S.m 593 is higher than S.m25175 and S.m 18.But the molar ratio of D-alanine to phosphorus in S.m 18 is lowest.The expression of dltABCD gene in S.m 593 is more than S.m25175 and S.m 18.The expression level of S.m 25175 is higher than S.m 18.

Conclusion:The LTA in S.m 593(Streptococcus mutans with higher cariogenicity) has the shorter chain,but per chain has more D-alanine ester residues.On the contrary,The LTA in S.m 18(Streptococcus mutans with lower cariogenicity) has the longer chain,but per chain has less D-alanine ester residues. The dlt mRNA level of S.m 593 is higher than S.m 18,that has the same tendency of the molar ratio of D-alanine to phosphorus.

【关键词】 Streptococcus mutans；Lipoteichoic acid；D-alanine；Chain length；Dlt

Role of D-alanylation of Streptococcus mutans Lipoteichoic Acid in Interspecies Competitiveness

吴敏婧　黄　珊　黄晓晶　福建医科大学附属口腔医院

【摘要】 Background: Lipoteichoic acid (LTA) is an important cell wall polymer in gram-positive bacteria, and it could be modified with D-Ala residues, which is called D-alanylation of LTA. The enzymes required for this process are encoded by the dltABCD operon. D-alanyl ester was demonstrated to effect on a number of important biological processes of bacteria. Streptococcus mutans (S.mutans) is one of the primary cariogenic bacteria，which could inhibit against other commensal oral bacteria by producing lactic acid and mutacins. D-alanine was demonstrated to be essential for the interspecies competitiveness of S. mutans. Objective: To investigate the role of D-alanylation of S. mutans LTA in interspecies competitiveness and clarify the mechanism that effect antagonism of S. mutans by LTA D-alanylation. Methods: SMUA159, S. sanguinis 10556, S. gordonii10558 were used in this study. SMUA159-dltC-ko was constructed by replacing the dltC gene with spectinomycin gene (add). The result was confirmed by gene sequence. Lack of D-alanylation in SMUA159-dltC-ko was shown by extraction of D- ala from parent and mutant strains. Biofilms were formed on bovine enamel blocks and placed in a vertical position in 24-well plates. Within the biofilms, pH, calcium concentration measurement and Colony-Forming Units were taken. Conditioned media assay and agar plates competition assay were taken to measure the wildtype and mutant interspecies competitive capacity. q-RT PCR was performed to quantify the levels of various mRNA transcripts. Results: Both single culture of SMUA159-dltC-ko and co-culture with S. sanguinis or S. gordonii showed higher pH and lower calcium concentration. The number of S. sanguinis or S. gordonii increased co-culture with SMUA159-dltC-ko (*p <0.05). SMUA159-dltC-ko showed less inhibition on S. sanguinis on agar plate and conditioned broth (*p <0.05) and mutacins and lactic acid related gene expression of early and late stage decreased. When SMUA159-dltC-ko was co-culture with S. gordonii, mutacins related gene (nlmABCD) expression decreased at the early stage while the acid producing related gene (ldh) expression increased at the late stage. Moreover, SMUA159-dltC-ko showed less inhibition on S. gordonii on agar plate and conditioned broth as well (*p <0.05). Conclusion: Within this study, the D-alanylation of LTA could increase S. mutans in interspecies competitiveness among oral commensal bacteria, S. sanguinis and S. gordonii, by regulation the mutacins and lactic acid produce.

【关键词】 Lipoteichoic acid；D-alanine；dlt operon；Streptococcus mutans；antagonism

新疆软紫草粗提物对口腔主要致龋菌体外作用的研究

袁曦玉　赵　今　新疆医科大学第一附属医院（附属口腔医院）

【摘要】目的：研究新疆软紫草粗提物对口腔主要致龋菌浮游状态及生物膜的生长、产酸、产糖、粘附的体外作用。方法 （1）通过微孔板法测定新疆软紫草粗提物对口腔主要致龋菌单菌最小抑菌浓度及生长抑制率，涂布平板法测定最小杀菌浓度；(2) 通过微量滴定板法测定新疆软紫草粗提物对口腔主要致龋菌单菌生物膜最低形成抑制浓度、生物膜最低清除浓度、最低清除已形成生物膜浓度（3）通过△ PH 值法测定 2 倍最小抑菌浓度、生物膜最低清除浓度及以下三个浓度新疆软紫草粗提物对测试菌株单菌浮游状态及生物膜产酸能力的影响，苯酚硫酸法测定 2 倍最小抑菌浓度、生物膜最低清除浓度及以下三个浓度新疆软紫草粗提物对测试菌株单菌浮游状态及生物膜产水不溶性胞外多糖能力的影响；(4) 采用玻壁法测定 2 最小抑菌浓度及以下三个浓度新疆软紫草粗提物对测试菌株粘附能力的影响；结果（1）新疆软紫草粗提物对变形链球菌、远缘链球菌、血链球菌、内氏放线菌、粘性放线菌和嗜酸乳杆菌的最小抑菌浓度分别为 1mg/mL、4mg/mL、1mg/mL、2mg/mL、4mg/mL、1mg/mL；最小杀菌浓度分别为 8mg/mL、8mg/mL、4mg/mL、4mg/mL、8mg/mL、4mg/mL；（2）新疆软紫草粗提物对变形链球菌、远缘链球菌、血链球菌、内氏放线菌、粘性放线菌和嗜酸乳杆菌的生物膜最低形成抑制浓度分别为 4mg/mL、4mg/mL、2mg/mL、2mg/mL、4mg/mL、2mg/mL；生物膜最低清除浓度分别为 16mg/mL、16mg/mL、8mg/mL、16mg/mL、16mg/mL、8mg/mL；最低清除已形成生物膜浓度分别为 8mg/mL、16mg/mL、8mg/mL、8mg/mL、8mg/mL、8mg/mL(3)2 倍最小抑菌浓度，生物膜最低清除浓度及以下三个浓度新疆软紫草粗提物对测试菌株的浮游状态及生物膜产酸及产水不溶性多糖的能力均有抑制作用，与阴性对照组相比差异均有统计学差异 ($P < 0.05$)；（4）2 倍最小抑菌浓度及以下三个药物浓度新疆软紫草粗提物均可抑制测试菌株的粘附能力，与阴性对照组相比差异均有统计学意义 ($P < 0.05$)。结论：新疆软紫草粗提物对口腔主要致龋细菌单菌浮游状态及生物膜的生长、产酸、产糖、粘附均具有一定抑制作用。

【关键词】 新疆软紫草；粗提物；口腔主要致龋菌；作用

氟化物对乳牙龈上菌斑微生态影响的宏基因组学研究

张倩霞　空军军医大学第三附属医院

【摘要】 目的：采用宏基因组学测序技术（16SrDNA 测序）检测氟化物对乳牙菌斑微生物多样性的影响及其动态变化，为氟化物防龋作用提供分子微生物参考数据。方法 以西安市某幼儿

园 3 岁儿童为研究对象，要求未接受过氟化物防龋措施，进行口腔检查并记录龋坏情况，分为高龋组 (dmft>=7)、低龋组（dmft=2）和无龋组 (dmft=0)，分别在涂氟前、涂氟后第 3 天、涂氟后第 2 周末采集符合 WHO 采样标准的龈上菌斑样本，基于 Thermofisher 的 IonS5TMXL 平台进行 16S V3-V4 区域测序并对比分析。结果 1. 平均每个乳牙龈上菌斑样本产生 79069 个 CleanReads 可用于分析。2. 高龋组和无龋组涂氟前相对丰度较高的菌门为放线菌门、拟杆菌门、变形菌门、厚壁菌门、梭杆菌门等；相对丰度较高的菌属为棒状杆菌属、放线菌属、二氧化碳嗜纤维菌属、纤毛菌属、普雷沃氏菌属、弯曲杆菌属、奈瑟菌属、变异链球菌属等。3. 涂氟前，高龋组中的微球菌目、肉杆菌科、颗粒链菌属、α - 变形菌属、变异链球菌种的相对丰度高于无龋组（P ＜ 0.05），而无龋组中韦荣球菌属、纤毛菌属、硒单胞菌属、普雷沃氏菌等菌种的相对丰度高于高龋组（P ＜ 0.05）。4. 高龋组、低龋组、无龋组乳牙龈上菌斑微生物群落均存在多样性。5. 高龋组涂氟前后菌群组成和相对丰度变化不大。高龋组涂氟后二氧化碳嗜纤维菌属的相对丰度先下降后升高（P ＜ 0.05）。无龋组涂氟后放线菌门、Tannerella 的相对丰度先升高后下降（P ＜ 0.05），厚壁菌门、普雷沃氏菌属的相对丰度先下降后升高（P ＜ 0.05），且都恢复至接近涂氟前水平。结论 不同患龋程度 3 岁龄儿童乳牙菌斑微生物群落均呈现多样性，氟化物能够抑制菌斑中某些微生物的属种驻存，且这种抑制作用是暂时的，为乳牙龋的微生物因素及其防治研究提供了新数据。

【关键词】 16SrDNA 测序技术；龈上菌斑微生态；氟化物；乳牙

数字化口腔医学

Confocal imaging of mouse mandibular condyle cartilage

何　瑶　重庆医科大学附属口腔

【摘要】 Mice are commonly used to study the temporomandibular joint (TMJ) and to model human TMJ disease. However, evaluating TMJ pathology in mice using standard histologic methods is time consuming, labor intensive, and dependent upon investigators’ expertise at consistently orienting and sectioning across tiny specimens. We describe a method that uses confocal microscopy to rapidly and reliably assess indicators of mandibular condyle cartilage pathology in mice. We demonstrate the utility of this method for detecting abnormalities in chondrocyte distribution in mice lacking lubricin (Prg4), the major boundary lubricant of articular cartilage. We further show that the method can provide information about recombination sites and efficiency in mandibular cartilage for Cre-driver strains. Because specimen preparation and data acquisition with confocal microscopy are simple and fast, the method can serve as a primary screening tool for TMJ pathology, before proceeding to complicated, time consuming, secondary analyses.

【关键词】 mandibular condyle cartilage; confocal imaging; 3D reconstruction; Prg4; aggrencan

基于髁突骨小梁解剖特征的仿生结构单元研究

李　帆　北京大学口腔医院

【摘要】 目的：通过分析髁突骨小梁三维结构数据，进而观察其三维方向上结构单元的形态学分布，研究三维方向上结构单元骨小梁的解剖特征，为进一步分析其仿生应力分布特点提供研究基础。

方法：本研究对象为 78 岁女性的右侧髁突，扫描 Micro-CT。从髁突骨小梁三维重建结构中选取出 2×2mm 的圆柱体兴趣单元（Volume of interest，VOI），得到多个三维分布的符合髁突骨小梁特异性解剖特征的 VOI 结构单元。

结果：VOI 结构单元共选取 33 个，从上至下共 5 层，第 1 层 8 个，第 2 层 8 个，第 3 层 7 个，第 4 层 6 个，第 5 层 4 个。其形态学参数在髁突骨小梁三维分布是不均匀的。

结论：本研究基于 VOI 结构单元对髁突骨小梁进行划分，获得骨小梁的解剖分布特征。髁突骨小梁三维方向上结构单元的形态学分布不均匀，在前侧、内侧及第 1 层骨量较高，在外侧及第 4、5 层前中侧骨质较疏松。利用该方法，进一步扩大样本量，可以获得髁突骨小梁分布普遍性规律，为仿生应力分布及临床应用创造条件。

【关键词】 髁突；骨小梁；解剖特征；结构单元

口腔用光固化三维打印精度评价方法建立及应用效果研究

萧　宁　赵一姣　王　勇　北京大学口腔医学院

【摘要】 目的：光固化三维打印技术在口腔修复临床诊疗中应用广泛，尤其以牙颌模型制作应用较多，本研究建立了一种光固化三维打印技术精度评价用牙颌参考模型，并借助该模型建立光固化三维打印牙颌模型准确度的多维评价方法，为临床应用提供参考。方法：参考既往文献报道中国人群恒牙及恒牙列形态学研究的统计分析数据，在 3ds Max 2018 软件中设计一副以简化标准长方体组合模型模拟真实牙颌模型特征的牙颌参考模型。用五款不同打印原理的光固化三维打印机进行模型打印： Objet30 Pro 打印机（PJ 技术）、Projet 3510 HD Plus 打印机（MJP 技术）、Perfactory DDP 打印机（DLP 技术）、DLP 800d 打印机（DLP 技术）和 Form 2 打印机（SLA 技术）。在 Geomagic 2012 软件中基于扫描数据分析打印模型的整体 3D 偏差、特征面的平面度、平行度和垂直度误差。利用数显卡尺对打印模型牙冠特征指标和牙列特征指标进行测量，分析打印层内和打印层高误差。结果：Objet30 Pro 打印模型的整体 3D 偏差和平行度误差最小，分别为 45 μm

和 0.138°；Projet 3510 HD Plus 和 Perfactory DDP 打印模型分别在垂直度和平面度方面表现最优，分别为 89.905°和 0.074mm；Objet30 Pro 打印机模型的打印层内和打印层高误差综合表现最优，分别为 0.02% 和 -0.06%。结论：本研究建立的牙颌参考模型及配套准确度评价方法可提供较客观全面的评价结果，具有较好的通用性。

【关键词】 三维打印；牙颌模型；数字化分析；精度评价

一种口内扫描结合 CBCT 重建三维冠根融合模型的精度研究

朱玉佳　赵一姣　王　勇　北京大学口腔医院

【摘要】 目的：具有全面完整信息的三维牙列模型在正畸、种植等领域有着越来越广泛的应用。本实验基于三维口内扫描模型与三维 CBCT 模型数据，获得完整的三维冠根融合模型，研究其建模精度并得到精度较高的三维冠根融合模型参数模式，以期为临床应用提供参考和指导。

方法：

1. 临床获取 10 颗人离体牙，应用精度为 10 μ m 的 SHINING DS-EX Pro 模型扫描仪进行离体牙扫描，得到离体牙的三维参考模型。

2. 通过在猪的下颌骨模型上按照牙列形态植入离体牙，构建模拟牙颌模型。

3. 应用精度为 20 μ m 的 3shape 口内扫描仪扫描模拟牙颌模型 , 得到模拟牙列的三维口扫模型。

4. 大视野 NewTom CBCT 扫描模拟牙颌模型，在 Mimics17.0 软件中重建模拟牙颌模型的三维 CBCT 模型。

5. 模拟牙列三维 CBCT 模型在 Geomagic Studio 2012 软件中与模拟牙列三维口内扫描模型基于临床牙冠进行配准。对模拟牙列三维口扫模型进行冠龈分界线提取，边界线向根方偏置不同距离（釉牙骨质界冠方、釉牙骨质界、釉牙骨质界根方）及投影，模型裁剪等操作，并通过曲率和切线连续算法实现三维冠根模型的自然过渡缝合 , 每颗牙可得到 6 个三维冠根融合模型。

6. 将获得的 60 个三维冠根融合模型分别与对应的离体牙三维参考模型进行整体及解剖牙冠部的三维偏差分析，采用析因资料的方差分析评价不同融合参数下牙齿模型精度的差异。

结果：针对本研究构建的模拟牙颌模型，基于“模拟冠根分界线”位于釉牙骨质界冠方进行曲率融合所获得的三维冠根融合模型精度最高，其整体和牙冠部 RMS 均值分别为 0.0813mm、0.0427mm。“冠龈分界线”偏置位置对有精度的影响有统计学差异，两种过渡算法对于精度的影响无显著差异。

结论：本研究中冠根三维数据融合方法，实现了三维 CBCT 模型与三维口内扫描模型的高精度融合，可以满足临床需求，并且可以为后续研发自动化算法程序提供参考依据。该方法基于活体牙的体内精度评价有待进一步研究。

【关键词】 CBCT；口内扫描；模型扫描；三维图像融合

下颌髁突功能面三维运动轨迹的初步推算和模拟

黄　超　北京大学口腔医院

【摘要】 目的探讨下颌运动过程中髁突功能面的三维运动轨迹，为颞下颌关节窝的设计提供理论基础。

方法对 1 名来源于北京大学口腔医学院·口腔医院的研究生志愿者颅颌面部进行锥形束 CT 扫描，数据重建得到颅颌面三维模型；同时利用虚拟架的牙列三维运动轨迹跟踪装置记录志愿者下颌运动轨迹，结合颅颌面三维模型和下颌骨运动轨迹数据，推算和模拟髁突三维运动轨迹。进一步确定髁突功能面，对髁突功能面在下颌张口、前伸、侧方运动过程中的三维形态进行拟合，推算髁突功能面的三维运动形态。

结果经推算模拟可见，下颌张口运动时髁突功能面先向下方运动，继续加大开口度的过程中，功能面向前上方运动，髁突功能面起始位置与终末位置的直线距离为 8.34mm。下颌前伸运动时髁突功能面向前下方滑动，滑动距离为 8.64mm。下颌侧方运动时工作侧髁突功能面运动范围较小，仅为轻微转动，最大运动幅度为 1.97mm；而非工作侧髁突功能面较工作侧运动幅度大，运动方向为向下前内方，移动距离为 7.65mm。

结论虚拟架的牙列三维运动轨迹跟踪装置与数字化建模技术结合，可实现对下颌骨髁突运动轨迹的准确模拟，并可进一步推算髁突功能面的三维运动形态。

【关键词】 下颌骨髁状突； 颌关系记录；数字化技； 髁突三维轨迹

基于模型的动态导航口腔种植手术相关学习曲线分析

黄婉如　滨州医学院

【摘要】 目的：评估基于模型研究的动态导航种植手术相关学习曲线。

方法：研究纳入 3 名无动态导航经验的临床种植医生，在同一种植颌骨模型上使用动态导航系统（易植美®，迪凯尔，中国）模拟种植手术，将种植体（威高 Jericom® 实验植体）植入计划的位点中，植入后对模型进行锥形束扫描，将实际种植体位置与虚拟计划位置进行比较精度验证：①植入点距离差②末端距离差③植入角度差。通过累积求和分析法 （CUSUM），得出种植动态导航技术的学习曲线。

结果：32 颗种植体植入点距离差平均 1.036±0.4mm，末端距离差平均 0.993±0.493mm，植入角度差 2.704° ±1.208。12 例手术后，CUSUM 学习曲线 k 值为负。

结论：通过累积求和分析法得出种植动态导航技术的学习曲线特征，并且在 12 例以后可以跨

越学习曲线。

【关键词】 动态导航；计算机辅助手术；学习曲线；累积求和法

数字化导航和三维打印模型技术相结合指导腓骨瓣在下颌骨缺损修复中的对比研究

倪幼康　浙江大学医学院附属第一医院

【摘要】 目的：腓骨瓣已广泛应用于下颌骨缺损修复重建中，但其精确度及对面型的恢复还有待提高，本文旨在用导航和三维打印模型技术指导腓骨瓣修复来提高腓骨瓣的应用。材料和方法：将 34 例接受腓骨瓣修复的口腔肿瘤患者按照使用导航技术分为导航组（13 例，使用数字化导航和三维打印模型技术）和对照组（21 例，使用导航技术），通过收集患者住院信息，测量术前及术后六个月的开口及开口型、面型不对称、外形满意度、疤痕满意度、华盛顿生活质量量表评分、CT 数据等来做出比较。结果：所有患者均顺利完成手术，导航组的手术时间长于对照组（10.36±1.87vs9.00±1.34h)。术后早期并发症二者没有显著性差异，住院天数及住院费用等二者无显著性差异。术后导航组在开口受限、面型不对称、疤痕满意度等方面和对照组无明显差异，在开口型异常、外观满意度上，导航组优于对照组。在生活质量评分中的外貌、情绪、焦虑的得分高于对照组。CT 结果显示下颌角偏差、颏偏斜，导航组优于对照组（1.72±1.29° vs 3.69±1.67°；2.45±1.39 vs 5.19±2.13）。结论：导航技术与三维打印技术相结合能够提高腓骨瓣修复下颌骨缺损手术的准确性，改善术后患者面容，不明显增加患者术后并发症、患者花费和时间成本，值得在临床上进一步推广。

【关键词】 下颌骨缺损重建；数字化导航；三维打印模型技术；腓骨瓣

CT-MRI Image Fusion Based Computer-assisted Navigation Management of Communicative Tumors Involved the Infratemporal-middle Cranial Fossa

杨　榕　郭玉兴　郭传瑛　北京大学口腔医院

【摘要】 Purpose: CT and MRI are crucial for preoperative assessment of the three-dimensional (3D) spatial position relationships of tumor, vital vessels, brain tissue and craniomaxillofacial bones precisely. The value of CT-MRI based image fusion was explored for the preoperative assessment, virtual planning and navigation surgery application during the treatment of communicative tumors

involved the infratemporal fossa (ITF) and middle cranial fossa.

Methods：Eight patients with infratemporal-middle cranial fossa communicative tumors (ICFCT) were enrolled in this retrospective study. Plain CT, contrast CT and MRI image data were imported into a workstation for image fusion, which were used for 3D image reconstruction, virtual surgical planning and intraoperative navigation sequentially. Therapeutic effect was evaluated through the clinical data analysis of ICFCT patients after CT-MRI image fusion based navigation-guided biopsy or surgery.

