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·综述·

甲状旁腺激素与甲状旁腺激素相关肽在调节牙萌出中作用的研究进展

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【摘要】 牙萌出是指牙冠形成后向𬌗平面移动，穿过牙槽骨与口腔黏膜到达功能位置与对颌牙接触的一系列复杂生理过程。甲状旁腺激素（parathyroid hormone，PTH）与甲状旁腺激素相关肽（parathyroid hormone-related peptide，PTHrP）是体内钙磷代谢的重要调节因子，在牙齿的萌出中起着重要作用，其调控作用具有复杂的时空特点，且其背后的机制尚未完全明确。近年来，国内外学者对PTH/PTHrP在牙齿萌出中的作用及机制研究越来越多，主要集中在对牙囊形成、基部牙槽骨形成、冠部牙槽骨吸收、牙根形成、牙周膜形成等方面。文献复习结果表明：PTH/PTHrP调节着骨代谢，协调OPG/RANK/RANKL、cAMP/PKA和Wnt/β-catenin等多种信号通路，并受Ca^{2+}和ATP变构调节，参与牙囊的发育，并通过牙囊发出信号，聚集破骨细胞促进冠部牙槽骨吸收以形成萌出通道，也参与基部牙槽骨形成、牙根发育、牙周膜形成以形成萌出动力，经过严格的时空调控，多方协同合作，使得牙槽骨重塑来完成牙齿萌出这一复杂的发育过程。未来还需进一步研究PTH/PTHrP作用背后的机制，以及给药方式、剂量、时间和频率。

【关键词】 甲状旁腺激素；　甲状旁腺激素相关肽；　牙齿萌出；　破骨；　牙囊；　牙槽骨；　牙根；　牙周膜
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Research progress on the role of parathyroid hormone and parathyroid hormone-related peptide in regulating tooth eruption

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【Abstract】 The emergence of teeth is a complex physiological process characterized by the formation of the tooth crown, its movement towards the occlusal plane, and subsequent penetration through the alveolar bone and oral mucosa to achieve functional positioning for contact with opposing teeth. Parathyroid hormone (PTH) and parathyroid hormone-related peptide (PTHrP) are critical regulators of calcium and phosphorus metabolism in the body, playing significant roles in tooth emergence. Their regulatory functions exhibit intricate temporal and spatial dynamics, with underlying mechanisms that remain incompletely understood. In recent years, an increasing number of researchers both domestically and internationally have investigated the role and mechanisms of PTH/PTHrP in tooth emergence, primarily focusing on aspects such as dental sac formation, basal alveolar bone development, coronal alveolar bone resorption, root formation, and periodontal ligament development. Literature reviews indicate that PTH and PTHrP regulate bone metabolism, coordinate various signaling pathways including OPG/RANK/RANKL, cAMP/PKA, and Wnt/β-catenin, and are allosterically modulated by Ca^{2+} and ATP. These processes contribute to the development of dental sacs, which transmit

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signals to recruit osteoclasts and promote the resorption of crown alveolar bone, thereby forming an eruption pathway. Additionally, PTH/PTHrP plays a role in the formation of basal alveolar bone, root development, and the periodontal ligament, generating the force necessary for tooth eruption. Through precise spatiotemporal regulation and coordinated efforts, alveolar bone remodeling is achieved, facilitating the intricate process of tooth eruption. Through stringent temporal regulation and multi-faceted cooperation, remodeling of the alveolar bone occurs to complete this intricate developmental process of tooth emergence. Future research should further elucidate the mechanisms underlying PTH/PTHrP actions while also considering optimal dosage regimens regarding timing and frequency for therapeutic applications.

【Key words】 parathyroid hormone; parathyroid hormone related peptide; tooth eruption; osteoclasis; dental follicle; alveolar bone; tooth root; periodontal ligament

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牙萌出是指牙冠形成后向𬌗平面移动，穿过牙槽骨和口腔黏膜到达功能位置的一系列复杂生理过程[1]。钙磷代谢在骨形成和骨吸收中发挥重要作用。甲状旁腺激素（parathyroid hormone，PTH）是由甲状旁腺主细胞合成、分泌的一种碱性单链多肽类分子，是调节钙、磷代谢及骨转换的重要肽类激素之一[2]。甲状旁腺激素相关肽（parathyroid hormone-related peptide，PTHrP）与PTH类似，生物学作用相似，两者都参与调控颌骨内骨的合成代谢[3]，体内磷、钙和PTHrP的改变导致钙感应受体缺陷小鼠牙齿和牙槽骨形成缺陷[4]。这2种激素都调节血清钙，任何一种激素的缺失都可能会导致低钙血症和高磷血症。PTH/PTHrP与高钙血症及恶性肿瘤方面的研究已很多，但近年来发现PTH/PTHrP在颅面发育和重塑功能方面也受到了人们的关注[5]。在口腔中尤其是牙齿发育与牙槽骨发育中发挥着重要作用，故本文就PTH和PTHrP在牙齿萌出中作用作一综述。