Results：High-quality CT-MRI image fusion and 3D reconstruction were obtained in all eight cases. Image fusion combined with 3D image reconstruction enhanced the preoperative assessment of ICFCT, and improved the surgical performance via virtual planning. Definite pathological diagnosis was obtained in all four navigation-guided core needle biopsies. Complete removal of the tumor was achieved with one exception among the seven navigation-guided operations. Postoperative cerebrospinal fluid leakage occurred in one patient with recurrent meningioma.

Conclusions: CT-MRI image fusion combined with computer-assisted navigation management, optimized the accuracy, safety and surgical results for core needle biopsy and surgery of ICFCTs.

【关键词】 Image fusion；CT；MRI；Computer-aided navigation；Infratemporal-middle cranial fossa

特殊人群口腔保健

Identification of a novel candidate gene KDF1 and novel mutations in tooth agenesis

曾秉辉　赵　玮　余东升　中山大学光华口腔医学院·附属口腔医院，广东省口腔医学重点实验室

【摘要】 Objective: Tooth agenesis (TA) is a disorder characterized by congenital tooth loss. There are two sub-types of TA: non-syndromic TA (NSTA) and syndromic TA (STA). Hypohidrotic ectodermal dysplasia (HED), characterized by sparse hair, oligodontia, and reduced sweating, is a kind of STA. Mutations of EDA, EDAR, EDARADD and WNT10A underlie TA. This study investigated the genetic causes of TA families.

Materials and Methods: Peripheral blood of 13 HED and 5 NSTA families was obtained. EDA, EDAR, EDARADD and WNT10A genes were analyzed by PCR and Sanger sequencing. Whole exome sequencing, bioinformatics analysis and structural modeling were performed. Immunohistochemical staining was performed to investigate whether kdf1 is expressed in developing tooth germs. CRISPR/Cas9 was used to construct the KDF1 c.G908C mutation knocked-in mice.

Results: By Sanger sequencing, we identified 12 EDA, 2 EDAR and 4 WNT10A mutations

in the genomes of 13 HED and 4 NSTA families. Whole exome sequencing identified KDF1 as a novel candidate gene of NSTA. Six of those mutations were novel mutations. Novel mutations were predicted as damaging, probably damaging, and disease-causing by SIFT, PolyPhen2, and Mutation Taster, respectively. Structural modeling results showed significant changes of the mutated proteins. Immunohistochemical staining of kdf1 in developing tooth germs indicated that kdf1 expression is important for the development of teeth. The KDF1 c.G908C mutation knocked-in mice was constructed by CRISPR/Cas9.

Conclusions: This study revealed the genetic basis of 13 HED and 5 NSTA families and expanded the mutational spectrum. KDF1 was identified as a novel candidate gene for NSTA. The KDF1 mutation knocked-in mice was constructed successfully.

【关键词】 tooth agenesis; KDF1; hypohidrotic ectodermal dysplasia; EDA; WNT10A

修　复

PIPS 技术联合 MTAD 溶液对纤维桩粘接强度的影响

万　书　郭　玲　西南医科大学附属口腔医院

【摘要】 背景及目的：桩道预备后根管内牙本质表面覆盖了大量的玷污层，研究表明大量玷污层的存在可阻碍牙本质－粘接剂的有效粘接，从而影响纤维桩的粘接效果。本实验的通过微推出实验，评价 PIPS 技术联合 MTAD 溶液对纤维桩粘接强度的影响。方法：将 44 颗完成根管治疗的下颌单根管前磨牙经桩道预备后，根据不同根管预处理方法随机分成 A、B、C、D 四组， A 组用蒸馏水预处理根管；B 组用 MTAD 溶液预处理根管；C 组用 PIPS 技术预处理根管；D 组用 PIPS 技术联合 MTAD 溶液预处理根管。每组随机选取一个样本通过扫描电镜观察牙本质玷污层和牙本质小管开发情况，每组剩余样本粘接纤维桩后进行微推出实验，检测纤维桩的粘接力，并进行统计分析。结果：1. 扫描电镜观察结果：A 组可见根管内壁牙本质小管完全被玷污层覆盖，未见牙本质小管开放；B 组和 C 组均可见部分牙本质小管开口和散在的玷污层覆盖；D 组极少玷污层覆盖，几乎可见所有的牙本质小管开放。2. 微推出实验结果： A 组具有最低的粘接强度值（P<0.05）。B、C、D 组粘接强度大于对照组，差异有统计学意义。D 组具有最高的粘接强度值（P<0.05）。结论：PIPS 技术和 MTAD 溶液单独预处理桩道根管内壁均能显著提高纤维桩的粘接强度，且两者联合使用效果最佳。

【关键词】 PIPS；MTAD；玷污层；纤维桩；微推出强度

牙槽外科学

MEG3 regulate the development and progression of head and neck squamous cell carcinoma by decreasing the expression of miR-421 and promoting the expression of E-cadherin

侯韵雯　季叶枫　南京医科大学附属口腔医院

【摘要】 Objectives: MEG3, a long chain non-coding RNA (lncRNA), has been verified in several tumors to function as tumor suppressors. However, the downstream mechanism of MEG3 in regulating the molecular mechanism of epithelial-mesenchymal transformation (EMT) in head and neck squamous cell carcinoma (HNSCC) progression is still need to be further explored. Methods: The expression of MEG3 was confirmed in 51 cases of HNSCC tissues compared to adjacent normal tissues by quantitative real-time polymerase chain reaction (qRT-PCR) analysis. Luciferase report assay was used to detect the association between miR-421 and MEG3, miR-421 and E-Cadherin in HNSCC cell lines. CCK8 and transwell invasion assays were used to assess cell proliferation and invasion capacity. Scratch wound assay was used to assess cell migration capacity. Results: This study demonstrates that expression of MEG3 is significantly downregulated in HNSCC compared to adjacent normal tissues. In vitro, overexpressed MEG3 inhibits cell proliferation, migration and invasion. MEG3 upregulated the expression of E-cadherin, which was instead downregulated by MiR-421. MiR-421 is negatively regulated by MEG3 in HNSCC. MEG3 therefore regulates EMT by sponging miR-421 targeting E-cadherin in HNSCC. Conclusions: This study suggests that the MEG3-miR-421-E-cadherin axis may be a new therapeutic target for HNSCC.

【关键词】 Head and neck squamous cell carcinoma (HNSCC）；MEG3；miR-421；E-cadherin；epithelial-mesenchymal transition(EMT)

BMP-2、VEGF 和 TGF-β 联合应用诱导成骨分化作用和机制的研究

王志浩　青岛大学口腔医学院

【摘要】 目的：研究联合应用生长因子 BMP-2、VEGF 和 TGF-β 诱导成骨的质量和效率，从而获得最有利于成骨的联合应用方式，同时研究联合应用诱导成骨的网络调控机制，为组织工程骨构建提供理论基础。

方法：体外培养小鼠胚胎成骨细胞前体细胞（MC3T3-E1）和牙髓间充质干细胞（DPSCs），以成骨诱导培养基（oeteogenic medium，OM) 中添加 BMP-2、VEGF 和 / 或 TGF-β1 排列组合设计实验分组，以单纯 OM 培养基为对照组（OM 组）。ccK-8 实验检测各组细胞的体外增殖能力，碱性磷酸酶 (alkaline phosphatase，ALP) 染色、茜素红染色及其定量检测分析成骨水平，RT-PCR 法检测成骨相关基因的表达情况， Western blotting 研究成骨诱导相关机制。

结果： 应用 BMP-2、VEGF 或 TGF-β1 不会影响 MC3T3-E1 和 DPSCs 的早期增殖。诱导 3 天后，联合应用 BMP-2、VEGF、 TGF-β1 时 ALP 染色及定量检测均高于其余实验组和对照组（P ＜ 0.05）。诱导第 7 天和 14 天后，联合应用 BMP-2 和 VEGF 组 de ALP 染色和茜素红染色及其定量检测均高于联合应用 BMP-2、VEGF、 TGF-β1 及其余组。时效关系改进后，前期联合应用 BMP-2、VEGF 和 TGF-β1 后期联合应用 BMP-2、VEGF 时，诱导第 7 天和第 14 天时，ALP 染色及定量检测和成骨矿化结节染色及钙沉积定量检测均高于 BMP-2+VEGF 联合应用组及其余实验组（P ＜ 0.05）。同时时效关系改进后 Runx2 的表达量也较其余实验组显著提高（P ＜ 0.05），ALP、OCN 的表达量也高于其余组。Western blotting 也显示，通过经典的 BMPs-Receptor-Smad 信号转导通路来促进成骨分化，MAPK 下游通路 P38 和 ERK1/2 信号通路的磷酸化辅助调节成骨分化能力。

结论：依据时效关系联合应用 BMP-2、VEGF 和 TGF-β 能够显著提高成骨分化诱导能力，主要通过经典的 BMPs-Receptor-Smad 信号转导通路来促进成骨分化，MAPK 下游通路 P38 和 ERK1/2 信号通路的磷酸化辅助调节成骨分化能力，从而提高成骨质量和效率。这一研究结果将为构建高效组织工程骨提供理论依据，进而为制作具有临床实用价值的组织工程骨奠定基础。

【关键词】 BMP-2；VEGF；TGF-β：成骨作用；时效关系

BMAL1 Regulates Development of Mandibular Condyle through Hedgehog Signaling

余少玲　Tang Qingming　华中科技大学同济医学院附属协和医院

【摘要】 Chondrogenesis and endochondral ossification in mandibular condyle play crucial roles in maxillofacial morphogenesis and function. Circadian regulator brain and muscle arnt-like 1 (BMAL1) is proven to be essential for embryonic and postnatal development. Although there are some indications that BMAL1 plays a regulatory role in skeletal development, its roles in chondrogenesis and endochondral ossification of mandibular condyle have not been explained. The goal of this study was to define the functions of BMAL1 in the postnatal growth of mandibular condylar cartilages (MCC). we verified that global knockout of BMAL1 can result in short malformation of mandible by impairing the sequential differentiation of chondrocytes in mandibular condyle. Furthermore, genome-wide RNA sequencing in mandibular condyle tissues from Bmal1-/- mice and even-aged wild-type mice uncovered that hedgehog signaling pathway is the potential target of BMAL1. Dual-luciferase assays illuminated that BMAL1 regulates the sequential differentiation of chondrocytes in MCC through directly binding to the promoter of protein patched homologue 1 (Ptch1), modulating target of hedgehog signaling which is indispensable for chondrogenesis and endochondral ossification. Importantly, the short malformation of mandible caused by BMAL1-deficiency can be rescued by SAG, a hedgehog signaling activator. Collectively, our results indicate that BMAL1 plays critical roles on chondrogenesis and endochondral ossification of MCC, giving a new insight on potential therapeutic strategies for facial dysmorphism.

【关键词】 endochondral ossification；mandibular condyle；hedgehog signaling pathway；BMAL1

LncRNA PVT1 对口腔鳞状细胞癌生物学特性的影响及机制

邹　波　李克义　袁道英　聊城市人民医院

【摘要】 目的：拟通过对口腔鳞状细胞癌基因芯片数据集进行生物信息学分析，筛选出在口腔鳞癌发生发展过程中起关键作用的 lncRNA，并验证其调控口腔鳞状细胞癌发生发展的机制，以寻找可靠的 lncRNA 作为口腔鳞状细胞癌预后判断的标志物和潜在的治疗靶点。

方法：应用公共数据库筛选与 OSCC 患者临床病理特征相关的 lncRNA PVT1；应用慢病毒基因敲除技术敲除 CAL-27 和 TCA-83 细胞中的 PVT1，应用相应的技术手段检测细胞的增殖、克隆

形成、迁移和侵袭能力以及体内成瘤能力的变化。通过转录组测序技术，筛选敲除 PVT1 前后的差异表达基因，验证差异基因对 OSCC 生物学特性的影响，采用荧光素酶报告基因检测 PVT1 对差异基因的调控。

结果：1. 通过生物信息学研究发现，PVT1 在口腔鳞状细胞癌中表达明显上调，并且 PVT1 表达与口腔鳞状细胞癌的临床分期、预后呈明显相关性。2. 在 CAL-27 和 Tca-83 两个细胞系中，验证了 PVT1 敲除能够抑制细胞增殖和克隆形成，并且抑制细胞迁移和侵袭能力；此外，裸鼠荷瘤实验证实了敲除 PVT1 抑制口腔鳞状细胞癌细胞的成瘤能力和肿瘤生长速度。3. 转录组测序和生物信息学分析 4 个口腔鳞状细胞癌数据集发现 PLAU 是 PVT1 的靶基因。敲除 PLAU 能够抑制口腔鳞状细胞癌细胞增殖、迁移和侵袭，过表达 PLAU 能够部分阻断敲除 PVT1 对细胞增殖、细胞迁移和侵袭的抑制作用。此外敲除 PVT1 能够下调 PLAU 启动子活性。

结论：本研究首先采用生物信息学分析手段，筛选出与口腔鳞状细胞癌临床病理特征有明显相关性的 lncRNA PVT1，并且通过细胞生物学实验和荷瘤实验验证了 PVT1 对口腔鳞状细胞癌发生发展的促进作用；并发现 PVT1 通过在转录水平调控 PLAU 的表达促进口腔鳞状细胞癌发生发展。提示 PVT1 可能作为口腔鳞状细胞癌预后判断的标志物和潜在的治疗靶点。

【关键词】 PVT1；长链非编码 RNA；口腔鳞状细胞癌；PLAU；生物信息学

升支高度变化及成角畸形对儿童髁突骨折患者治疗方式选择的影响分析

常士平　马　秦　空军军医大学第三附属医院

【摘要】 研究目的：儿童髁突骨折的治疗目前尚无明确的治疗规范。由于儿童髁突的生长潜力，髁突骨折后保守治疗即能改建复位愈合，因此保守治疗是儿童髁突骨折患者首选方式，但其目前并无明确适应证。本研究拟对我院近 5 年治疗成功的儿童髁突骨折患者的髁突骨折评估参数进行分析，量化升支高度变化、成角畸形对治疗方式选择的影响，以期为临床选择保守或开放治疗提供明确的参考数据。研究方法：检索我院 2012—2016 年收治的儿童髁突骨折患者，对 CT 数据进行分析，量化骨折导致的升支高度降低值及成角畸形值。根据复诊记录或随访信息，满足以下 3 个条件者定义为治疗成功，纳入分析。同时根据手术治疗或保守治疗进行分组。Ø 最大开口度 35mm 或三横指以上；Ø 口内咬合无严重的咬合错乱关系；Ø 无自觉主诉的关节不适症状对保守治疗成功组和手术治疗成功组的升支高度降低值和成角畸形值进行独立样本 t 检验。研究结果：46 人（35 男，11 女）纳入本次研究，受累髁突

74 侧，42 侧接受保守治疗，32 侧接受手术治疗。不考虑骨龄情况下，囊内骨折及颈部骨折患者升支高度降低 6mm 以上者，手术治疗更安全；骨龄 1、2 组患者升支高度降低 10mm 以内，保守或手术都能达到治疗目标。颈部骨折病例的成角畸形均值在手术治疗组和保守治疗组中具有统计学差异；成角畸形值在 60° 以上的病例选择手术治疗是更安全的。研究结论：升支高度降低值、

成角畸形值可以作为治疗方法选择的参考因素。

【关键词】 髁突骨折；治疗方式；保守治疗；手术治疗；参考因素

Application of digital mandibular movement record and masticatory muscle electromyography in the evaluation of stomatognathic function in patients with mandibular tumor

陈俊鹏　郭传瑛　北京大学口腔医院

【摘要】 Objective: To study the clinical characteristics of mandibular movement and masticatory muscle function in preoperative and postoperative patients with unilateral mandibular tumors in the region of mandibular body and ramus by combining digital mandibular movement records with electromyography, and to preliminarily explore the relationship and mechanism between movement and masticatory muscle function.Methods: Six preoperative patients with tumor in unilateral body and ramus of mandible were included, and three postoperative patients with unilateral segmental resection and reconstruction of mandibular bone were included. The mandibular movement recording system and surface electromyography system were used to collect the movement trajectory of the patients’ mandibular marginal movement and chewing movement, and the surface electromyography of bilateral masseter and temporalis was recorded concurrently. The surface electromyography of bilateral masseter and temporalis was collected when the patients were at relaxation and at maximal voluntary clenching (MVC). The motion trajectory was observed on the digital virtual model, and the motion amplitude and direction of mandibular marginal movements were analyzed. The characteristics of masticatory electromyogram (EMG) activity in affected and unaffected sides at relaxation, MVC and bilateral mastication were analyzed, and the asymmetry indexes and activity indexes were calculated. Results: The preoperative mean maximum opening of the patients was (35.20±6.87) mm. Three patients had mild mouth opening limitation, and all the patients’ mouth opening trajectory was skewed to the affected side. During lateral movements, the mean range of motion of the affected side [(10.34±1.27) mm] and that of the healthy side [(6.94±2.41) mm] were significantly different. The maximum opening of the postoperative patients was (30.65±17.32) mm, and the mandibular marginal movement characteristics were consistent with those of the patients before surgery. During MVC in the preoperative patients, the median EMG activities of the masseter muscle [44.20 (5.70, 197.90) μV] and the temporalis muscle [42.15 (22.90, 155.00) μV] on the affected side were slightly lower than those of the masseter [45.60 (7.50, 235.40) μV] and the temporalis muscle [63.30 (44.10, 126.70) μV] on the healthy side. In the postoperative patients, individualized changes occurred. Some patients suffered from weakened electromyographic activity on the affected side, while some other ones showed

hyperelectromyographic activity on the affected side.Conclusion: Both benign and malignant tumors as well as their surgery can cause abnormal mandibular movements and change of electromyographic activity of bilateral masseter and temporalis muscles.

【关键词】 Mandibular movement；Electromyography；Head and neck tumor；Rehabilitation and reconstruction；Masticatory muscle

Subcutaneous Injection of Hyaluronic Acid to Decrease Acute Skin Toxicity after Adjuvant Interstitial Brachytherapy in Parotid Gland Cancer Patients: A Non-Randomized Controlled Trial

高　雅　北京大学口腔医院

【摘要】 Purpose: The aim of this trial was to evaluate safety and efficacy of subcutaneous injection of hyaluronic acid to decrease acute skin toxicity after adjuvant interstitial brachytherapy in parotid gland cancer patients.

Methods: In this non-randomized controlled trial, patients with histologically proven parotid gland cancer who were indicated for adjuvant interstitial brachytherapy were included. Participants were non-randomly divided into experimental group and control group. Participants in the experimental group were injected with hyaluronic acid subcutaneously immediately after interstitial brachytherapy during the operation. The acute toxicity was evaluated in the first two months. Results: Thirty consecutive participants with parotid gland cancer who were indicated for adjuvant interstitial brachytherapy were included from April 2018 to September 2018. Twenty participants were in the experimental group and 10 were in the control group. The median dosage of hyaluronic acid was 8mL (4-11mL) according to the size of target area. The D90 of the affected skin was 2732cGy (1049-5733cGy). The difference of D90 of the affected skin was significant between the pre-plan (mean, 3693cGy) and the actuarial quality verification (mean, 2770cGy) in the experimental group (p=0.004). The difference of scoring of acute akin toxicity was significant between the experimental group and the control group (p=0.001). There was no clear correlation between the D90 of the affected skin and the scoring of acute akin toxicity (p=0.266). Conclusions: Subcutaneous injection of hyaluronic acid was safe and efficient to decrease acute skin toxicity after adjuvant interstitial brachytherapy in parotid gland cancer patients.

【关键词】 Hyaluronic Acid; Acute; Skin Toxicity; Brachytherapy; Parotid

口腔颌面部恶性肿瘤术后感染相关因素分析

郭治辰　新疆医科大学附属口腔医院

【摘要】 目的：口腔颌面部恶性肿瘤患者术后出现继发感染的机率很高，通过分析此类感染病源菌的分布及特点，对于治疗和预防颌面部恶性肿瘤术后感染提供理论依据。

方法：收集 2007 年 1 月 -2018 年 1 月期间我科收治的 312 例口腔颌面部恶性肿瘤患者的病例资料，并进行回顾性分析，分析术后感染几率，病源菌的分布，运用 Logistic 回归分析相关指标来揭示引起恶性肿瘤术后感染的相关危险因素。

结果：312 例恶性肿瘤患者术后发生感染 39 例（12.5%），感染的常见部位是呼吸道和术区；病源菌类型分布：需氧菌 35 例（89.74%），厌氧菌 36 例（92.31%）。运用单因素分析得出：年龄、肿瘤部位、BMI 指数、糖尿病、手术时间、Charlson 并发症指数、手术方法、输血及术前放疗为恶性肿瘤术后感染的相关危险因素；多因素分析得出：BMI 指数、手术方式、糖尿病、手术时间和手术方式是口腔颌面部恶性肿瘤患者术后感染的独立危险因素。

结论：通过本研究发现 BMI 指数、糖尿病、手术时间和手术方式是口腔颌面部恶性肿瘤患者术后感染的独立危险因素，故术前需要全面评估术后可能出现感染的风险，并在术前积极给予相关处理。

【关键词】 口腔颌面部肿瘤 / 并发症 / 感染 / 糖尿病

3D 打印供牙模型在自体牙移植中的应用优势总结

惠小勇　空军军医大学第三附属医院

【摘要】 目的：总结 3D 打印供牙模型在自体牙移植中的应用。方法：收集 2017 年 11 月至 2018 年 3 月进行自体牙移植且术中采用 3D 模型辅助受牙窝预备的病例 37 例，从患者对供牙模型的接受度与认可度、受牙牙窝预备时间与试植次数、供牙游标卡尺测量、供牙与 3D 模型数据比较、3D 模型试植，植入位置调整、影像资料保存等方面进行总结。结果：37 例病例制作了 3D 打印模型，患者对模型的接受度和认可度均为 100%；受牙牙窝预备的平均时间为 10.33±1.83min，模型试植次数为 3.11±1.74 次，供牙试植次数为 1.65±0.79 次；供牙及其 3D 模型在牙冠近远中和颊舌径的直径偏差分别为 0.28±0.11mm、0.28±0.09mm，牙根长度偏差 0.27±0.10mm；影像资料显示，使用 3D 模型有助于调整并选择理想的近远中向、颊舌向位置及咬合关系。结论：在自体牙移植手术中应用 3D 打印供牙模型有助于手术简单、高效和理想的完成。

【关键词】 3D 打印；供牙；模型；自体牙移植

局部 5% 普萘洛尔乳膏治疗浅表型婴幼儿血管瘤的效果评价

姜莉铖　李克义　张　彬　聊城市人民医院

【摘要】 婴幼儿血管瘤（IH）是一种临床常见的的良性血管性肿瘤，病理学表现为血管内皮细胞增殖性病变。尽管它有自行消退的趋势，但部分患者会出现严重并发症，影响患者美观及生活。国际上推荐早期干预治疗，防止并发症发生。本研究回顾分析了我治疗中心两年多来用 5% 普萘洛尔乳膏治疗的浅表性婴幼儿血管瘤全部病变 150 例，对其流行病学，疗效评分和安全性进行评估。结果发现婴幼儿血管瘤的头颈部发病率较其他部位稍高；治疗效果与患儿性别、病变部位无明显差异，但与病变面积及深度有关，病变面积越大，治疗效果越明显，病变深度越深，治疗效果越差；浅表型婴幼儿血管瘤干预越早，治疗效果可能越好，越能够减缓血管瘤的发展，进而减少并发症。总之，我们认为局部应用 5% 普萘洛尔乳膏治疗浅表型婴幼儿血管瘤的临床安全性好，且临床效果显著，值得临床推广。

【关键词】 婴幼儿血管瘤；普萘洛尔乳膏；消退

聚多卡醇硬化治疗小涎腺粘液腺囊肿的疗效及安全性

刘建林　李克义　张　彬　聊城市人民医院

目的：小涎腺粘液囊肿多见于导管损伤，粘液渗入组织间隙，粘液腺体阻塞，导致囊性病变形成和小导管扩张。目前，其治疗方法众多但治疗效果差异较大。本研究旨在探究聚多卡醇治疗小涎腺粘液囊肿的疗效及安全性。方法：对 112 例确诊为小涎腺粘液囊肿的患者注射聚多卡醇，并对其疗效和安全性进行系统评价。结果：122 例中治愈 102 例，显效 8 例，部分缓解 2 例。随访期间未发现复发，均有效，总治愈率为 91.07%；在治疗或随访期间未观察到严重的副作用；性别间疗效无显著性差异 (P=0.490)；与舌尖下表面粘液囊肿相比，下唇粘液囊肿硬化治疗更有效 (P=0.035)。结论：聚多卡醇硬化治疗小涎腺粘液囊肿疗效满意，尤其对于儿童，具有无需麻醉、疼痛度轻、创伤小、操作简单、配合度好的优点。

【关键词】 聚多卡醇；硬化治疗；粘液腺囊肿

内倾型深覆殆非拔牙矫治前后软硬组织变化的研究

闫昱文　刘　奕　中国医科大学附属口腔医院

【摘要】 目的：

研究内倾型深覆殆患者采用非拔牙矫治配合口外弓治疗前后软硬组织的变化，探讨该类患者的临床矫治效果。

方法：

选择中国医科大学附属口腔医院正畸科就诊的 24 例内倾型深覆殆患者，所有患者均采用非拔牙矫治方案，采用固定矫治器配合口外弓增强口内支抗及颌间牵引的治疗方案，通过配对 t 检验对治疗前后头颅侧位片测量数据进行统计分析，比较治疗前后软硬组织的变化。

结果：

矫治结束，软组织测量值 LLP 距增加（-0.94±1.83）mm，EP-LL 距增加（-0.65±1.54）mm，差异有统计学意义（P ＜ 0.05），表明下唇在矫治结束后前移；Cm-Sn-U1 角略增大，但差异无统计学意义（P ＜ 0.05）。硬组织骨性测量值 SNA、SNB、ANB 略增大，差异无统计学意义（P ＜ 0.05）；MP-SN 增加（-0.20±1.56）°，ANS-Me 增加（-0.21±1.63）mm，差异有统计学意义（P ＜ 0.05），提示矫治结束后下面高增加。硬组织牙性测量值 U1-SN 增加（14.20±4.31）°，U1-L1 减小（25.10±8.23）°，差异有统计学意义（P ＜ 0.05），表明矫治结束后上切牙牙轴唇倾，牙冠唇向移位；L1-MP 增加（8.00±1.56）°，差异有统计学意义（P ＜ 0.05），表明矫治结束后下切牙牙轴代偿性唇倾。

结论：

内倾型深覆殆患者非拔牙矫治配合口外弓治疗，上下切牙代偿性唇倾可获得良好的覆殆覆盖关系，且远期疗效稳定可靠。组织改建在骨骼及软组织上作用较弱，主要以牙性改建为主。矫治结束下唇前移获得协调的鼻唇颏形态，远期观察软组织侧貌良好。

【关键词】 内倾型深覆殆；非拔牙矫治；软组织侧貌；口外弓

下颌第三磨牙冠切除术临床预后的研究

闫子玉　崔念晖　北京大学口腔医学院

【摘要】 研究目的：采用分组对照前瞻性的研究方法，按照定量感觉测试程序（quantitative sensory testing, QST）比较牙冠切除术与牙拔除术对下牙槽神经（inferior alveolar nerve, IAN）功能的影响，并应用 CBCT 评估冠切术后剩余牙根转归。

内容与方法：选取经 CBCT 确认牙根与下颌神经管接触的下颌智齿拔除病例，遵从伦理原则分为两组，试验组行牙冠切除术，对照组行牙拔除术。1）两组分别于术前、术后 24 小时和术后 1 周对患侧颏孔区进行 QST 检查；2）试验组分别于术后即刻、术后 6 月行 CBCT 检查。

结果：试验组（n=91，27.19±4.31y ）对照组（n=49，28.04±4.26y ）

1）试验组 IAN 管骨壁缺失长度（IAN 损伤风险）（P ＜ 0.05）显著大于对照组，但术后疼痛，感染等并发症发生率无显著差异；2）QST 结果示：术后机械感觉异常率变化显著（P ＜ 0.001），温度感觉异常率无显著变化； 温度感知阈值（神经永久性损伤的敏感指标），试验组波动较对照组小；3）牙根术后可发生位移甚至旋转，牙根表面成骨情况各异，其转归可能与患者年龄、牙根位置、形态、大小、与 IAN 距离等有关。

结论： 对于与 IAN 关系密切的智齿拔除病例，1）牙冠切除术手术创伤可能小于牙拔除术；2）牙拔除术对 A δ，C 神经的损伤比牙冠切除术大；3）保留牙根的转归可能与患者年龄、牙根位置、形态、大小、与 IAN 距离等有关。

【关键词】 下颌第三磨牙；牙冠切除术；定量感觉测试；下牙槽神经；剩余牙根

改良自体脂肪移植技术联合真皮组织瓣治疗半侧颜面萎缩

张　凯　李云鹏　张浚睿　空军军医大学第三附属医院

【关键词】 半侧颜面萎缩是一种发生于颌面部原因不明的先天性软组织发育畸形，受累侧出现渐进性软组织全层萎缩。该病治疗难度较大，传统的治疗方法主要依靠游离组织瓣修复，患侧软组织体积恢复效果欠佳，而经典的自体脂肪移植技术存在术后血管化程度差，体积留存率较低的缺点，尤其是对于口周等肌肉运动频繁的区域，脂肪受压吸收较明显，单纯依靠脂肪移植难以取得满意的效果。近年来我科结合自身技术特长，在 Coleman 脂肪移植技术基础上进行改良，采用富血小板纤维蛋白（Platelet Rich Fibrin, PRF）和基质血管成分（Stromal Vascular Fraction, SVF）提高自体脂肪移植后体积留存率，借助自体脂肪移植技术恢复患侧面部软组织体积，配合真皮组织瓣修复口周形态，取得了良好的修复效果。

【关键词】 半侧颜面萎缩；自体脂肪移植；基质血管成分；富血小板纤维蛋白；游离组织瓣

牙髓病学

LncRNA DANCR 竞争性结合 miR-216a 在牙髓防御修复中的作用研究

陈玲玲　林正梅　中山大学附属口腔医院

【摘要】 目的

促进牙髓细胞（DPCs）成牙本质向分化是牙髓牙本质复合体再生的关键。我们前期发现 lncRNA DANCR 调控 DPCs 分化参与牙髓防御修复过程，但其机制未明。

方法

首先，筛选 DPCs 分化过程差异表达的 lncRNAs，并检测特异性表达的 DANCR 在 DPCs 成牙本质向分化及牙髓防御中的作用；接着，通过信息学分析及功能验证实验，探索 DANCR 是否发挥转录后调控作用并筛选其作用靶点；进一步采用荧光素酶技术及 RNA 结合蛋白免疫沉淀实验验证 DANCR 的机制；最后，阐明 DANCR 的靶标在 DPCs 分化中的作用。

结果

我们发现 DANCR 参与牙髓防御修复过程，低表达 DANCR 促进 DPCs 分化。进一步实验证实 DANCR 与 miR-216a 结合，且两者负相关。DANCR 通过阻遏 miR-216a 发挥作用，而 miR-216a 可靶向沉默 c-Cbl 的表达。与此同时，敲低 miR-216a 可解除对 c-Cbl 的抑制，并逆转敲低 DANCR 对 DPCs 分化的影响。

结论

DANCR 可竞争性结合 miR-216a，解除对 c-Cbl 的靶向沉默，进而调控 DPCs 分化参与牙髓修复再生。本研究可为牙髓修复再生研究提供新思路。

【关键词】 长链非编码 RNA DANCR；牙髓细胞；微小 RNA-216a；竞争性内源 RNA；修复反应

METTL3 regulates alternative splicing of MyD88 upon the lipopolysaccharide-induced inflammatory response in human dental pulp cells

冯智慧　中山大学附属口腔医院珠江新城门诊部

【摘要】 Dental pulp inflammation is a widespread public health problem caused by oral bacterial infections and can progress to pulp necrosis and periapical diseases. N6-methyladenosine (m6A) is

a prevalent epitranscriptomic modification in mRNA. Previous studies have demonstrated that m6A methylation plays important roles in cell differentiation, embryonic development and stress responses. However, whether m6A modification affects dental pulp inflammation remains unknown. To address this issue, we investigated the expression of m6A and N6-adenosine methyltransferase (METTL3, METTL14) as well as demethylases (FTO, ALKBH5) and found that the levels of m6A and METTL3 were up-regulated in human dental pulp cells (HDPCs) stimulated by lipopolysaccharide (LPS). Furthermore, we knocked down METTL3 and demonstrated that METTL3 depletion decreased the expression of inflammatory cytokines and the phosphorylation of IKKα/β, p65, and IκBα in the NF-κB signalling pathway as well as p38, ERK, and JNK in the MAPK signalling pathway in LPS-induced HDPCs. The RNA sequencing analysis revealed that the vast number of genes affected by METTL3 depletion were associated with the inflammatory response. Previous research has shown that METTL3-dependent N6-adenosine methylation plays an important role in mRNA splicing. In this study, we found that METTL3 knockdown facilitated the expression of MyD88S, a splice variant of MyD88 that inhibits inflammatory cytokine production, suggesting that METTL3 might inhibit the LPS-induced inflammatory response of HDPCs by regulating alternative splicing of MyD88. These data shed light on new findings in epitranscriptomic regulation of the inflammatory response and open new avenues for research into the molecular mechanisms of dental pulp inflammation.

【关键词】 N6-methyladenosine；METTL3；alternative splicing；MyD88；lip polysaccharide；dental pulp inflammation

EZH2 对牙髓炎症中胶原纤维降解的作用及其机制

何　婕　惠甜倩　北京大学口腔医院

【摘要】 目的：研究 EZH2 对牙髓组织炎症反应过程中细胞外基质的降解及胶原纤维的作用及机制。

方法：用 20ng/mL EZH2 重组蛋白及 2uMol/L 的 EZH2 抑制剂 EI1 刺激人牙髓细胞（human dental pulp cells，HDPC）不同时间（0h、2h、4h、24h）后，定量即时聚合酶链式反应（q-PCR）测定细胞基质金属蛋白酶（MMP1、MMP2、MMP3、MMP8、MMP9、MMP10、MMP13）及 I 型胶原的基因表达变化。在体内实验中，选取 SD 雄性六周龄大鼠 12 只，对其磨牙进行开髓封药，建立大鼠牙髓炎模型，将大鼠分成 3 组： LPS（10mg/ml）组；LPS(10mg/ml)+EZH2（20ng/mL）组；LPS(10mg/ml)+EI1（20ng/mL）组，分别在 1d、3d 后处死，HE 染色观察其牙髓组织病理变化，马松三色染色法验证 EZH2 及其抑制剂 EI1 对牙髓中胶原纤维的影响。q-PCR 结果显示：EZH2 重组蛋白刺激 HDPC 2h、4h、24h 后，MMP3 mRNA 水平为对照组的 2.032± 0.1969、2.244± 0.1374、1.664± 0.06682 倍（P<0.01），MMP8 的 mRNA 水平为对照组的 4.113± 0.06374、3.918 ± 0.9280、

1.914 ± 0.06330 倍（P<0.05）；type I collagen 的 mRNA 水平为对照组的 8.45%、24.55%、9.217% 左右（P<0.001）。EI1 刺激 HDPC 2h、4h 后，MMP3 的 mRNA 变化无统计学差异，24h 为对照组的 56.46% 左右（P<0.001）。MMP8 的 mRNA 水平为对照组的 26.05%、22.45% 、 22.67% 左右（P<0.001）；type I collagen 的 mRNA 水平叫对照组上调 15 倍左右（P<0.001）。

在体内实验中，HE 染色结果显示：LPS（10mg/ml） 组；LPS(10mg/ml)+EZH2 组；LPS(10mg/ml)+EI1 组均可见开髓孔处密集的炎细胞浸润，局部组织液化坏死。马松三色结果显示：封药 1 天及 3 天后，LPS （10mg/ml ）+EI1 组中胶原纤维含量较 LPS（10mg/ml）组与 LPS(10mg/ml)+EZH2 组多。

结论：EZH2 上调了人牙髓干细胞中 MMP3、MMP8 的表达， 抑制了 type I collagen 的表达。抑制 EZH2 可以抑制人牙髓干细胞中 MMP3、MMP8 的表达，使 type I collagen 的表达上升。在大鼠牙髓炎模型中， EZH2 的下调促进了胶原纤维的形成 ，提示 EZH2 可能参与了牙髓炎症中胶原的降解过程，在牙髓炎症发展中发挥作用。

【关键词】 牙髓炎；EZH2；胶原纤维；基质金属蛋白酶

牙髓修复的干细胞分化与 Notch3 蛋白的表达研究

何圆培　西南医科大学附属口腔医院 牙体牙髓科；复旦大学附属华山医院 口腔科

【摘要】 目的：探讨 Schwann 细胞来源的间充质干细胞参与牙髓损伤修复的过程，检测 Notch3 信号蛋白在此过程中的时空表达。

方法：利用 PLP1-CreERT2/ Rosa26-GFP 基因型谱系追踪模式鼠，PCR 技术筛选阳性基因模式鼠，选取 4 周龄小鼠进行 Tamoxifen 灌胃诱导 GFP 阳性细胞表达，对牙髓损伤后不同时间段的小鼠切牙进行免疫荧光染色。

结果：牙髓损伤后 2 小时，GFP 阳性细胞在牙体组织中极少量表达；牙髓损伤后 6 小时，GFP 阳性细胞在牙尖及根尖表达量增加，与 Notch3 信号蛋白出现共染；牙髓损伤后 24 小时，GFP 阳性共染细胞在小鼠切牙牙尖部、牙中部的表达量明显增加，而根尖部表达量减少；牙髓损伤后 3 天，在牙尖处成牙本质细胞的位置，高柱状 GFP 阳性细胞大量表达，而该部分 GFP 阳性细胞与 Notch3 信号蛋白并未发生共染。

讨论： Schwann 细胞来源的间充质干细胞参与了牙髓损伤修复的过程，同时 Notch3 信号蛋白可能在 Schwann 细胞来源的间充质干细胞向成牙本质细胞分化的中期发挥了重要作用。

【关键词】 牙髓损伤；Schwann 细胞；间充质干细胞；Notch3 信号蛋白

OCT4A and its related LncRNA FTX modulate the self-renewal of dental pulp cells under inflammatory microenvironment

洪　弘　中山大学附属口腔医院
Wei Xi　中山大学附属口腔医院

【摘要】 Objectives: Regulating the pluripotency of human dental pulp cells (hDPCs) is the key for the self-repair of dental pulp. We previously reported that OCT4A promotes the cell proliferation and odontogenic differentiation of hDPCs. Recent studies showed that long non-coding RNAs (lncRNAs) regulate the effects of OCT4A on embryonic stem cells (ESCs). The present study aimed to explore the underlying roles of OCT4A and its related lncRNAs on the self-renewal of hDPCs under inflammatory microenvironment.

Methods: Human LncRNA microarrays were applied to screen out the differentially expressed lncRNAs in OCT4A overexpression and control hDPCs. LPS from E.coli was used to simulate the inflammatory microenvironment. The effects of OCT4A and lncRNA FTX on the proliferation and multi-differentiation of hDPCs were observed by CCK-8, realtime PCR, western blot, alizarin red and oil red O staining. The possible mechanisms of FTX were detected by investigating its effects on the gene expression of pluripotent transcription factors OCT4A, SOX2 and c-MYC.

Results: LncRNAs FTX were validated from 978 potential differentially expressed lncRNAs. OCT4A improved the cell proliferation and differentiation capacities of hDPCs with LPS stimulation. However, overexpression of FTX exhibited opposite results. Moreover, OCT4A negatively regulated FTX expression in hDPCs. Knockdown of FTX up-regulated the expression of pluripotent transcription factors OCT4A, SOX2 and c-MYC, whereas overexpression of FTX down-regulated their expression.

Conclusions: OCT4A was a crucial factor to maintain the self-renewal of hDPCs under inflammatory conditions. While lncRNA FTX suppressed the pluripotency of hDPCs by inhibiting the expression of OCT4A, SOX2 and c-MYC. FTX and OCT4A may form a feedback regulation loop to modulate the pluripotency of hDPCs.

【关键词】 “Octamer-binding transcription factor 4”“Long noncoding RNA”“Dental pulp cells”“Pluripotency”

The metabolic regulation of bone mesenchymal stem cell differentiation

李波儿　刘梦余　叶　玲　四川大学华西口腔医学院，口腔疾病研究国家重点实验室

【摘要】 Objective:

Accumulating evidences have demonstrated that in addition to growth factors and extracellular matrix cues, various metabolic pathways provide important signals for the self-renewal and differentiation potency of stem cells. Changes to energy metabolism can regulate stem cell reprogramming and cell differentiation. These studies indicated that cell metabolism may be a potential target to regulate cell differentiation. However, the role of energy metabolism in BMSC remains unclear. The purpose of this study was to investigate the changes and influence of cell metabolism in bone marrow mesenchymal stem cell (BMSC) differentiation.

Methods:

BMSC was cultured in osteogenic and adipogenic induction media respectively. The Seahorse XF assay was used to measure the oxygen consumption and extracellular acidification. The mitochondrial number was evaluated by citrate synthase assay. The mitochondrial aggregate/monomeric JC-1 ratio was used for the mitochondrial membrane potential. The cellular NAD+ and NADH content was measured using cell lysate. The NAD+ salvage pathway inhibitor FK866 was applied to suppress the NAD+ level in BMSC and investigate the role of NAD during osteogenesis.

Results:

The mitochondrial respiration was upregulated during BMSC osteogenic and adipogenic differentiation. The basal extracellular acidification rate was decreased during osteogenesis but increased during adipogenesis, indicating glycolysis flux was changed. The energy map showed the distinct metabolic profile of BMSC during osteogenesis and adipogenesis that the osteogenic BMSC preferred aerobic pathway whereas the adipogenic BMSC preferred glycolytic energy metabolism. Consistently, the glycolytic rate detected by seahorse assay was decreased in BMSC during osteogenesis. To further investigate the difference of mitochondrial respiration during BMSC differentiation. We evaluated the mitochondrial function. Specifically, the osteogenic BMSC had an approximately 110% higher membrane potential when compared undifferentiated BMSC. Furthermore, both osteogenic and adipogenic BMSC had more mitochondria than undifferentiated BMSC. As literature reported, the NAD+/NADH ratio played an important role in glycolysis and mitochondrial respiration. In our study, we found that the NAD+/NADH ratio was significantly increased during osteogenesis but decreased during adipogenesis, which may be correlated with metabolism state

and protein acetylation. What’s more, the expression of NAMPT, a key enzyme in NAD+ salvage pathway was dramatically increased during osteogenesis. The NAMPT inhibitor FK866 could impair osteogenesis in BMSC, indicated that NAD related energy metabolism was involved in BMSC differentiation.

Conclusion:

The osteogenic and adipogenic differentiation of BMSC showed distinct metabolic profiles. NAD metabolism was involved in osteogenesis of BMSC. Manipulation of the cell metabolism may become a potential method to regulate BMSC cell fate decision and differentiation.

【关键词】 cell metabolism；bone marrow mesenchymal stem cell；differentiation；NAD

Nell-1 促进牙髓干细胞、脐静脉内皮细胞联合应用血管再生的研究

李孟月　山东大学口腔医学院

【摘要】 有体内实验研究证明，相比于牙髓干细胞单独培养，牙髓干细胞与脐静脉内皮细胞 1：1 共培养时，单位面积内有更多的血管形成，本课题组已经研究发现 Nell-1 对牙髓细胞神经样分化有促进作用、在成牙本质细胞的分化及牙本质形成中发挥调节作用，本实验拟探讨 Nell-1 对于联合牙髓干细胞及脐静脉内皮细胞是否有促进血管再生的作用。

【关键词】 牙髓再生；血管再生；Nell-1；牙髓细胞；脐静脉内皮细胞

Spatio-temporal Distribution of Gli1+ Odontoblastic Progenitors during Dentin Formation

厉超元　同济大学附属口腔医院

【摘要】 Objective: This study aims to investigate the spatio-temporal relationship between newly formed odontoblasts, directly transformed from Gli1+ dental mesenchymal progenitors with indirect interaction to enamel epithelium, and early postnatal dentin formation. Materials and Methods: Gli1-CreERT2; R26-tdTomato (GT) mice were generated and were injected by onetime tamoxifen at postnatal days 3 (P3), sacrificed 1, 7, 14, 21 days after induction. EdU was injected 2 hours before sacrifice. Mandibles were fixed in 4% paraformaldehyde overnight and decalcified by EDTA (pH 7.4) at 4℃ , followed by either cryosection and immune-staining with anti-Nestin monoclone antibody. Flu-

orescent cell images were captured by SP5 Leica confocal microscope. Quantification of increased odontoblast processes was counted from the images shot by 63x oil lens to ensure the visible individual processes. Mice mandible 1st molars were scanned by micro-CT at P4, P8, P10, P17, P28, P56. Results: The representative confocal images showed numerous dendritic Gli1+ pulp cells (EdU-) and newly formed odontoblasts (Od) directed from the pulp center toward Od layer, indicating Gli1+ pulp cells form odontoblasts and odontoblast processes without direct interactions with epithelial cells postnatally. Three weeks later, the newly formed (Gli1+) Od-processes occupy almost the entire dentin tubules in the coronal dentin after induction at P3. Red Od-processes overlapped nearly all Nestin+ Od-processes gradually in the first month afterbirth with the thickening dentin mass ($P < 0.05$). Through micro-CT scan and 3D reconstruction, measured dentin volume continuously expanded until reaching full crown size at age P28 ($P < 0.05$), compared with that at P56 ($P > 0.05$). The lineage relationship between dentin volume, the number of newly formed odontoblasts and Od-process length was depicted at postnatal stage. Rapid growth of dentin volume occurred during the period from P7 to P10 while newly formed Od getting less after P7. Similarly, mineral contents are rapidly increased during this period. Conclusions: The postnatal formation rate of odontoblasts directly transdifferentiated from Gli1+ progenitors are spatio-temporally related to dentin mineralization extent.

【关键词】 dentinogenesis；odontoblast；cell lineage tracing；tooth development；odontoblast process；dentin mineralization

PI3K 在 LPS 作用下破骨细胞中表达研究

史东梅　徐慧君　大连医科大学口腔医学院

【摘要】 目的：在脂多糖 LPS 介导的炎症环境下，研究 PI3K 在破骨细胞表达情况，从而为根尖周炎的治疗提供实验依据。

方法：将 RAW264.7 用 RANKL 诱导 5 天后，通过光学显微镜下观察、TRAP 染色及 RT-qPCR 的方法，验证破骨细胞是否诱导成功；破骨前体细胞 RAW264.7 诱导成功后，分别加入 100ng/ml 和 0ng/mlLPS 作用于破骨细胞，通过实时荧光定量 PCR 检测脂 PI3K、破骨细胞分化标志因子 TRAP 及其相关转录因子 NFATC1 基因水平的表达情况。

结果：实时荧光定量 PCR 结果发现脂多糖 LPS 刺激后破骨细胞中 PI3K、TRAP、NFATC1 的 mRNA 表达量明显增高（$P < 0.05$），具有统计学意义。

结论：PI3K 参与了慢性根尖周炎的骨破坏反应进程。

【关键词】 脂多糖；破骨细胞；PI3K；慢性根尖周炎

Association between Increased Inducible Costimulator/ Inducible Costimulator Ligand Expression with the Bone Destruction in Apical Periodontitis

陶祎伟　xing/ 邢　quan/ 泉　中山大学附属口腔医院

【摘 要】 Introduction: The aim was to assess the association of inducible co-stimulator (ICOS) and ICOS-ligand with bone destruction in apical periodontitis (AP). Methods: Lesion specimens from AP patients were obtained during apicoectomy and subjected to histopathological analysis and molecular assessment of ICOS/ICOS-ligand. In addition, experimental AP was induced by exposing the pulp of the first mandibular molars in rats. Histological and radiographic examinations were carried out to validate the periapical lesions. The immunolocalization and mRNA expression of ICOS/ICOS-ligand were evaluated. The osteoclastic activities in periapical lesion, including the lesion size, the expression of the tartrate-resistant acid phosphatase (TRAP) and the receptor activator of NF-kappa B ligand (RANKL), were recorded and followed by correlation analysis with ICOS/ICOS-ligand expression. Results: In excisional specimens from AP patients, a significantly increased expression of ICOS/ICOS-ligand was found by quantitative real-time polymerase chain reaction (qRT-PCR) and immunofluorescenc staining, compared with the control. In the experimental AP samples, the expression of ICOS/ICOS-ligand, TRAP and RANKL were significantly elevated in inflamed periapical tissues (AP group) when compared to the control group (day 0). The number of ICOS+/ICOS-ligand+ cells was highly correlated with the periapical lesion size ($r = 0.892$, $P < 0.001$; $r = 0.930$, $P < 0.001$). Conclusions: The increased expression of ICOS/ICOS-ligand in periapical lesions was associated with the inflammatory infiltration and alveolar bone destruction of AP.

【关键词】 ICOS; ICOS-Ligand; Apical periodontitis; Osteoclast; T cell

A Switch from Dentinogenesis to Osteogenesis: BMP is the Key

王　骏　谢旭东　四川大学华西口腔医院

【摘 要】 OBJECTIVES: Jawbone and dentin share many common features, although which one evolutionarily comes first is still under debate. The goal of this study was to investigate the role of BMP2 and BMP4 in controlling the fate of pulp cells during molar root formation.

METHODS: The Gli1-CreER mice were crossed with Bmp2flox/flox and Bmp4flox/flox mice in Rosa26-tdTomatobackground to specifically inactivate Bmp2 and/or Bmp4 (two key BMP ligands) in the dental pulp cells. A single dose of tamoxifen was injected at postnatal day 5 and animals were harvested at postnatal week 4 with EdU injection 3 hours before sacrifice. The combined approaches of X-ray, μCT, in vivo cell lineage-tracing, histology, and immunostaining were used.

RESULTS: The deletion of single Bmp2 or Bmp4 led to minor dentin defects, while double knockout (dKO) mice displayed profound defects in molar roots, characterized by short and thin root dentin with few dentinal tubules. The quantitative μCT data demonstrated that these changes were statistically significant (n=6, $P < 0.05$). Mechanistic studies (including cell lineage tracing analysis) showed 1) an ectopic bone-like structure formed in pulp; 2) a change of dentin matrix to bone-like matrix, in which bone-like cells were buried; 3) a great increase in pulp cell proliferation and bone marker expression; 4) a sharp reduction in odontoblast markers such as Nestin and DSPP; and 5) increased expression of osteogenic transcription factors (Runx2 and Osterix) and decreased expression of odontogenetic transcription factors (Klf4 and Sox2). Together, data supported a vital role of BMP signaling in preventing the cell fate change from odontoblast lineage to osteoblast lineage during root dentin formation.

CONCLUSIONS: Our findings demonstrated that BMP signaling (a combined role of BMP2 and BMP4) is essential for determining the cell fate of Gli1+ pulp progenitor cells during molar root formation.

【关键词】 dentin；bone；BMP signaling；osteodentin；knockout mouse

壳聚糖及其衍生物对粪肠球菌的抑菌作用

王　楠　王　帅　青岛大学口腔医学院

【摘要】 难治性根尖周炎是一种长期、慢性的根尖周病，反复发作且不易治愈，微生物感染是一个重要原因。其中，粪肠球菌与难治性根尖周炎具有密切关系，在已充填根管中经常被检测和分离培养。随着抗生素的广泛使用，微生物耐药性相继出现，新抗菌药物的研发是被广泛关注的热点。壳聚糖和季铵盐壳聚糖因其优良的生物学特性被广泛用于生物医学领域，且已被证明具有广谱抗菌性，但季铵盐壳聚糖对于根管微生物的作用以及两种抗菌剂抗根管微生物作用的差异尚未清楚。因此，本实验的目的是探索壳聚糖及其衍生物对不同来源的粪肠球菌菌株及其细菌生物膜的抑菌作用。

【关键词】 壳聚糖；季铵盐壳聚糖；粪肠球菌；最低杀菌浓度；细菌生物膜

Foxq1 mediates polarity differentiation of dental papilla cells via Wnt5a signaling

项露赛　凌均棨　中山大学附属口腔医院
郑骏明　佛山科学技术学院附属口腔医院·佛山市口腔医院

【摘要】 Objective

Polarity of dental papilla cells is crucial for odontoblast differentiation and dental pulp repairing. Forkhead-Box Q1 (Foxq1) is a novel transcription factor highly expressed in odontoblast cells by comparing bone marrow stromal cells and odontoblast cells through gene microarray. However, Foxq1’s roles in tooth development and its molecular mechanisms are elusive. This study is to illuminate Foxq1’s role on regulation polarity formation of dental papilla cells via Wnt5a signaling.

Methods

Foxq1 expression was mapped by in situ hybridization from E11.5 to E14.5, and by immunohistochemistry from P1 to P11. E14.5 tooth germs were isolated and manipulated by Foxq1 overexpression and downregulation by lentivirus transfection. E14.5 dental papilla cells were characterized with flow cytometry(FCM) and immunofluorescence. Alizarin red, Oil red and Alcian blue were performed to evaluate differentiation ability of E14.5 dental papilla cells. Foxq1/Wnt5a overexpression/inhibition for dental papilla cells were conducted by lentivirus transfection. Foxq1, Wnt5a, odontogenic and polarity related genes were detected by qRT-PCR and Western Blot. Alizarin red staining was carried out to evaluate Foxq1’s effect on mineralization. Wnt5a’s rescuing effect for tooth development inhibition caused by Foxq1 suppression in dental papilla cells were evaluated with qRT-PCR and tooth germ culture. Fluorescence in situ hybridization (FISH) localized the distribution of Foxq1 and Wnt5a. Foxq1’s binding targets for Wnt5a were evaluated with ChIP-assay. All quantitative data were considered statistically significant if $p<0.05$.

Results

Foxq1 expression was first identified in dental epithelium at E11.5. By E14.5, Foxq1 was expressed in dental mesenchyme, and continued its robust expression also in the inner enamel epithelium by E16.5. From P1 to P11, Foxq1 became gradually pronounced in odontoblasts, and peaked between P3 to P7, during which active dentin formation and maturation occurs. Foxq1 knockdown in E14.5 dental mesenchyme reduced tooth-germ size, disrupted odontoblast polarity and dentin formation. Contrastingly, Foxq1 overexpression promoted dentin thickness and odontoblast polarization. E14.5 dental papilla cells were isolated from mice tooth germ, and showed robust expression of vimentin and fibronectin. FCM showed high expression of CD105, CD73 and less expression of CD11, CD45,

CD14, I-A/I-E, CD19, CD34 and CD49. These cells exhibited well Osteogenic, adipogenic and chondrogenic differentiation ability, indicating mesenchymal stem cells characteristics. Manipulation of Foxq1 influence the expression of pEzrin, ZO-1, Dspp, Dmp-1 Dlx1/2, Msx1/2 and Pax9. Foxq1 and Wnt5a regulate pEzrin and ZO-1 in the same direction, as shown in qRT-PCR and Western Blot assay. Alizarin red staining showed Foxq1 promote mineralization. Recombinant Wnt5a protein restored the disruption in tooth germ development caused by Foxq1 inhibition. qRT-PCR results indicated Wnt5a supplement rescued expression of Dmp1, Dspp, pEzrin, ZO-1, Runx2, Alp and Ocn in Foxq1 knockdown dental papilla cells. FISH showed co-localization of Foxq1 and Wnt5a. ChIP-assay results confirmed that Foxq1 bound to Wnt5a's locus.

Conclusions

Foxq1 plays previously unrecognized roles in dental papilla polarity differentiation and dentin formation. Foxq1 appears to signal via Wnt5a in regulating dental mesenchyme maturation.

【关键词】 Foxq1；Wnt5a；odontogenesis；polarity

Effect of SDF-1α combined with BMP-2 dual controlled release treatment on odontogenic differentiation of human stem cells from apical papilla cultured in the VitroGel 3D system

肖　敏　空军军医大学

【摘要】 Objective: Pulp-dentin regeneration in apical region of immature permanent teeth is currently a difficult problem. Tissue engineering using bioactive molecules and scaffolds may have the potential to regenerate apical natural structure of these teeth as a better alternative to existing treatment regimens. Stromal-derived factor-1α (SDF-1α) is a chemokine signaling molecule that binds to the transmembrane receptor CXC chemokine receptor-4 (CXCR4) and carries out important functions in development tissue homeostasis. SDF-1α signaling via CXCR4 regulates the recruitment of stem cells and precursor cells to support tissue-specific repair or regeneration. The aims of this study were i) to evaluate the VitroGel 3D system, an animal origin-free polysaccharide hydrogel,as a possible injectable scaffold for pulp-dentin regeneration and ii) to investigate the effects of stromal cell- derived factor-1α (SDF-1α) and bone morphogenetic protein-2(BMP-2) dual controlled release cotreatment on odontogenic differentiation of human stem cells from apical papilla (SCAP) cultured in the VitroGel 3D system.

Methods: The morphology, viability and proliferation of SCAP cultured in the VitroGel 3D system

were measured via scanning electron microscopy (SEM), live and dead cell staining and CCK-8 assays. Alkaline phosphatase (ALP) activity, real- time reverse transcriptase polymerase chain reaction (real-time RT-PCR) and Western blot analysis were further used to evaluate the odontogenic differentiation of SCAP cultured in the VitroGel 3D system in vitro. Meanwhile, SDF-1α/BMP-2 double controlled release system were constructed. The morphology and structure of microspheres were observed by SEM, and the release curves were measured by ELISA in vitro. The effect of hydrogel combined with SDF-1α/BMP-2 double release system on the odontogenic differentiation of SCAP in vivo through ectopic subcutaneous injection was evaluated by Von Kossa staining 、 H&E, Masson trichrome and human nuclear antigen 、 CD31 、 DSPP and OCN immunohistochemical staining.

Results: SEM showed that there were homogeneous pores in the VitroGel 3D hydrogel, which could effectively increase the intercellular junction and facilitate the diffusion of nutrition and metabolite. In VitroGel 3D system, SCAP secreted a large amount of extracellular matrix. SCAP cultured in 3D hydrogel presented favorable viability and proliferation. SDF-1α and BMP-2 co-treatment enhanced odontogenic differentiation-related gene (ALP、Runx-2、DMP-1、DSPP、OCN and BSP)and protein (Runx-2、DMP-1、DSPP、BSP and OCN) expression in vitro and promoted odontogenic differentiation of SCAP in vivo. SDF-1α rapid release microspheres and BMP-2 slow release microspheres were successfully constructed, and VitroGel 3D hydrogel combined with SDF-1α/BMP-2 dual controlled release system could enhance angiogenesis, cementoid and mineral deposition in vivo. The positive staining of DSPP and OCN showed that they could promote the odontogenic differentiation of SCAP.Conclusion：our present study demonstrated that VitroGel 3D system promoted SCAP proliferation and differentiation. SDF-1α can significantly promote the migration of SCAP. SDF-1α has synergistic effects on BMP-2 induced odontogenic differentiation of human SCAP cultured in VitroGel 3D system in vitro. BMP-2/SDF-1α dual controlled release system with injectable hydrogel promoted odontogenic differentiation of SCAP in vivo.

【关键词】 stem cells from apical papilla; stromal cell-derived factor-1α; bone morphogenetic protein-2; odontoblastic differentiation; controlled delivery

炎性环境下破骨细胞中 BTK 的表达研究

徐慧君　左美娜　大连医科大学

【摘要】 目的：通过粪肠球菌 LTA 介导炎症微环境，研究布鲁顿酪氨酸激酶 (BTK) 在破骨细胞中的表达情况，以进一步探讨 BTK 在根尖周炎骨破坏中的作用机制。结果：通过光学显微镜下观察及 TRAP 染色结果显示破骨细胞诱导成功；免疫荧光阳性定位结果显示 Btk 表达于破骨细胞胞浆及细胞核内，LTA 作用后，表达量明显增高；与对照组相比， 10ug/ml 的 LTA 作用于破骨细

胞，PCR 结果显示： BTK、 CTSK 和 TRAP 的 mRNA 表达明显，增高（ P<0.05），WB 结果显示：BTK、 CTSK 和 TRAP 的蛋白表达量也明显增高；与 NC 对照组相比，敲低 BTK 后， CTSK 和 TRAP 的蛋白 表达水平明显降低，加入 rhBTK 后， CTSK 和 TRAP 的蛋白表达水平明显增高。结论：在粪肠球菌 LTA 介导的炎症微环境下， BTK 在破骨细胞中有表达且表达增高。

【关键词】 破骨细胞；LTA；根尖周炎；BTK

Gαs 经 Hedgehog 信号通路调控胚胎发育期颅颌面膜内成骨的研究

徐若诗　周学东　口腔疾病研究国家重点实验室，国家口腔疾病临床医学研究中心，四川大学华西口腔医院

Yang Yingzi　美国哈佛大学牙学院，长木大道 188 号，波士顿，马萨诸塞州，美国

【摘要】颅颌面畸形是先天或后天因素导致的骨生长发育异常，影响患儿颅颌面后续生长发育、心理成长和社会适应。先天基因异常导致的颅颌面畸形常表现为综合征，治疗困难。GNAS 基因编码 Gαs 蛋白，参与鸟嘌呤核苷酸结合蛋白偶联受体（GPCR）介导的跨膜信号转导。人 GNAS 基因功能获得型突变导致骨纤维异常增殖症，人 GNAS 基因功能缺失型突变导致进行性骨发育异常。人 GNAS 基因突变是罕见病，其疾病发展机制尚不明确，现有治疗方案只能对症止痛或手术切除，潜在的生物治疗方案有待开发。

为了寻找 GNAS 基因突变所致颅颌面畸形的潜在生物治疗方案，并探究 Gαs 对颅颌面生长发育的调控机制，本研究首次建立颅颌面 Gnas 功能获得型和 Gnas 功能缺失型突变模型：

①体内模拟颅颌面骨纤维异常增殖症和进行性骨发育异常，发现 Gαs 减弱胚胎发育期成骨前缘延伸，延迟颅颌面膜内成骨。

②分析 Hedgehog 信号通路，发现 Gαs 通过减弱 Hedgehog 信号通路激活，延迟颅颌面膜内成骨。

③选用靶向 Hedgehog 小分子抑制剂，首次尝试小鼠体内治疗进行性骨发育异常的颅颌面表型，发现异位成骨得到部分缓解，为临床上对 GNAS 突变所致颅颌面畸形的潜在治疗方案提供重要的基础研究依据。

【关键词】 胚胎发育；成骨细胞；信号通路；膜内成骨；小分子抑制剂

D- 蛋氨酸增强氯己定对变异链球菌生物膜分散作用的研究

闫昱文　刘　奕　中国医科大学附属口腔医院

【摘要】 目的：研究 D- 蛋氨酸对变异链球菌生物膜的分散作用，通过添加 D- 蛋氨酸，增强氯己定含漱液对变异链球菌生物膜的杀菌效果，减少龋病的发生。

方法：本实验分为未处理组（菌 + 培养液）、100ppm 氯己定组、50ppmD- 蛋氨酸组和 100ppm 氯己定 +50ppmD- 蛋氨酸组

（1）采用扫描电镜对生物膜表面形貌观察分析；

（2）通过平板计数法，评估 D- 蛋氨酸增强氯己定杀菌的效果；

（3）通过结晶紫染色法，检测经 D- 蛋氨酸和氯己定混合物处理后变异链球菌形成生物膜量；

（4）通过对核酸、蛋白、多糖含量检测分析 D- 蛋氨酸对变异链球菌生物膜胞外多糖含量的影响；

（5）通过激光共聚焦显微镜活死染色分析评估处理后变异链球菌活死细菌的含量；

（6）通过 ATP 含量检测分析比较不同实验组条件下 D- 蛋氨酸对变异链球菌生物膜的影响。

结果：50ppm D- 蛋氨酸增强了 100ppm 氯己定对变异链球菌生物膜抑制效果，但 50ppm D- 蛋氨酸单独作用时对变异链球菌生物膜无明显抑制作用。

结论：D- 蛋氨酸与氯己定具有协同作用，能够分散变异链球菌生物膜，增强氯己定对变异链球菌的杀菌效果，但 D- 蛋氨酸单独并不具有杀菌作用

【关键词】 D- 蛋氨酸，氯己定，生物膜，变异链球菌

OPN Promotes Bone Destruction in Periapical Periodontitis by Activating the NF- κ B Pathway

于新新　董　明　大连医科大学

【摘要】 Background/Aims: Periapical periodontitis is caused by bacterial infection and results in both bone destruction and tooth loss. Osteopontin (OPN) is a secreted phosphorylated glycoprotein that participates in bone metabolism. Methods: Thirty-three patients with chronic periapical periodontitis and 10 patients who had undergone the orthodontic removal of healthy tooth tissue (control) at the periodontal ligament were investigated, and an animal model of mouse periapical periodontitis was established for an in vivo analysis. The relationship between OPN and bone destruction during periapical periodontitis was analyzed. Osteoblasts and osteoclasts were cultured in vitro and treated with lipopolysaccharide. An inhibitor of NF- κ B was used to pretreat the transfected cells. Results:

OPN increased osteoclast proliferation and differentiation, but reduced osteoblasts proliferation and differentiation. OPN activated the NF-κB pathway during periapical periodontitis and accelerated the transfer and phosphorylation of P65 from the cytoplasm to the nucleus. Conclusion: This study demonstrated that OPN played important roles in the progression of periapical periodontitis, and a dual role in bone metabolism during periapical periodontitis, linking osteoclasts and osteoblasts. The underlying mechanism may be related to the NF-κB pathway

【关键词】 OPN；Bone absorption；Periapical periodontitis；NF-κB

The Effect of propolis,MCJ,neem and sodium hypochlorite on hDPSCs and hPDLFs

张 蕾 一曼街 143 号哈尔滨医科大学口腔医学院

【摘要】 Objective

To compare the effects of propolis, MCJ, neem and NaClO on hSCAPs and hPDLFs.

Methods

The highest optimal concentration of each group was determined by CCK-8 test.The scratch test was performed to evaluate the migration capacity of hSCAPs and hPDLFs.The expressions of DSPP and DMP-1 were detected by Western blot with ALP staining to investigate the ALP activity of hSCAPs in each group.The live-dead cell staining test and the Actin and nuclear staining was used to find the effect for proliferation and morphology on two cells.

Results

CCK-8 showed that MCJ had little effect on the proliferation of hSCAPs and hPDLFs after 24 hours,while propolis and neem had less effect than NaClO at 72 hours.The scratch test showed that all three herbs could promote the migration of hSCAPs compared with NaClO,especially in MCJ. Western blot showed that the expression of DMP-1and DSPP in hSCAP for all three herbs are higher than in NaClO. ALP research showed that ALP stain in MCJ and propolis are deeper than in NaClO and neem,together with the ALP activity higher in MCJ and propolis.showed that the fluorescent of living hSCAPs and hPDLFs in all three herbs are higher than in NaClO at 3days,with no significant defference between MCJ and control group.The live-dead cell staining test showed that the fluorescent of living hSCAPs and hPDLFs in all three herbs are higher than in NaClO at 3days,with no significant defference between MCJ and control group.And the Actin and nuclear stainingshowed that the morphology of living hSCAPs and hPDLFs in MCJ and propolis are better than in neem and NaClO at 3days,which showed that the cytoskeleton spread better in the former two groups,especially in MCJ.

Conclusions

MCJ,propolis, and neem have less influence of proliferation, migration ,morphological change and odontogenic differentiation on hSCAPs and hPDLFs than NaClO ,being expected to be the ideal irrigant for RCT.

【关键词】 herb；hSCAPs；hPDLFs；RCT

镁离子通过免疫调节促进 BMSCs 成骨向分化的作用研究

张旭芳　陈庆飘　毛学理　中山大学附属口腔医院

【摘要】 目的：在骨组织工程中，生物材料的骨免疫特性对干细胞的成骨向分化和骨再生的效果至关重要。镁金属具有可降解性，良好的生物相容性和成骨活性，在骨组织工程领域具有较好的应用潜质。但由于镁的降解速度过快，过高的镁离子浓度反而引起体内炎症反应，限制了镁在骨组织工程中的应用。因此，明确不同镁离子浓度的免疫特性至关重要。本课题研究不同浓度的镁离子对炎症反应的调控作用，并建立干细胞－巨噬细胞共培养模型，研究镁的骨免疫调节及对干细胞成骨向分化的影响和机制。

方法：以 LPS 激活巨噬细胞 RAW264.7 模拟炎症环境，检测镁离子对 RAW264.7 表型转化的影响，RT-PCR 和 Western blot 检测炎症相关因子表达、NF-κB 信号通路的激活水平及成骨相关因子 mRNA 和蛋白表达水平；取镁离子刺激 RAW264.7 细胞培养的上清液，作为条件培养基，检测条件培养基对 BMSCs 成骨向分化的影响以及 BMP/SMAD 信号通路的激活水平。

结果： 100mg/L 的镁离子浓度可显著促使 RAW264.7 向 M2 型细胞转换增多，促进活化的巨噬细胞分泌抗炎因子 IL-10 和 IL-1ra（Fig 1），并上调成骨相关基因 BMP2 和 VEGF 的表达（Fig 2）；同时 100mg/L 的镁离子抑制 RAW264.7 细胞内 NF-κB 信号通路的激活（Fig 3）。在镁离子浓度为 100mg/L 时，镁离子 / RAW264.7 条件培养基显著上调 BMSCs 的 ALP 活性，增强 BMSCs 成骨相关因子 ALP、OPN、OCN 和 Runx-2 的基因和蛋白表达（Fig 4），以及 BMP/SMAD 信号通路中 SMAD4、SMAD5、BMPR1A 的基因和蛋白表达水平（Fig 5）。

结论：适宜浓度镁离子（100mg/L）对炎症反应具有抑制作用，并通过免疫调节作用促进 BMSCs 成骨向分化。本研究为镁基生物材料在骨组织工程中的应用提供体外研究基础。

【关键词】 镁；成骨分化；骨髓间充质干细胞；骨免疫调节

Odonto-immunomodulatory properties of exosomes derived from dental pulp stem cells (DPSCs-EXO) and its manipulation of immune response for odontogenesis by transfer of microRNAs

郑健茂　中山大学附属口腔医院

【摘要】 Abstract

Background：Immune responses play pivotal roles in determining the in vivo fate of dental pulp capping materials in pulp regeneration. It has been recognized that biomaterials should create a favorable immune microenvironment for successful biomaterials-mediated pulp regeneration. Therefore, it is pivotal to investigate the effects of immune cells in biomaterial-stimulated odontogenesis. Macrophages are major effector cells in the immune response of implanted materials and are essential for odontogenesis. Their heterogeneity and plasticity make macrophages a target for immune system modulation. However, little is known about the effects of macrophages on biomaterials-modulated odontogenesis. Exosomes derived from dental pulp stem cells (DPSCs-EXO) are reported as ideal biomimetic material for odontogenesis. In this study, we used DPSCs-EXO as a biomimetic material to investigate the role of macrophages on the material stimulated odontogenesis.

Methods: Transmission electron microscopy (TEM), fluorescent labeling and nano-flow cytometry were used to identify the DPSCs-EXO. Elisa, qPCR, automatic western blot and flow cytometry analysis were used to investigate the effects of DPSCs-EXO on modulating the macrophages functions for odontogenesis. The microRNA-sequencing and pathway analysis were performed to explore the microRNA profile and its functions in DPSCs-EXO.

Results: DPSCs-EXO stimulated the macrophages to switch their phenotype to M2 by inhibiting the TLR receptor and NFκB signaling pathway, which resulted in the up-regulation of anti-inflammatory cytokines IL-1ra and IL-10. Moreover, we found that DPSCs-EXO switched the macrophages toward a more pro-healing extreme by transfer of exosomal microRNAs. Interestingly, the DPSCs-EXO-stimulated macrophages up-regulated BMP2 expression, which activated the BMP signaling pathway in dental pulp stem cells (DPSCs), resulting in odontogenic differentiation.

Conclusions: DPSCs-EXO acted as a biomimetic material to modulate the immune response of macrophages, and shifted the immune microenvironment towards one that favored odontogenesis. These findings provided valuable insights into the mechanism of biomaterial-stimulated odontogenesis, and a strategy to optimize the evaluation system for the in vitro odontogenesis capacity of dental pulp

capping biomaterials.

【关键词】 DPSCs；macrophages；immunomodulation,odontogenesis

Bivalent Histone Modifications of WNT5A in Dental Papilla Cells Differentiation

周雅川　Zhou Xuedong　Zheng Liwei　四川大学华西口腔医院

【摘要】 Objectives: Cytodifferentiation is an essential biological program during odontogenesis, which is activated by several lineage-associated genes. Such genes are modified by colocalization of H3K4me3 and H3K27me3 at promoter region in progenitors. These modifications, named as “bivalent domains” maintain genes in a “poised” state and then resolved for later activation or repression during differentiation. WNT5A has been reported to promote odontogenic differentiation in dental mesenchyme. However, it is still unknown whether WNT5A is modulated by bivalent histone modifications in human dental papilla cells (hDPCs) differentiation. This study aimed to establish the histone modification profiles of WNT5A and investigate the underlying mechanisms during odontogenic differentiation.

Methods: qRT-PCR and western blot were tested to map expression patterns of methylases, demethylases and WNT5A. ChIP-qPCR was performed to establish histone modification profiles within±2.0kb of WNT5A TSS. The lentivirus with JMJD3 shRNA was transfected into cells. Co-immunoprecipitation were conducted to investigate the combination of enzymes.

Results: In cultured hDPCs, H3K4me3 and H3K27me3 co-localized at promoter of WNT5A expressed at very low levels. During odontogenic differentiation, WNT5A was detected upregulated. Simultaneously, the repressive mark H3K27me3 was markedly decreased and the binding of JMJD3, a specific H3K27me3 demethylase, was increased. H3K4me3 level at WNT5A promoter was raised with enrichment of WDR5. When JMJD3 was knockdown in transfected cells, odontogenic differentiation was suppressed. The depletion of JMJD3 epigenetically repressed WNT5A transcription by increased H3K27me3 marks and decreased H3K4me3 marks. Additionally, JMJD3 can physically interact with ASH2L to form a coactivator complex, coordinately modulating the histone modifications of WNT5A.

Conclusions: Our study reveals the histone modification patterns that regulate WNT5A activation during odontogenic differentiation in hDPCs. Bivalently marked WNT5A is initiated transcription by resolution of bivalent domains and tightly mediated by JMJD3 and KMT2 coactivator complex, ultimately modulating odontogenic commitment in human dental papilla cells.

【关键词】 Histone modification; WNT5A; JMJD3; KMT2; dental papilla cells

下颌第一磨牙近中中根管和峡区发生相关因素

黄紫荆　黄柱伟　张晓磊　中山大学附属口腔医院

【摘要】 研究目的：通过 CBCT 调查中国人群下颌第一磨牙近中中根管和峡区的发生率及相关因素，分析 MFMs 近中根管根尖 1/3 峡区的发生与其个体特征的关系。

方法：调取我院 2010 年至 2018 年就诊患者的 CBCT 影像。在轴向面观察到近中颊根管（MB）与近中舌根管（ML）之间有圆形透射根管影像时判定其为 MM，观察到 MB 与 ML 之间的带状缝隙时判定其为峡区。我们记录了患者的年龄、性别、左右，MM 和峡区的发生与位置、MB-ML 根管口距离和 MB-ML Weine 分类。

结果：本研究共纳入 823 个样本。在 MFMs 近中根，MM 根管和峡区的发生率分别为 10.8%（89/823）和 64.6%（532/823）。峡区的发生率随着年龄增大而减小，MM 发生率在 41-60 岁人群中最高（16.7%），两者的发生率与性别和左右无关。　　根尖 1/3 峡区的发生率为 41.3%（340/823），20.8%（171/823）的 MFMs 存在根中 1/3 到根尖 1/3 或局限于根尖 1/3 的峡区。Logistic 回归显示患牙越年轻、MB-ML 根管口距离越短以及 Weine II 类根管越可能出现根尖 1/3 峡区。

结论：在中国人群中，MFMs 近中根管峡区的发生率高，而 MM 的发生率较以往报道的低。年龄、MB-ML 根管口距离和 Weine 分类可以帮助临床医师更好的预测根尖段峡区的存在，

【关键词】 根管形态；峡区；近中中根管；下颌第一磨牙；锥形束 CT

上颌第二恒磨牙牙根及根管解剖的 CBCT 研究

宋　欣　青岛大学附属医院

【摘要】 目的：应用 CBCT 技术研究青岛地区人群上颌第二恒磨牙牙根及根管的解剖结构，分析牙根数目及类型、根管数目及类型、髓室高度、根管口间距离、MB2 位置、牙根及根管对称性、四根牙形态及其与年龄、性别之间的关系。方法：收集 2018 年 1 月至 2018 年 4 月于青岛大学附属医院口腔医学中心放射科拍摄 CBCT 患者的影像学资料，按严格的纳入标准和排除标准选择研究对象，记 录纳入研究对象的籍贯、姓名、性别、年龄，同时记录并分析研究以下内容：①牙位；②牙根数目及类型；③根管数目及类型；④髓室高度及根管口之间的距离；⑤ MB2 的位置；⑥牙根及根管的对称性，并分析以上研究内容与年龄、性别之间的关系。采用 CBCT 软件 KaVo i-CAT Vision 和影像处理软件 KaVo Invivo 5 观察牙根及根管系统的解剖形态并测量记录研究指标，测量数据使用 SPSS 20.0 软件进行统计学分析。结论：青岛地区人群上颌第二恒磨牙牙根及根管系统

复杂多变。3 根 3 根管为主要的牙根及根管形式；女性牙根的融合趋势高于男性；年龄增长，根管口间距离及髓室高度逐渐减小，MB2 检出率逐渐下降；男性根管口间距离大于女性；MB2 的解剖位置相对 MB 较为恒定。CBCT 加深了对上颌第二恒磨牙牙根及根管解剖形态的认识，为临床治疗提供参考依据。

【关键词】 上颌第二恒磨牙；牙根；根管；CBCT

牙周病学

Mitochondria Transfer Improves the Viability of MSCs Under Oxygen and Serum Deprivation Condition in Vitro

迟晓培　郭雨思　邓旭亮　北京大学口腔医院

【摘要】 Objectives: To detect the effects of mitochondria transfer on mesenchymal stromal cell (MSC) viability under oxygen and glucose deprivation condition in vitro.

Methods: Mitochondria from donor rat MSCs was extracted and artificially transferred into recipient rMSCs in different concentrations. The effective of mitochondria transfer was validated and quantified by imaging and fluorescence-activated cell sorting (FACS) analysis. Recipient rMSCs were cultured under oxygen and serum deprivation (ORD) condition. The viability of recipient rMSCs was detected by CCK-8 and Annexin V-FITC/PI detection.

Results: Uptake of donor mitochondria by the recipient rMSCs increased in a dose-dependent manner. When rMSCs was cultured in an ORD condition, rMSCs CCK-8 activity was significantly down-regulated and the percentage of Annexin V-FITC/PI staining cells was significantly upregulated compared with controls. Artificial mitochondria transfer in recipient rMSCs rescued ORD-induced both decrease of cell CCK-8 activity and increase of the percentage of Annexin V-FITC/PI positive cells.

Conclusions: Mitochondria transfer increases rMSCs’ viability under ORD condition, which may contribute to improve bone repair in future.

【关键词】 Mitochondria transfer; MSCs; Qxygen and glucose deprivation

Oxytocin facilitates the proliferation, migration and osteogenic differentiation of human periodontal stem cells in vitro

葛　斌　山东大学口腔医学院

【摘 要】 Objective: To explore the effect of oxytocin (OT) on the proliferation, migration, and osteogenic differentiation of periodontal ligament stem cells (PDLSCs) in vitro.

Design: PDLSCs were obtained by limiting dilution method. Immunofluorescence (IF), cell-counting kit-8 (CCK8), cell migration assay, Alizarin Red S staining, cetylpyridinium chloride (CPC) colorimetry, quantitative real-time polymerase chain reaction (qRT-PCR), and western blot analysis were used to examine the effect of OT on oxytocin receptor (OTR) expression, cell proliferation, migration and osteogenic differentiation of PDLSCs.

Results: Our study showed that PDLSCs expressed OTR. One hundred nanomolar OT exhibited the maximal effect on migration, while only 50 nM OT significantly promoted proliferation of PDLSCs, as well as mineralized

nodule formation and calcium deposition ($p < 0.05$). Furthermore, 50 nM OT significantly up-regulated expression of osteogenesis-related genes—alkaline phosphatase (ALP), Collagen I (Col I), runt related transcription factor 2 (Runx 2), osteopontin (OPN) and osteocalcin (OCN)—at specific time points compared with osteogenic inductive medium ($p<0.05$). In addition, western blot analysis demonstrated that 50 nM OT enhanced protein levels of ALP, Col I, and Runx 2 at day 7 and day 14 ($p<0.01$), as well as activating the phosphorylation of extracellular-signal-regulated kinase (ERK) and protein kinase B (AKT) pathway; notably, 50 nM OT inhibited phosphorylation of the phosphatidylinositol 3-kinase (PI3K) pathway ($p < 0.05$).

Conclusions: OT promoted proliferation, migration, and osteogenic differentiation of PDLSCs in vitro. Furthermore, the effect of OT on osteogenic differentiation was mediated through ERK and AKT pathway. Thus, OT may have potential for use in periodontal regeneration.

【关键词】 periodontal ligament stem cells; oxytocin; osteogenic differentiation

Building capacity for macrophage modulation n high-stiffness hydrogels for periodontal regeneration: Experimental studies in vitro and in rats

贺小涛　Li Xuan　空军军医大学第三附属医院牙周病科

【摘要】 Objective: Periodontitis is characterized by inflammation-induced progressive destruction of tooth-supporting alveolar bone due to the persistent bactrial insult. Dictating the host immune response based on biomaterial design may be a potential stratergy for the regeneration of the lost hybrid periodontal tissues. As one of the predominant immunological regulators, macrophages have receieved considerable attention as modulators of disease pathogenesis and tissue repair following injury. Herein, we envisioned a proactive immunomodulatory stratergy via tuing macrophges towards M2 phenotype based on a tailored high-stiffness hydrogels to promote in situ periodontal tissue regeneration.

Materials & Methods: Firstly, conditioned mediums (CMs) generated by different polarized macrophages (M0, M1 and M2) were used to explore the effects of different polarized macrophages on the cellular behaviors of bone marrow stromal cells (BMSCs) in 2D culture conditions. Susequently, gelatins with gradient concentrations were crosslinked with transglutaminase to obtain hydrogels with different stiffness. The transwell co-culture systems and CM systems were then used to interrogate the effects of macrophages encapsulated in high-stiffness hydrogels on the osteogenesis of gel-encapsulated BMSCs in 3D culture conditions. Finally, a crical-sized periodontal defects in rats were established to explore whether the incorporation of immunomodulatory molecule IL-4 and homing factor SDF-1 in high-stiffness hydrogels could exploit the power of macrophages and stem cells to promote in situ periodontal tissue regeneration.

Results & Discussion: In 2D culture conditions, CMs generated by M1-polarized macrophages supported the proliferation and adipogenic differentiation of BMSCs, whereas CMs generated by M2-polarized macrophages faciliated BMSC osteogenesis and promoted robust matrix production of BMSCs. When gelatin was crosslinked with transglutaminase, hydrogels with highly interconnnected pore structure and tunable matrix stiffness were successfully synthesized for 3D culture of BMSCs or macrophages. In 3D culture conditions, increasing the matrix stuffness could harness the osteogenic differentiation of BMSCs directly, but high-stiffness matrix could also coax macrophages towards a pro-inflammatory M1 phenotype, which indirectly compromised the osteogenic potentials of BMSCs. When IL-4 was incorporated in high-stiffness hydrogels, the osteogenesis of BMSCs increased sigficantly in either direct or indirect co-culture of macrophages and BMSCs in 3D culture conditions. Furthermore, the in vivo experiments showed that the fibrosis in the periodontal defetcs were also

disappeard when hydrogels containing IL-4 and/or SDF-1α was transplanted. Moreover, the combined use of IL-4 and SDF-1α in high-stiffness hydrogels could significantly improve the therapeutic outcomes of periodontal tissue regeneration than IL-4 or SDF-1α alone.

Conclusions: The involvement of macrophages may change previously identified material-related influences on cellular behaviors of stem cells, which frequently causes inconsistencies between in vitro and in vivo studies. Development of proactive immunomodulatory stratergy by finly tuning macrophages towards M2 phenotype may be a effective stratergy to exploit the power of host immune response to promote in situ periodontal tissue regeneration.

【关键词】 Periodontal tissue regeneration；macrophages；endogenous regeneration

Gut microbiota regulates inflammatory alveolar bone loss under estrogen deficiency

贾小玥　四川大学华西口腔医院

【摘要】 Postmenopausal osteoporosis (PMO) is a potential risk factor for inflammatory alveolar bone diseases, periodontitis and periapical periodontitis included [1, 2]. Current medications for PMO, such as bisphosphonates and estrogen supplements, can prevent the aggravated inflammatory alveolar bone loss due to estrogen deficiency [2, 3]. Gut microbiota, which closely relates to physiological bone remodeling, has been recognized as a promising therapeutic target for PMO [4-6]. Gut microbial regulators, including natural alkaloid berberine and probiotics, have shown their effectiveness in the treatment of metabolic diseases such as obesity and diabetes via regulating gut microbiota [7, 8]. We hypothesize that berberine and probiotics can ameliorate inflammatory alveolar bone loss under estrogen-deficient condition through regulating gut microbiota. By establishing experimental periodontitis and periapical periodontitis animal models in ovariectomized (OVX) rats, we have demonstrated that estrogen deficiency increases alveolar bone loss in periodontitis/periapical-periodontitis and aggravates systemic and local inflammatory responses. Further studies have showed that intestinal epithelial paracellular permeability affected by gut microbial metabolite butyrate is closely associated with circulating endotoxin level as well as systemic and local inflammatory responses, subsequently participating in the regulation of alveolar bone remodeling and alveolar bone loss. Berberine/probiotics treatment enhance intestinal epithelial barrier function by increasing gut butyrate-producing bacteria and butyrate production, thus attenuating systemic and local inflammatory responses and inhibiting the enhanced alveolar bone loss induced by estrogen deficiency in both periodontitis and periapical periodontitis. Taken together, gut microbiota can be a potential target for the treatment of inflammatory alveolar bone diseases under estrogen deficient condition, and berberine/

probiotics represent a promising adjuvant therapeutic against inflammatory alveolar bone loss in postmenopausal women by modulating gut microbiota.

【关键词】 Gut microbiota；estrogen deficiency；butyrate；periodontitis；periapical periodontitis

Pg-LPS 对人体牙周细胞共培养下的人脐动脉平滑肌细胞钙化能力影响

李　静　青岛大学附属医院

【摘要】 目的：利用 Transwell 小室建立体外人牙周膜细胞（HPDLCs）和人脐动脉平滑肌细胞（HUASMCs）共培养系统，初步探究 Pg-LPS 刺激时，对 HPDLCs 共培养条件下的 HUASMCs 增殖和 ALP 活性以及对其相关钙化基因 mRNA（ALP、Cbfα1、BSP）表达的影响。

方法：利用 Transwell 小室建立 HPDLCs-HUASMCs 体外共培养系统。通过 CCK-8 法检测 HUASMCs 增殖。采用钙化诱导液诱导 HUASMCs 成骨分化后使用茜素红 S 染色定量检测细胞钙化结节。利用 Real Time PCR 检测钙化相关因子 (ALP、Cbfα1、BSP 等) 的表达。

结果：共培养组中 HUASMCs 的增殖和 ALP 活性分别强于单独正常培养；且共培养组中 HUASMCs 的增殖和 ALP 活性强于单独培养的组。钙化诱导各组较普通培养各组钙化结节明显增多。Pg-LPS 促进钙化结节的形成；而共培养钙化诱导各组钙化能力分别强于单独培养钙化诱导各组。Cbfα1、ALP、BSP 在钙化诱导组的表达分别明显高于普通培养组的；在含 Pg-LPS 的各组的表达显著高于不含 Pg-LPS 的各组；Pg-LPS 或钙化诱导液以及两者同时存在的时候，共培养各组的钙化能力分别高于单独培养的各组。

结论：Pg-LPS 可能通过促进 HUASMCs 增殖增强、ALP 活性和上调钙化相关基因（ALP、Cbfα1、BSP）的表达进而影响其钙化；且与 HPDLCs 共培养条件下对 HUASMCs 的钙化作用更强；提示牙周炎可能比单纯的炎症更能促进血管钙化的发生发展，牙周炎对心血管疾病的发生发展有一定的促进作用。

【关键词】 共培养；HUASMCs；Pg-LPS；细胞增殖；钙化

Integrative of GWAS and eQTL identifies AIM2 as a risk gene for periodontitis

李文静　Meng Huanxin　北京大学口腔医院

【摘要】 Background: Periodontitis is one of the most prevalent causes of disease worldwide and accounts for a vast burden of healthcare spending. Recent large-scale genome-wide association studies

(GWAS) have identified some risk variants that show association with periodontitis. Nevertheless, how the identified risk variants confer risk of periodontitis remains largely unknown.

Objective: To identify risk variants that are associated with gene expression in peripheral blood and to identify genes whose expression change may contribute to the susceptibility of periodontitis.

Material and methods: We systematically integrated the genetic associations from GLIDE consortium Meta-GWAS data (17,353 periodontitis cases and 28,210 controls) and blood expression quantitative trait loci (eQTL) data (N = 369) using a Bayesian statistical framework (Sherlock). Then explored the expression analysis of candidate genes and construct a co-expression and enrichment analysis.

Results: Sherlock integrative analysis identified 10 genes whose expression level may have a role in periodontitis. We further explored the expression level of these 10 genes and found that AIM2 was consistently upregulated in periodontium and peripheral blood of periodontitis cases compared with controls. Our study identifies AIM2 as a risk gene for periodontitis and suggests that risk variants may contribute to periodontitis susceptibility through affecting AIM2 expression.

Conclusion: Our results suggested that periodontitis-associated variants may confer periodontitis risk through affecting AIM2 expression. The significant upregulation of AIM2 in periodontitis also suggests that AIM2 may be targeted in future as a potential marker for future therapeutics and diagnostics.

【关键词】 periodontitis；AIM2；GWAS；eQTL；Sherlock

Autophagy preserves the osteogenic ability of periodontal ligament stem cells under high glucose conditions in rats

李治冶　第四军医大学口腔医院

【摘要】Objective: To investigate how a high glucose environment influences the osteogenic ability of periodontal ligament stem cells (PDLSCs) and the function of autophagy in this process, we explored whether the osteogenic ability of PDLSCs could be protected by autophagy.

Methods: PDLSC proliferation and osteogenesis were evaluated by CCK-8 and western blotting under gradient glucose conditions. The Autophagy RT2 Profiler PCR Array was used to screen autophagy-related mRNA expression during PDLSC osteoblastic differentiation on 5.5 mM + osteogenic induction (OI) medium or 25 mM + OI medium on day 3. Autophagy was regulated by an inducer (rapamycin) and inhibitor (bafilomycin) to investigate its protective effects on PDLSCs. A periodontal trauma model was established in diabetic rats to verify the effects of enhanced autophagy activity on PDLSCs.

Results: A high glucose concentration (25 mM) impeded PDLSC proliferation on day 1, and compared with the control condition, high glucose also decreased the osteogenic ability of PDLSCs. The Autophagy RT2 Profiler PCR Array showed obvious fluctuations in many autophagy-related genes, such as ULK1 (9.27), MTOR (3.15), MAP1LC3B (4.22), GABARAPL1 (7.09), ATG10 (6.5), AMPK14 (4.47), WIPI1 (3.29), and IGF1 (24.65). Compared with the control condition, an autophagy inducer or inhibitor markedly impaired or enhanced osteogenic differentiation in cells. The diabetic rat periodontal trauma model demonstrated that periodontium tissue partly recovered in the autophagy-enhanced cell injection diabetic rat group.

Conclusions: High glucose inhibited the activity of PDLSCs, and regulating autophagy protected cell function. Upregulating autophagy partially reversed the adverse effect of high glucose conditions on PDLSCs.

【关键词】 Autophagy；Osteogenic ability；Periodontal ligament stem cells；High glucose

骨植入材料表面微纳米形貌通过调控 MΦ 极化影响骨结合的研究

王津津　中国人民解放军空军军医大学第三附属医院牙周病科

孟凡辉　中国人民解放军空军军医大学第三附属医院口腔材料学教研室

【摘要】 本研究拟通过探究骨植入材料表面形貌在体内外对巨噬细胞（Macrophage, MΦ）极化方向的调控作用，以及该作用对骨髓间充质干细胞（Bone Marrow Mesenchymal Stem Cells, BMSCs）成骨分化的调节作用，阐明骨植入材料成骨微环境中 MΦ 极化方向对材料体内诱导骨结合具有重要意义。我们通过将具有不同表面微纳米形貌的骨植入材料植入小鼠股骨远心部干骺端或者接种 BMSCs 进行成骨诱导培养，发现体内外结果并不一致，即具有大管径纳米管形貌材料在体外可以更好地诱导 BMSCs 成骨分化，而具有小管径纳米管形貌材料在体内具有较强诱导骨结合的能力，且材料周围浸润 MΦ 类型与大管径纳米管形貌材料不同；继而通过将 MΦ 培养于不同形貌材料表面，发现其可诱导 MΦ 向不同方向极化，小管径纳米管形貌材料更多诱导 MΦ 向 M2 极化并分泌抑炎相关细胞因子，而大管径纳米管形貌材料更多诱导 MΦ 向 M1 方向极化并分泌促炎相关细胞因子，将材料表面 MΦ 与 BMSCs 进行间接共培养后，发现在巨噬细胞参与下，材料表面形貌诱导 BMSCs 成骨分化的能力发生了逆转，与体内结果相一致；进一步通过 M1 极化阻断小鼠体内实验，我们进一步验证了 MΦ 极化对材料在小鼠体内诱导骨结合的能力具有重要调控作用。

【关键词】 骨植入材料；微纳米形貌；巨噬细胞极化；成骨分化；骨结合

牙龈间充质干细胞外泌体对炎症状态下巨噬细胞极化的调节作用

王　茹　青岛大学口腔医学院

【摘要】 牙周炎是最常见的牙周病之一，是导致牙齿脱落的最主要的疾病。牙周炎的组织学特征是炎症细胞的积聚，如白细胞、巨噬细胞和淋巴细胞，诱导促炎和抗炎介质浸润牙周组织。研究发现，巨噬细胞在牙周炎中占据重要地位。

巨噬细胞受内环境的影响，可以发生极化。巨噬细胞可以分为两种类型：M1 巨噬细胞和 M2 巨噬细胞。M1 巨噬细胞可以产生致炎因子，如 TNF-α，IL-1β，IL-12,IL-6 等，参与早期炎症反应，导致组织损伤。M2 巨噬细胞可以产生抗炎因子。如 IL-10,CD163 等，参与炎症反应的修复。有研究证实间充质干细胞可以减轻 M1 巨噬细胞的炎症反应，促进 M2 巨噬细胞的转化，在此过程中间充质干细胞是以旁分泌途径发挥功能的。

外泌体是一种直径 30-150nm 的小囊泡，可以参与多种炎症反应的过程，可以调节组织的损伤和修复，但是牙龈间充质干细胞的外泌体是否会对炎症状态下的巨噬细胞是否有调节作用，尚未有报道。

本研究探索牙龈间充质干细胞外泌体在炎症状态下对巨噬细胞极化作用的影响，为牙周炎的的治疗提供一种新的可能性。

【关键词】 牙龈间充质干细胞外泌体；巨噬细胞；极化；炎症因子

医用聚醚醚酮表面等离子改性对人牙龈成纤维细胞和细菌早期行为的影响及机制探索

王　笑　上海交通大学医学院附属第九人民医院

【摘要】 目的：采用等离子体浸没离子注入技术（PIII），在碳纤维增强聚醚醚酮（CFRPEEK）材料表面构建纳米氧化钛微纳结构，评价改性后材料对人牙龈成纤维细胞及口腔相关细菌行为的影响，为其运用于口腔种植体材料提供理论依据。

方法：采用 PIII 技术进行材料表面改性并检测材料表面理化性质；体外细胞实验探查 Ti 注入改性 CFRPEEK 材料表面对人牙龈成纤维细胞粘附、增殖、迁移和胶原分泌行为的影响；体外抗菌实验探查改性后表面对种植体周围炎相关细菌粘附及增殖行为的影响。

结果：采用 Ti 等离子体注入技术在 CFRPEEK 表面构建纳米颗粒和纳米多孔共存的多级纳米结构，Ti 元素以 TiO2 形式存在，分布于纳米孔结构壁和底部。注入改性后的 CFRPEEK 表面弹性恢复能力大幅改善。体外细胞实验表明，此多级结构可有效促进 HGFs 粘附、增殖、迁移以及胶原分泌。此外，TiO2 纳米颗粒的存在赋予材料抗菌性，使其对种植体周围炎易感菌有一定抵抗能力。

结论：Ti 等离子体注入后的 CFRPEEK 表面多级微纳结构具有良好的生物相容性，不仅有利种植体周围软组织细胞的粘附，同时还可以抑制细菌生长繁殖。为改性后 CFRPEEK 应用于临床提供理论依据。

【关键词】 聚醚醚酮；等离子体浸没离子注入技术；抗菌性；牙龈成纤维细胞

敲低 N-WASP 对牙周组织炎症的调控作用

王旖嘉　山东大学口腔医院

【摘要】目的：神经组织来源的 WASP 蛋白（neuronal wiskott-aldrich syndrome protein，N-WASP）是 WASP 家族成员之一，与 wiskott-aldrich 综合征蛋白（wiskott-aldrich syndrome protein，WASP）的同源性最高，是肌动蛋白细胞骨架的关键调节因子，在促进细胞迁移、受体信号传导、免疫炎症反应中具有重要的作用。已有研究表明敲除 N-WASP 的小鼠可以引起免疫缺陷，主要表现为生长发育迟缓及皮肤炎症的变化。慢性牙周炎也是一种慢性炎症，但 N-WASP 在牙周炎中的作用未见报道。因此，本研究拟通过敲低人牙龈成纤维细胞中的 N-WASP，来检测敲低前后炎症因子表达量的改变并探讨相关通路的变化。

方法：通过 H&E 染色检测敲除 N-WASP 小鼠的牙龈组织中的炎症反应；体外培养健康的人牙龈成纤维细胞（human gingival fibroblasts，HGFs），通过 si-RNA 技术敲低 HGFs 中 N-WASP；通过实时定量 PCR 筛选最佳敲除序列并利用免疫荧光检测敲低效果；通过实时定量 PCR 检测白细胞介素（interleukin，IL）-6、IL-8、趋化因子 CC 基序配体 2（chemokine（C-C motif）ligand 2，CCL2）、编码锰超氧化物歧化酶 2（superoxide dismutase ,SOD-2）和前列素内环氧化物合成酶 2（prostaglandin endoperoxide synthase，PTGS-2）在转染 6h，24h 和 48h 后表达量的改变；应用免疫印迹法检测敲低 N-WASP 对 NF-κb（p65）和 MAPK（p38、JNK、ERK）信号通路的激活作用。

结果：H&E 结果显示敲除 N-WASP 小鼠的牙龈组织出现炎症反应，有明显的大量淋巴细胞浸润，上皮钉突伸长，腺泡形态丧失，被淋巴细胞替代；选取最佳 siN-WASP 敲低序列并用该序列转染 6 h，24 h 和 48 h 后发现相关炎症因子表达显著上调 （$P < 0.001$，$P < 0.001$，$P < 0.001$）；并且证明敲低 N-WASP 使 p65、p38、JNK、ERK 的磷酸化水平明显升高（$P < 0.001$，$P < 0.05$，$P < 0.001$，$P < 0.01$）。

结论： 小鼠体内敲除 N-WASP 后引发牙龈组织炎症，在体外 HGFs 中敲低 N-WASP 表现出炎症因子表达量升高以及炎症通路的激活，提示 N-WASP 缺失后可引起牙周组织炎症，该蛋白在体内可起到保护作用，为进一步了解牙周炎的发病机制提供了新的思路。

【关键词】 N-WASP；HGFs；牙周炎

Ctsk 通过 TLR9 相关的细胞自噬调节关节炎加重牙周炎作用机制的研究

卫 韡 尹无为 王 敏 四川大学华西口腔医院

【摘要】 目的：大量流行病学调查发现牙周炎和类风湿关节炎（Rheumatoid arthritis, RA）会相互促进病程进展。同时研究表明自噬是这两种疾病共通的特点，且 Toll 样受体 9（Toll-like receptor 9, TLR9）对自噬至关重要。然而，TLR9 相关的自噬通路对 RA 加重牙周炎的作用机制尚不清楚。本实验旨在探讨 TLR9 相关自噬通路的新靶点，组织蛋白酶 K（Cathepsin K, Ctsk）， 对关节炎加重牙周炎过程的影响及机制。

方法：采用牙龈卟啉单胞菌（Porphyromonas gingivalis, P.g）局部定植和胶原蛋白注射的方法建立 RA 和牙周炎小鼠疾病模型。使用腺相关病毒（Adeno-associated virus, AAV）抑制小鼠体内 Ctsk 的表达。采用显微计算机断层扫描、免疫组化及荧光、蛋白免疫印迹、实时定量聚合酶链反应检测牙周炎和 RA 疾病模型中 TLR9 相关自噬通路的表达。应用小干扰 RNA 和 CpG 寡脱氧核苷酸（CpG oligodeoxynucleotides, CpG ODN）刺激巨噬细胞后，采用蛋白免疫印迹、细胞免疫荧光、实时定量聚合酶链反应等方法检测体外样本，从而对体内结论进行验证。

结果：RA 可以促进牙周炎骨吸收，抑制 Ctsk 可有效阻止牙周炎骨破坏。在伴有 RA 的牙周炎病变组织中，巨噬细胞浸润、TLR9 相关自噬蛋白显著增加。在牙周区域局部抑制 Ctsk 后，上述反应均明显降低。细胞实验与动物实验的变化趋势相符。在巨噬细胞中，通过 CpG ODN 激活 TLR9 后，抑制 Ctsk 可以抑制 TLR9 下游信号和自噬相关蛋白。

结论：本研究提出了 Ctsk 在 TLR9 相关自噬通路中的新作用，为阐明类风湿关节炎促进牙周炎进展的分子机制提供了新的视角。

【关键词】 牙周炎；关节炎；组织蛋白酶 K；Toll 样受体 9；自噬

Axin2+-mesenchymal PDL Cells, Instead of K14+ Epithelial Cells, Directly Contribute to Postnatal Root Cementum Growth

谢旭东 王 骏 四川大学华西口腔医院

【摘要】 To date, attempts to regenerate functional periodontal tissues (including cementum) are largely unsuccessful due to a lack of full understanding about the cellular origin (epithelial or

mesenchymal cells) essential for root cementum growth. To address this issue, we first showed a close relationship between the expression patterns of Axin2 and β-catenin within cementum-forming PDL cells using either X-Gal staining or immunohistochemistry, and identified a rapid cementum growth window at ages of postnatal day 28 (P28) to P56. Next, cell lineage tracing studies revealed an Axin2+-mesenchymal PDL cell population that rapidly expands and directly contributes to postnatal cementum growth, whereas there are few K14+ epithelial cells during rapid cementum formation from P28 to P56. The in vivo cell ablation of these Axin2+ cells using Axin2CreERT2/+; R26RDTA/+ mice led to severe cementum hypoplasia, whereas constitutive activation of β-catenin in the Axin2+ cells resulted in acceleration in cellular cementogenesis plus a transition from acellular cementum to cellular cementum. Thus, we conclude that it is Axin2+-mesenchymal PDL cells, instead of K14+ epithelial cells, that directly contribute to both cellular and acellular cementum growth postnatally.

【关键词】 cementum；PDL；Wnt/β-catenin signaling；Axin2；mesenchymal cells

人尿源干细胞来源外基质对人牙周膜干细胞增殖、铺展和分化的影响

熊　雪　周建萍　重庆医科大学附属口腔医院

【摘要】全世界有许多人因为牙周疾病、创伤、肿瘤等造成牙周组织缺损；牙周病是其主要原因，累及全世界高达 90% 的人群。牙周膜干细胞（PDLSC）自 2004 年被发现被发现，在一定的体外培养条件下可分化为牙周骨细胞、成骨细胞、脂肪细胞等 , 是牙周组织再生的优良选择。

然而在细胞治疗中，干细胞来源有限，体外大规模扩增干细胞并且保持其性能仍是一个难题，长时间体外培养扩增容易使干细胞生物特性发生改变。

细胞外基质（ECM）来源于间充质干细胞（MSCs）最近被证明能够在培养扩增过程中增强 MSCs 的分化潜能，恢复衰老 MSCs 的活性，提示 MSC ECM (MECM) 可能是增强 MSCs 生物材料支架生物活性的合适培养基。几乎绝大部分供体干细胞采集样本的方法都需要针插入、活检或通过刮除进行物理剥离。我们能否找到一种新的来源的干细胞进行生产 ECM，并应用于牙周组织工程呢？ 2008 年人的尿液中首次分离出干细胞，被命名为尿源干细胞，表达间充质干细胞表面分子表型，具有多向分化潜能。尿源干细胞具有来源广泛、完全无创获取、价格低廉等优点。

本实验研究目的是想探究 USC 来源细胞外基质对于 PDLSC 增殖、铺展和分化的作用。也许 USC 外基质可以成为体外培养和扩增干细胞的一种安全广泛和低廉来源，甚至在支架表面改性方面可以扮演重要角色。

【关键词】 尿源干细胞；牙周膜干细胞；细胞外基质；细胞增殖；细胞分化

多西环素下调牙龈卟啉单胞菌 LPS 介导的人 牙龈成纤维细胞 NLRP3 炎症小体的研究

徐　烁　吉秋霞　青岛大学附属医院

【摘要】 目的　探究牙龈卟啉单胞菌 LPS（P.g-LPS）诱导人牙龈成纤维细胞（HGFs）表达 NLRP3 炎症小体相关蛋白的效果，并用多西环素（DOX）对其进行干预，观察细胞疗效，明确作用机制。

方法　利用 CCK-8 筛选合理 P.g-LPS 浓度，1 μg/ml P.g-LPS+5 μM 三磷酸腺苷（ATP）刺激 HGFs 12 小时，收集细胞提取总 RNA 及蛋白，分别用 qRT-PCR、Western Blot 检测总 RNA 及蛋白中 NLRP3、ASC、Caspase-1 表达量，ELISA 检测 IL-1β 在 HGFs 细胞上清液中的表达水平。选用浓度为 10 μg/ml 多西环素对已建立的细胞炎症模型干预 1 小时，收集细胞提取总 RNA 及蛋白，qRT-PCR、Western Blot 检测总 RNA 及蛋白中 NLRP3、ASC、Caspase-1 表达量，ELISA 检测 IL-1β 在细胞上清液中的表达水平。

结果　qRT-PCR 结果显示 P.g-LPS 刺激后的 HGFs 中 NLRP3、ASC、Caspase-1 的 mRNA 表达量均升高，多西环素干预后其 mRNA 表达量均降低；Western Blot 结果显示 NLRP3、ASC、Caspase-1 蛋白表达水平均升高，多西环素干预后其蛋白表达水平均降低；ELISA 结果显示 IL-1β 在细胞上清液中的表达水平升高，多西环素干预后其表达水平降低；SPSS 24 t 检验 $P<0.05$，差异具有统计学意义。

结论　P.g-LPS 对 HGFs 具有致炎作用，且在 ATP 激活后会上调其 NLRP3 炎症小体相关 mRNA 及蛋白的表达水平；多西环素对 P.g-LPS 介导的 HGFs 中 NLRP3 炎症小体相关 mRNA 及蛋白的表达水平有一定的下调作用，对临床上的药物使用有一定的指导意义，丰富了多西环素疗效的评价标准。

【关键词】多西环素；牙龈卟啉单胞菌 - 脂多糖；牙龈成纤维细胞；NLRP3 炎症小体；白介素 -1β

间接共培养人尿源干细胞对人牙周膜干细胞成骨 / 成牙骨质分化的影响

杨　潇　熊　雪　重庆医科大学附属口腔医院

【摘要】 背景：人牙周膜（PDL）干细胞（PDLSCs）作为一种潜在的种子细胞在牙周组织再生研究中得到了广泛的应用。但是体外获取和扩增 PDLSC 不仅过程繁琐而且具有侵入损伤性，因

此为了进一步满足牙周组织再生的需要，提高 PDLSC 的增殖和分化能力是有必要的。

方法：体外分离 PDLSCs 和人尿源干细胞（USCs）, 以 1/0.5、1/1 和 1/2 的比例进行间接共培养，研究 USCs 对 PDLSCs 增殖和多向分化的影响。将 PDLSCs/USCs 比例为 1/2 的间接共培养的 PDLSCs 膜片移植到裸鼠皮下，以观察体内分化的效果。

结果：相比于对照组，进行间接共培养的三个组中 PDLSCs 的增殖速率从第 5 天开始明显上升，组间无明显差异。PDLSCs 的成骨和成牙骨质相关基因和蛋白的表达随着间接共培养 USCS 比例的增加而显著提高。此外 ,PDLSCs/USCs 比率为 1/2 时的 PDLSC 膜片在显示出更致密的胶原层，对成骨和成牙骨质相关蛋白具有更高的表达。体内实验结果表明，与未经 USCS 处理的 PDLSC 膜片相比， PDLSCs/USCs 比值为 1/2 时的 PDLSCS 膜片在形成了更多的硬骨样结构，免疫组织化学染色显示表达了更高的成骨和成牙骨质相关蛋白。

结论：我们的研究结果表明，随着间接共培养 USCs 比例的增加， PDLSC 的成骨和成牙骨质分化能力也越强。此外，USCs 通过间接共培养促进体外 PDLSC 膜片的形成与分化，而且进一步促进 PDLSC 膜片体内再生骨 / 牙骨质样结构，为临床再生牙周组织提供了一种新的策略。

【关键词】 牙周组织工程；牙周膜干细胞；尿源干细胞；细胞膜片

MFN2 silencing promotes neural differentiation of embryonic stem cells via the Akt signaling pathway

易思琦　Luan Qingxian　Department of Periodontology, Peking University School and Hospital of Stomatology

【摘 要】 Mitofusin2 (MFN2) is a regulatory protein participated in mitochondria dynamics, cell proliferation, death, differentiation and so on. This study is to reveal the roles of MFN2 in pluripotency and primitive differentiation of ESCs. A dox inducible silencing and routine overexpressing approach was used to down-regulate and up-regulate MFN2 expression, respectively. We have compared the morphology, cell proliferation, expression level of pluripotent genes in various groups. We also employed the directed differentiation methods to test the differentiation capacity of various groups. Akt signaling pathway was explored by WB assay. MFN2 up-regulation in ESCs exhibited typical cell morphology and similar cell proliferation, but decreased pluripotent genes markers. In addition, MFN2 overexpression inhibited the ESCs differentiation into mesendoderm. While MFN2 silencing ESCs exhibit normal cell morphology, slower cell proliferation and elevated pluripotency markers. For differentiation, MFN2 silencing in ESCs have enhanced three germs differentiation ability. Moreover, the protein levels of phosphorylated Akt308 and Akt473 decreased in MFN2 silenced ESCs, and recovered in neural differentiation process. When treated with Akt inhibitor, the neural differentiation capacity of the MFN2 silenced ESCs can reverse to normal level.

Together, the data indicated that the appropriate level of MFN2 expression is essential for the

pluripotency and differentiation capacity in ESCs. The increased neural differentiation ability by MFN2 silencing are strongly related to Akt signaling pathway.

【关键词】 MFN2；Embryonic stem cells(ESCs)；neural differentiation；Akt signaling pathway

牙周干预对 2 型糖尿病伴慢性牙周炎大鼠颈动脉血管病变及血清 hs-CRP 水平的影响

尹　馨　赵　勇　山西医科大学口腔医院

【摘要】 慢性牙周炎（chronic periodontitis，CP）是发生在牙支持组织的慢性炎症性疾病。T2DM（Type Ⅱ Diabetes Mellitus，T2DM）是一种以高血糖为特征的慢性代谢性疾病。越来越多的证据表明，两种疾病具有双向关系。多项研究发现，超敏 C 反应蛋白（hypersensitive C-reactive protein，hs-CRP）等在 CP、T2DM 及血管病变的过程中发挥着重要的作用。目前已有研究通过中间替代指标探讨牙周炎与糖尿病之间的关系，但是有关牙周炎对血管 As 病变及牙周干预措施对血管病变影响的研究仍较少，动物实验文献偏少，而且出于伦理学原因并不能直接研究相关血管组织病变。

【关键词】 糖尿病；慢性牙周炎；超敏 C 反应蛋白；颈动脉

纤维内矿化胶原复合浓缩生长因子 引导牙周组织再生的研究

于　敏　LIU YAN　北京大学口腔医院正畸科生物仿生纳米材料实验室

【摘要】 研究目的：如何实现牙周组织再生是口腔科学研究中的热点与难点，本研究旨在探讨纤维内矿化胶原（IMC）复合浓缩生长因子（CGF）在引导牙周组织再生中的作用。

材料与方法：首先采用 ELISA 来检测不同生长因子的释放情况，包括 PDGF-BB、TGF-β1、VEGF、IGF-1、bFGF、C3a 和 C5a。然后将复合材料植入大鼠下颌牙周缺损区域和裸鼠皮 下，8 周后采用 micro-CT 和组织学染色来观察牙周组织的再生效果。

研究结果：CGF 在 IMC 中释放各生长因子总量更多，可缓慢释放至 28 天，在 14-28 天释放量显著增加。IMC 复合 CGF 材料可在牙周缺损区域形成连续完整的新生牙周膜、牙槽骨和牙骨质，并有丰富的新生血管结构，新生牙周膜胶原纤维较成熟；且可募集更多 CD146+ 和 STRO-1+ 的干细胞。

结论：IMC 复合 CGF 材料可为牙周缺损区域提供一种理想的生物支架，并缓慢有效地释放生长因子，募集自体干细胞，从而引导牙周组织再生。

【关键词】 纤维内矿化胶原；浓缩生长因子；缓释；牙周组织再生

Solitary Chemosensory Cells Serve as Immune Sentinels in Periodontal Tissue

郑　欣　四川大学华西口腔医院

【摘要】 OBJECTIVES. Taste-like chemosensory cells in the airways, gut and urogenital tract are involved in innate immune responses. These cells can detect the potentially harmful substances, such as the “bitter” quorum-sensing molecules from gram-negative bacteria, then trigger host defenses against these pathogens or irritants. Here we identified chemosensory cells in mouse gingival tissue and examined their role in oral microbiome regulation and in protection against periodontitis.

MATERIALS & METHODS. RT-PCR and immunofluorescence staining were utilized to identify which taste signaling molecules are expressed in gingival tissues. By measuring the distance from the cementoenamel junction of the 2nd maxillary molar to the alveolar bone crest, we assessed the severity of naturally occurring alveolar bone loss (ABL) and ligature-induced periodontitis in knockout mice lacking the taste G protein gustducin (Gnat3-/-), in which taste receptor mediated responses abrogated. Moreover, oral swab samples and bacterial samples recovered from sutures, from both wildtype (WT) and Gnat3-/- mice, were analyzed for microbial structure.

RESULTS. Ten Tas2r bitter taste receptors, alone with other chemosensory signaling components were expressed in mouse periodontal tissue. Gnat3-/- mice had elevated ABL at 16-weeks of age compared with WT controls. Furthermore, Gnat3-/- mice were more vulnerable to ligature induced periodontitis, with elevated ABL, higher bacterial load on sutures, up-regulated levels of pro-inflammatory cytokines and lower levels of antimicrobial peptides in gingival tissue. Moreover, 16S rRNA sequencing revealed that the lack of gustducin alters the oral microbiome in Gnat3-/- mice.

CONCLUSIONS. Taste-like chemosensory cells are present in mouse gingival epithelium and may serve as immune sentinels to modulate the oral microbiome, and thus protect against bacterially induced inflammation.

SIGNIFICANCE. Results from the current study provide novel potential targets for treating periodontitis and may lead to screens for susceptible individuals along with personalized treatments of oral infectious diseases.

【关键词】Solitary chemosensory cell; Taste receptor; Periodontitis; Oral microbiome; Innate immunity

慢性牙周炎患者颞下颌关节 CBCT 对比研究

郭晓倩　宁夏医科大学总院口腔医院

【摘要】 目的：探讨有慢性牙周炎患者双侧颞下颌关节（Temporomandibular joint，TMJ）在 CBCT 成像上可能存在差异的参考层面。方法：选取有慢性牙周炎患者 50 例，按牙周炎轻、中、重度分组，通过 CBCT 对颞下颌关节进行三维成像和重建， 垂直于髁突长轴的斜位与矢状位的关节结节斜度、关节窝深度和关节间隙，横断面的水平角；采用 SPSS19.0 软件对上述各测量指标做两配对样本 t 检验。结果：慢性牙周炎患者 TMJ 在矢状位 90° 关节间隙的测量值差异有统计学意义（$P < 0.05$）；重度牙周炎组，髁突内外极之间距离测量值差异有统计学意义，其余个分组的测量值均无统计学意义（$P > 0.05$）。结论：对于慢性牙周炎患者，矢状位 90° 关节间隙、髁突内外极之间距离是最早可以发生变化的颞下颌关节结构，在这个观察这两个参考值对诊断和对比研究更有参考价值。

【关键词】 慢性牙周炎；颞下颌关节；CBCT；对比研究

上颌窦底形态新分类及其与上颌窦底植骨术术式选择的关联

牛力璇　北京大学口腔医院

【摘要】 目的：选择合适的上颌窦底提升植骨术式较为复杂，缺乏共识。上颌窦形态在选择术式中非常关键，但关于形态的研究非常缺乏。根据我们多年的临床经验，提出新的基于 CBCT 影像的形态分类，并统计分析每种新分类的临床特点，针对每种类型的上颌窦给出最佳的术式选择的建议。

方法：上颌窦底形态分为五类：尖圆型、卵圆型、圆型、低平型和不规则型。前四类又分为：无凹陷、颊侧凹陷、腭侧凹陷。不规则型分为：牙根突入上颌窦底、不规则窦底、骨嵴 / 分隔。回顾 698 例患者的 CBCT 表现，测量第二前磨牙、第一磨牙、第二磨牙的上颌窦底宽度，进行统计分析。

结果：尖圆形在第二前磨牙占 88%，卵圆形在第一磨牙及第二磨牙占 50%。无凹陷者在第二前磨牙和第一磨牙占 62%，而在第二磨牙占 92%。3765 个牙位仅有 3 个存在颊侧凹陷。对每种类型及亚型，我们分别提出了最佳的术式选择建议。

结论：此新分类首次详述了上颌窦底形态与上颌窦提升植骨术式选择的关联。本分类一致性好，易于理解，实用性强。

【关键词】 上颌窦底形态；锥形束 CT；新分类

吸烟对牙周炎基础治疗前后龈沟液中 IL-17 及 TGF-β 水平的影响

齐雅丽　河北医科大学口腔医院

【摘要】 宿主自身免疫对炎症的反应影响牙周炎发展，受到刺激后 T 淋巴细胞会分化成不同的亚型：Th1、Th2、Th17、Treg 等。白介素 17（interleukin 17 ,IL-17）是一种主要由 Th17 细胞分泌的促炎因子，在牙周炎症过程中可破坏中性粒细胞的稳态，促使其向炎症部位聚集，并作用于破骨细胞促进牙槽骨吸收。转化生长因子 β（ transforming growth factor-β,TGF-β）是 Treg 等细胞产生、维持功能的重要细胞因子，是一种多效能细胞活性调节因子，同时发挥抗炎和促炎双重作用，能够作用于机体免疫应答、炎症反应、组织修复及胚胎发育等多方面。吸烟是促进牙周病发生和发展的重要危险因素。

【关键词】 牙周炎；牙周基础治疗；IL-17；TGF-β；龈沟液

遗　传

A Genome-wide association study identifies a new susceptibility locus for nonsyndromic cleft palate in a Chinese population

娄　姝　南京医科大学

【摘要】 Objectives: Nonsyndromic cleft palate only (NSCPO) is a common congenital disability that has a livebirth prevalence of 1 in 2,500. It occurs in the absence of other malformations or abnormalities and has a complex etiology of multiple genetic and environmental risk factors. To date, few susceptibility loci associated with risk of NSCPO have been characterized.

Methods: We performed the first two-stage GWAS of NSCPO using 185 NSCPO cases and 515 controls in discovery stage and 126 NSCPO cases and 612 controls in replication stage. All samples were genotyped using Illumina arrays and a systematic quality control analysis on the raw data was performed. We created a weighted genetic risk score (wGRS) which based on the odds ratios of previously reported SNPs and the significant NSCPO susceptibility SNP from the GWAS data. In

addition, we performed a gene-based analysis on imputed data from the susceptibility region using sequence kernel association test (SKAT) and MAGMA.

Results: A novel locus rs3826795, located in the intron of HIF3A, was found to have a significant association with the risk of NSCPO (Pcombine=3.40E-11, OR=1.94 (1.59-2.36). Based on previously reported variants and the identified variant, we achieved an area under the curve value of 0.662. HIF3A were significant in the gene-based analysis (P=3.57E-02 via SKAT and P=3.47E-05 via MAGMA). Moreover, the expression level of HIF3A is higher in dental pulp stem cells (DPSC) of NSCL/P cases than those in controls.

Conclusion: Our study identified rs3826795 as a novel locus of NSCPO in a Chinese population, providing clues for the screening of susceptible populations and help for implementing individualized prophylaxis and treatment.

【关键词】 nonsyndromic cleft palate；genome-wide association study；single nucleotide polymorphism

A rare FLNB mutation potentially underlies non-syndromic orofacial clefts in a pedigree with a subclinical phenotype

张杰铌　Lin Jiuxiang　北京大学口腔医院

【摘要】 Objective

This study aimed to identify the underlying genetic variants of a Han Chinese family with non-syndromic cleft lip and/or palate (NSCL/P) and a subclinical phenotype and to expand the spectrum of causal genes and variants.

Methods

Whole-exome sequencing (WES) was performed on two monozygotic twin probands and their parents in a family. The mother of the twins was later confirmed as a subclinical phenotype. Public databases, variant functions, inheritance models, in silico prediction software, filtering tools and literature review were used to screen the variants. Sanger sequencing was performed on five members of the family. Sixty-five unrelated Han Chinese control subjects were recruited to validate the allele frequency. Conservative analysis and homology modelling were conducted. Additionally, immunohistochemistry (IHC) was performed in embryonic mouse sections to detect the expression pattern of the candidate causal gene.

Results

A missense variant of filamin B (FLNB) (NM_001457.3; c. 7507A>G; p. Ser2503Gly) was identified. This variant is a rare variant and is predicted to be deleterious. Sanger sequencing was

used to validate the variant is rare. The resulting amino acid change, p. Ser2503Gly, is located in an evolutionarily conserved region of the hinge 2 domain of FLNB, which markedly changes the structure of the homology model. IHC indicated that the FLNB protein is expressed in the developing palate of mice, including the epithelium and mesenchyme of the palate.

Conclusions

This study demonstrated that FLNB c. 7507A ＞ G (p. Ser2503Gly) may underlie non-syndromic cleft lip and/or palate (NSCL/P) and the subclinical phenotype in the family, which provided a rationale for further investigations of the variant and gene, expanding the NSCL/P genetic spectrum. The study process suggested the significance of the subclinical phenotype in genetic research of orofacial clefts.

【关键词】 orofacial clefts；non-syndromic cleft lip and/or palate；FLNB；Whole Exome Sequencing

治　疗

PTH 通过促进 HDAC4 核转移治疗早期颞下颌关节骨关节炎

张　俊　四川大学口腔疾病研究国家重点实验室

【摘要】 目的：颞下颌关节骨关节炎（Temporomandibular Joint-Osteoarthritis, TMJ-OA）是一种颞下颌关节功能紊乱性疾病，其病理改变主要表现为软骨进行性变性，软骨下骨重建失衡。目前颞下颌关节骨关节炎的治疗方法主要为缓解颞下颌关节炎症状，缺乏明确的对因治疗，关节结构的病理性改变疗效不理想。PTH 作为调节钙磷代谢的激素，可以调控软骨细胞的分化和骨代谢。近年来，研究显示 PTH 通过促进 HDAC4 核转移调节骨代谢，并且 HDAC4 在软骨细胞的低表达与骨关节炎发病有着密切的关系。因此，本课题探讨 HDAC4 在颞下颌骨关节炎发病过程中的生物学作用，探索 PTH 调控 HDAC4 在颞下颌关节软骨和软骨下骨的表达，从而可调性的干预 TMJ-OA 的发病过程。

材料和方法：通过抬高大鼠咬合改变大鼠磨牙位置造成实验性异常殆力，一个月后行 micro-CT 扫描大鼠离体颞下颌关节组织，分析颞下颌关节软骨下骨组织相关参数 (BV/TV,Tb/Sp,Tb/Th)，组织切片免疫组化染色后观察关节软骨形态学改变与骨重建相关标记物（CollagenX ,MMP13）的表达情况。利用颞下颌关节炎模型，间断注射 PTH（1-34）一个月后观察颞下颌关节软骨及软骨下骨组织结构的改变情况。收集大鼠的颞下颌关节组织，通过 micro-CT 扫描分析骨相关参数并统计分析 (BV/TV，Tb/Sp，Tb/Th)；组织学切片并染色后观察关节软骨形态学改变与骨重建相关标记物的表达情况（如：CollagenX ，MMP13，TRAP，osterix）。通过免疫染色观察和 q-PCR 分析颞下颌关节炎模型的软骨和软骨下骨 HDAC4 表达情况；诱导下颌骨间充质干细胞骨

分化过程中，利用 Western blot 分析 PTH 调节下颌骨间充质细胞的 HDAC4 核转移的信号通路。

结果：异常咬合力诱导颞下颌关节软骨基质发生变性，软骨细胞高表达 MMP13 和 collagenX，软骨下骨骨量降低，TRAP 阳性细胞增加，osterix 阳性细胞减少，HDAC4 低表达在软骨细胞和软骨下骨。间断的给予 PTH 后，使得颞下颌关节炎模型的软骨层 CollagenX 和 MMP13 表达下降，软骨下骨的骨量增加，osterix 的阳性细胞增加。PTH 促进异常表达的 HDAC4 进入细胞核，从而抑制软骨细胞的 Runx2 的表达，促进下颌间充质干细胞的骨分化。

结论：在异常咬合力建立的早期颞下颌关节骨关节炎模型中，间断的给予 PTH，促进软骨和软骨下骨异常低表达的 HDAC4 核转移，从而缓解颞下颌关节骨关节炎发病早期的软骨和软骨下骨的结构变化。因此，PTH 可能是治疗颞下颌关节骨关节炎的潜在药物。

【关键词】 PTH；TMJ-OA；骨改建；髁突软骨下骨；HDAC4

口腔急诊危重症患者抢救 48 例回顾性分析

邵　校　北京大学口腔医学院

【摘要】 目的：回顾总结三级甲等口腔专科医院急诊科危重患者抢救情况，分析患者相关信息以及抢救过程、转归，对高危人群加强关注，同时合理配置急救资源、优化急诊抢救流程。

方法：收集北京大学口腔医学院急诊科 2006 年 3 月至 2018 年 12 月间危重患者抢救病历资料，进行分析总结。

结果：口腔急诊科 12 年间实施抢救的患者共 48 例，主要病因为一过性意识丧失（43.6%）、各种原因导致的颌面部出血（16.7%）及颌面部外伤（16.7%）；经抢救后生命体征稳定入院、转入外院或自行离院 44 例（91.7%），死亡 4 例（8.3%）；发生抢救事件时段集中于 2:00—4:00 及 15:00—20:00；值班医师到场时间大部分（91.7%）在 10 分钟内，抢救过程用时大部分（81.3%）在 90 分钟内；对合并全身症状患者常用的处置为监护、吸氧、补液。

结论：口腔急诊抢救患者以口腔颌面部合并全身急症为主，对高危人群应加强重视并尽可能提前预防危重抢救事件发生，通过制定优化抢救规范及对医护人员的相关培训，口腔专科医院医师及医疗资源可基本满足实施抢救的条件。

【关键词】 口腔急诊；危重；抢救

种　植

The Study of Antimicrobial Effect for A Novel Titanium Implant

吴千驹　厦门医学院附属口腔医院

【摘 要】 Objective: To evaluate antimicrobial effect in vitro of implant coating by introducing antimicrobial ion. Methods: A novel coating was prepared on dental implant surface via electrochemistry approach by introducing antimicrobial ion to recombine chemical composition, and concentrations of ions being released were measured. Then the biological performances were systematically explored as follows：(1) Survival situation of bacteria cultured on specimens was observed by CLSM; (2) Antimicrobial rate was calculated. Results: It was found that this functionalized implant controlled copper ions release in a sustained pattern. Additionally, it was capable of reducing viability of oral pathogens effectively, displaying its excellent antibacterial property. Conclusion: It suggests that implant coatings incorporated with antimicrobial element by electrochemistry approach for sustained release pattern and superior antimicrobial activity could be achieved, holding great promise for prevention of implant-associated infection.

【关键词】 Implants；Bioactive Ion；Controlled-release；Antimicrobial Performance

重　建

The Effects of Leptin on the Proliferation and Differentiation of Primary Chondrocytes in Vitro and Cartilage Regeneration in Vivo

傅润卿　上海交通大学医学院附属第九人民医院

【摘要】 Patients with cartilage damage have various discomforts, including pain, clicks, deformities, and dysfunction. Chondrocytes are a crucial component of cartilage restoration; however, their limited proliferative ability and degenerative specificity dramatically reduce their effectiveness. In the

present study, the effects of leptin on chondrocyte proliferation, chondrogenic and secretion marker gene expression, and chondrocyte cartilage matrix component secretion were evaluated in vitro. The roles of the mitogen-activated protein kinase (MAPK) and protein kinase B (AKT) signaling pathways in these processes were also investigated. More importantly, a leptin sustained release system was developed using a hydrogel with calcium alginate microspheres and was transplanted into cartilage defects in rabbit femurs to analyze the effect of leptin on promoting cartilage restoration. The results showed that leptin promoted cell proliferation and chondrocyte gene expression in a dose-dependent manner, and a concentration of 100 ng/mL leptin had the greatest effect. The activation of the P38 and AKT signaling pathways might be responsible for these effects. An improved in vivo restoration outcome was observed in the leptin sustained release group compared with the control group. These results suggest that leptin could be used as a suitable drug for cartilage restoration.

【关键词】 chondrocytes regeneration；leptin；P38；AKT

Chirality controls stem cell lineage diversification through mechanoresponses

江圣杰　北京大学口腔医院

【摘要】 Life biogenesis and tissue development are based on the heterogenesis of multipotent stem cells. However, the underlying mechanisms of stem-cell-fate specification are unclear. Chirality is one of the most initial niches in stem cells and is implicated in asymmetrical cell-morphology formation, however, its function in heterogeneous cell-fate determination remains elusive. Here, we report that the chirality of a constructed three-dimensional (3D) extracellular matrix (ECM) modulated mesenchymal stem cells (MSCs) to diverse lineages of osteogenic and adipogenic by providing primary heterogeneity. Molecular analysis showed that the left-handed chirality of the ECM enhanced the mechanosensor Itg α 5 clustering while right-handed chirality decreased this effect. These differential adhesion patterns further triggered distinct mechanotransduction events involving the contractile state, focal adhesion kinase (FAK)/ extracellular signal-regulated kinase (ERK)1/2 cascades, and yes associated protein (YAP)/ runt related transcription factor 2 (RUNX2) nuclear translocation, that direct heterogenous differentiation. Moreover, theoretical modeling demonstrated that diverse chirality mechanosensing is initiated by biphasic modes of fibronectin-tethering. Our findings of chirality-dependent lineage-specification of stem cells provide potential strategies for organism biogenesis and regenerative therapies.

【关键词】 matrix chirality；cellular mechanics；lineage diversification

LIPUS inhibited the expression of inflammatory factors and promoted the osteogenic differentiation capacity of hPDLCs by inhibiting the NF-κB signaling pathway

刘　杉　重庆医科大学附属口腔医院

【摘要】 Background and Objectives: As a chronic infectious disease, periodontitis can could lead to tooth and bone loss. Low-intensity pulsed ultrasound (LIPUS) is a safe, noninvasive treatment method to effectively inhibit inflammation and promote bone differentiation. However, the application of LIPUS in curing periodontitis is still rare. Our study aimed to explore the ability of LIPUS to inhibiting inflammatory factors and promote the osteogenic differentiation capacity of human periodontal ligament cells (hPDLCs), and its underlying mechanism.

Material and Methods: hPDLCs were obtained and cultured from the premolar tissue samples for experiments. First, hPDLCs were treated for 24 hours using lipopolysaccharide (LPS), and then exposed to LIPUS (10 mW/cm2, 30 mW/cm2, 60 mW/cm2, and 90 mW/cm2) to determine the appropriate intensity to inhibit expression of the inflammatory factors interleukin-6 (IL-6) and interleukin-8 (IL-8) expression. The expression of IL-6 and IL-8 was detected by real-time PCR and enzyme-linked immunosorbent assay (ELISA). The safety of the most appropriate intensity of LIPUS was tested by a cell counting kit 8(CCK-8) test and an apoptosis assay. Then, LPS-induced hPDLCs were treated in osteogenic medium for 7 ～ 21 days with or without LIPUS (90 mW/cm2, 30 min/day) stimulation. The osteogenic genes RUNX2, OPN, OSX, and OCN were measured by real-time PCR. Additionally, osteogenic differentiation capacity was determined using alkaline phosphatase (ALP) staining and alizarin red staining. The activity of the nuclear factor-kappa B (NF-κB) signaling pathway was determined by western blotting, real-time PCR, immunofluorescence, and pathway blockade assays.

Results: LPS significantly upregulated the production and gene expression of IL-6 and IL-8, while LIPUS stimulation significantly inhibited IL-6 and IL-8 expression in an intensity dependent manner. LIPUS (90 mW/cm2) was chosen as the most appropriate intensity and there was no detrimental influence on cell proliferation and status with or without osteogenic medium. In addition, consecutive stimulation with LIPUS (90mW/cm2) for 30 min/day for 7 days could also inhibit IL-6 and IL-8 gene expression, upregulate the expression of the osteogenesis-related genes RUNX2, OPN, OSX and OCN and promote osteogenic differentiation capacity in osteogenic medium in inflamed hPDLCs. The NF-κB signaling pathway was inhibited with LIPUS (90 mW/cm2) via inhibition of the phosphorylation of IκBα and the translocation of p65 into the nucleus in inflamed hPDLCs. Additional investigations

of the NF-κB inhibitor, BAY 11-7082, revealed that LIPUS (90 mW/cm2) acted similarly to BAY 11-7802 to inhibit the NF-κB signaling pathway and increase osteogenesis-related genes and promote the osteogenic differentiation capacity of inflamed hPDLCs.

Conclusions: LIPUS (90 mW/cm2) stimualtion could be a safe method to inhibit IL-6 and IL-8 in hPDLCs by inhibiting the NF-κB signaling pathway. The effect of LIPUS (90 mW/cm2) and BAY 11-7082 on LPS-induced inflammation demonstrated that both of these agents were capable of promoting osteogenesis-related gene expression and osteogenic differentiation in hPDLCs, suggesting that the effect of LIPUS on the promotion of osteogenic activity could be mediated in part through its ability to inhibit the NF-κB signal pathway. Hence, LIPUS could be a potential therapeutic method to cure periodontitis.

【关键词】 periodontal inflammation; Low-intensity pulsed ultrasound; NF-κB signal pathway; osteogenic capacity

MicroRNA-705 regulates the differentiation of mouse mandible bone marrow mesenchymal stem cells

王丽波　遵义医科大学附属口腔医院

【摘要】 The craniofacial skeleton is the foundation of most stomatological treatments, including prosthodontics and maxillofacial surgery. Although histologically similar to the appendicular skeleton, the craniofacial skeleton manifests many unique properties in response to external stimuli and signals. However, the mandibular or maxillary bone marrow mesenchyme, which is the intrinsic foundation of the functions of craniofacial skeleton, has not been well studied, and its homeostasis mechanism remains elusive. Osteoporosis is a systemic disease that affects all skeletons and is characterized by bone mass loss. Osteoporotic bone marrow mesenchymal stem cells (BMMSCs) exhibit disturbed homeostasis and distorted lineage commitment. Many reports have shown that microRNAs (miRNAs) play important roles in regulating MSCs homeostasis. Here, to obtain a better understanding of mandibular bone marrow MSCs homeostasis, we isolated and cultured mandible marrow MSCs from mouse mandibles. Using miR-705 mimics and an inhibitor, we demonstrated that miR-705 played a vital role in shifting the mandibular MSCs lineage commitment in vitro. Utilizing an osteoporosis mouse model, we demonstrated that MSCs from ovariectomized (OVX) mouse mandibular bone marrow exhibited impaired osteogenic and excessive adipogenic differentiation. miR-705 was found overexpressed in OVX mandibular MSCs. The knock down of miR-705 in vitro partially attenuated the differentiation disorder of the OVX mandibular MSCs by upregulating the expression of osteogenic marker genes but suppressing adipogenic genes. Taken together, our findings provide a better

understanding of the homeostasis mechanism of mandibular BMMSCs and a novel potential therapeutic target for treating mandibular osteoporosis.

【关键词】 MicroRNA-705；Differentiation；Bone marrow mesenchymal stem cells；Osteoporosis, Mandible bone

FAM20C 突变对成骨细胞行为的影响

王　瑜　滨州医学院

【摘要】 背景：序列相似性家族 20 代表了一个新的分泌蛋白家族，主要成员包括 FAM20A，FAM20B 与 FAM20C。每个家族成员的突变都可导致相应疾病发生，其中 FAM20C 突变引发的疾病临床上称为 Raine 综合征。此种疾病有两种不同的临床表现，一种为致死性骨硬化发育不良，另一种为非致死性低磷酸血盐佝偻病，同为 Raine 综合征为何出现相反临床表现？其病因与发病机制尚不清楚。本文利用课题组已拥有的成骨细胞系，转染携带有致死性与非致死性突变质粒，探究为何同一种基因的突变会引起两种完全相反的临床表现，不同位点的突变是否对细胞行为产生不同的影响。

目的：研究不同位点突变的 Fam20c 对成骨细胞的增殖、迁移、矿化等生物学行为的作用，及其对相关调控基因表达的改变。

方法：1. RT-PCR 检测基因表达差异；2. BrdU 染色检测细胞增殖变化；3. 划痕实验检测细胞迁移变化；4. 茜素红染色检测细胞矿化改变。

结果：1. Fam20c 缺失与突变对成骨 细胞增殖影响无显著性差异；

2. Fam20c 基因缺失和突变使 成骨细胞的迁移能力减弱

3. Fam20c 基因缺失和突变改变了 成骨细胞的基因表达

4. Fam20c 基因缺失使 成骨细胞矿化能力降低，Fam20c 基因缺失与突变对成骨细胞的矿化能力无显著性差异

结论： FAM20C 不同位点突变引起 Raine 综合征两种不同的临床表现，体外实验表明对成骨细胞增殖无显著性影响，但可引起成骨细胞迁移以及矿化的细胞学行为与功能改变。

【关键词】 FAM20C；位点突变；Raine 综合征；成骨细胞

一种用于创伤急救的三层仿生血管的研发与运用

张晏源　空军军医大学第三附属医院

【摘要】 颌面部肿瘤或外伤导致血管损伤，多数血管损伤后，采用结扎加缝扎的方法止血，

可能会引起供区器官功能障碍；同时，冠状动脉狭窄为代表的心血管疾病已经成为世界上发病率和致死率最高的疾病之一，仅我国须进行血管搭桥手术的患者达到 100，000 例 / 年。自体的血管组织远不能满足临床血管移植需求。近年来，小口径人工血管成为血管移植领域研究的热点，但在临床应用上存在易堵、易破等临床问题。因此需要研发兼具良好的生物学性能和力学性能的人工血管，本课题中采用静电纺丝技术构建聚已内酯（PCL）联合聚氨酯（PU）的三层仿生人工血管：①内、外两层为 PCL 可完全降解，具有较好的生物相容性，内层沿血管长轴静电纺丝的 PCL 微纳米纤维，可有效降低血流扰动，减少血管湍流，从而降低血管阻塞风险；②中间层为 PU/PCL 混合，具有耐疲劳、可加工性强等特点，弥补在材料降解新生血管未完全替代期间，出现的血管破裂或动脉瘤；③静电纺丝技术可实现血管三层有序复合，制备三层仿生人工血管。对于提高临床救治效果、减低伤亡率具有重要的意义。

【关键词】 仿生；静电纺丝；小口径人工血管；PCL；PU

ClC-7 Regulates the Pattern and Early Development of Craniofacial Bone and Tooth

张燕丽　空军军医大学

【摘要】 Human CLCN7 encodes voltage-gated chloride channel 7 (ClC-7); mutations of CLCN7 lead to osteopetrosis which is characterized by increased bone mass and impaired osteoclast function. In our previous clinical practice, we noticed that osteopetrosis patients with CLCN7 mutations had some special deformities in craniofacial morphology and tooth dysplasia. It is unclear whether these phenotypes are the typical features of CLCN7 involved osteopetrosis and whether ClC-7 could regulate the development of craniofacial bone and tooth in some signaling pathways.

Methods: First, we collected 80 osteopetrosis cases from the literature and compared their craniofacial and dental phenotypes. Second, four osteopetrosis pedigrees with CLCN7 mutations were recruited from our clinic for gene testing and clinical analysis of their craniofacial and dental phenotypes. Third, we used a zebrafish model with clcn7 morpholino treatment to detect the effects of ClC-7 deficiency on the development of craniofacial and dental phenotypes. General observation, whole mount alcian blue and alizarin red staining, whole mount in situ hybridization, scanning electron microscope observation, lysoSensor staining, Q-PCR and western blotting were performed to observe the in vivo characteristics of craniofacial bone and tooth changes. Fourth, mouse marrow stromal cells were further primarily cultured to detect ClC-7 related mRNA and protein changes using siRNA, Q-PCR and western blotting.

Results: Over 84% of osteopetrosis patients in the literature had some typical craniofacial and tooth phenotypes, including macrocephaly, frontal bossing, and changes in shape and proportions

of facial skeleton, and these unique features are more severe and frequent in autosomal recessive osteopetrosis than in autosomal dominant osteopetrosis patients. Our four pedigrees with CLCN7 mutations confirmed the aforementioned clinical features. clcn7 knockdown in zebrafish reproduced the craniofacial cartilage defects and various dental malformations combined the decreased levels of col10a1, sp7, dlx2b, eve1, and cx43. Loss of clcn7 function resulted in lysosomal storage in the brain and jaw as well as downregulated cathepsin K (CTSK). The craniofacial phenotype severity also presented a dose-dependent relationship with the levels of ClC-7 and CTSK. ClC-7/CTSK further altered the balance of TGF-β/BMP signaling pathway, causing elevated TGF-β-like Smad2 signals and reduced BMP-like Smad1/5/8 signals in clcn7 morphants. SB431542 inhibitor of TGF-β pathway partially rescued the aforementioned craniofacial bone and tooth defects of clcn7 morphants. The ClC-7 involved CTSK/BMP and SMAD changes were also confirmed in mouse bone marrow stromal cells.

Conclusion: These findings highlighted the vital role of clcn7 in zebrafish craniofacial bone and tooth development and mineralization, revealing novel insights for the causation of osteopetrosis with CLCN7 mutations. The mechanism chain of ClC-7/CTSK/ TGF-β/BMP/SMAD might explain the typical craniofacial bone and tooth changes in osteopetrosis as well as pycnodysostosis patients.

【关键词】 osteopetrosis；ClC-7；craniofacial bone；tooth；SB431542

天然丝蛋白基复合骨组织工程支架

郑　奥　上海交通大学医学院附属第九人民医院

【摘要】 基于干细胞的骨组织工程是具有前景的骨再生方式。支架材料是骨组织工程的最基本构架，因此筛选和制备出一种理想的支架材料对于骨组织工程的发展和临床应用至关重要。因此本实验尝试利用生物相容性较好的海藻酸钠与天然高分子丝蛋白材料，采用硅酸钙作为无机相进行复合，制备丝素蛋白 / 海藻酸钠 / 硅酸钙复合多孔支架。期望这一策略能构建出用于骨组织再生修复的具有良好生物相容性机械和理化性能的新型支架。

【关键词】 丝蛋白；海藻酸钠；支架；骨组织工程

STAT3 COOPERATES WITH MSX1 TO DRIVE OSTEOBLAST DIFFERENTIATION THROUGH DLX5 AND AFFECT SKELETAL DEVELOPMENT OF HIES PATIENTS

周巳入　Dai Qinggang　上海交通大学医学院附属第九人民医院

【摘要】 Hyper-IgE syndrome (HIES), or Job’s syndrome, is usually inherited in an autosomal dominant pattern caused by dominant-negative mutations in signal transducer and activator of transcription (STAT3). Bone fragility and craniofacial deformity are a defining feature of HIES patient besides recurrent staphylococcus aureus skin abscesses. However, the mechanisms of HIES-related craniofacial developmental malformation are still unknown and the contribution of STAT3 to skeletal metabolism in vivo remains to be elucidated. Here we reported that deletion of STAT3 in MSCs with Prx-cre and preosteoblasts with Osx-cre nor osteoclasts with Ctsk-cre induced frontal bones dysplasia, enlarged bone defects in the parietal bones, occipital and smaller mandible, bone fragility and osteoporosis , similar to those found in human patients with HIES. Stat3Osx mice displayed reduced bone formation. STAT3 deficiency in BMSCs displayed impaired osteoblast differentiation in vitro by markedly decreased ALP activity and mineralization. In addition , the mRNA levels of osteogenic genes were significantly downregulated. RNA sequence showed downregulated genes of Stat3Osx mice were enriched for associations with bone development and ossification. Among them, distal-less homeobox (DLX5) was downregulated significantly but the expression of Msh homeobox 1(MSX1) was remained relatively unchanged. Moreover, our results revealed a physical interaction between STAT3 and MSX1 nor DLX5. Mechanistic analysis revealed that STAT3 cooperated with MSX1 binds to DLX5 promoter and modulates its transcriptional activity. Overexpression DLX5 in BMSCs of Stat3Osx mice could promote osteoblast differentiation by enhanced ALP activity and mineralization. Taken together, our study demonstrated STAT3 cooperated with MSX1 to drive osteoblast differentiation through DLX5 and affect skeletal development of HIES patients.

【关键词】 HIES；STAT3；DLX5；MSX1；osteoblast differentiation