1　PTH和PTHrP的基本结构和功能

PTH是一种由甲状旁腺分泌的84个氨基酸构成的多肽激素，由甲状旁腺主细胞分泌，在体内调节体内钙磷代谢，通过直接影响人体骨骼和肾脏和间接影响人体肠道发挥重要作用[6-7]。PTH是钙磷稳态中重要的调节因子，对骨代谢有着双重调节作用，既能促进骨的形成，也能加速骨的吸收[8]。PTH对骨代谢的双重影响主要取决于其给药剂量、给药方式及机体自身的PTH水平[9-10]。PTH间歇性给药、短时间刺激能促进成骨细胞介导的骨形成[10-11]，PTH大剂量给药、长时间连续刺激能明显增加破骨细胞活性，促进骨吸收[12]。以上情况意味着PTH不仅具有促进骨形成，而且具有刺激骨吸收的能力。PTHrP最开始是在研究恶性肿瘤相关性高钙血症中发现的，因其和PTH在空间构象和信号传导方面有相同或相似之处，故称为甲状旁腺激素相关肽[13-14]。PTHrP是由141个氨基酸组成的多肽，其N-端与PTH具有高度同源性，由各种组织合成和表达，包括骨骼、皮肤、血管、生长板软骨细胞、平滑肌和神经元组织，主要发挥PTH样作用，参与调节体内钙磷平衡，在成骨分化等方面发挥作用[15-16]。PTH是一种经典的内分泌肽激素，PTHrP主要以自分泌/旁分泌方式发挥作用[15，17]。有学者发现[18]，在甲状腺功能减退小鼠中，PTHrP补偿了PTH的作用，促进了体内骨积累的情况。

PTH与PTHrP通过激活相同受体PTH/PTHrP受体（type 1 PTH/PTHrP receptor，PTH1R）发挥作用。PTH1R是B类G蛋白偶联受体（G protein-coupled receptors，GPCR）家族成员之一，在骨组织、肾脏、乳腺中高度表达[15，19]。GPCR激活的经典模型是配体结合时异源三聚体G蛋白信号传导的刺激仅发生在细胞表面，并且刺激的持续时间是短暂的，以防止过度刺激。GPCR信号转导通过G蛋白偶联受体激酶（G protein-coupled receptor kinase，GRK）的受体磷酸化和随后募集β-arrestin而被关闭，导致受体内化到内体中。然后，内化的受体可

以循环回细胞表面或被转运到溶酶体进行降解。内化的GPCR继续通过来自内体的G蛋白发出信号。PTH1R就是这种情况，它在PTH刺激后参与来自内体的持续环磷酸腺苷（cyclic adenosine monophosphate，cAMP）信号传导[20]。

PTH和PTHrP与骨重塑过程有关，介导合成代谢和分解代谢效应。实验表明，PTH1R受正变构调节剂细胞外Ca^{2+}的调节，Ca^{2+}通过延长PTH在PTH1R上停留的时间，导致受体激活延长并通过cAMP增强内体信号传导[21]。Ca^{2+}诱导了PTH1R变构信号通路，Ca^{2+}的关键结合进一步促进受体的正变构活化，促进了PTH1R与Gs蛋白的α5螺旋（spep）之间的相互作用，Ca^{2+}的结合稳定了PTH1R-PTH-spep复合物的构象，特别是细胞外环1（ECL1）[21]。Li等[22]发现，Ca^{2+}的存在增强了PTH和PTH1R跨膜结构域（transmembrane domain，TMD）内的通讯，增强了PTH1R的活化，也印证了这一结果。Ca^{2+}的调节，使得PTH/PTHrP更好的发挥作用。

牙齿萌出过程涉及牙槽骨变化，即骨形成与骨吸收，通过牙根部形成牙齿萌出动力，以及牙冠部形成牙齿萌出通道，最终穿过牙槽骨和口腔黏膜从而完成这一复杂的萌出过程[23]。PTH与PTHrP已在以往研究中发现与骨代谢有关[24-26]，因而引起了学者们对它们在牙齿萌出中作用的研究，越来越多的证据证明PTH/PTHrP在牙萌出中起着不可或缺的作用。

2　PTH和PTHrP参与牙齿萌出

目前，许多研究证明PTH和PTHrP与牙齿萌出有着不可分割的关系[27-28]。牙萌出的机制尚未完全明确，已有研究表示[23, 29]，该机制主要涉及两大方面：一是牙齿萌出通道形成，需要成熟破骨细胞使牙囊冠部牙槽骨吸收；一是牙齿萌出动力，需要牙周膜、根尖周组织及牙囊基部牙槽骨形成等多因素相互作用推动牙齿萌出。在这个过程中，涉及牙囊、牙槽骨、破骨细胞、成骨细胞及多种细胞因子参与共同调控。

2.1　PTH和PTHrP对牙囊的作用

牙囊是牙齿正常萌出过程中不可缺少的条件[30]。Larson等[31]在犬下颌前磨牙萌出前4周摘除外层牙囊，前磨牙不能萌出；而当将摘除牙囊重新放置在成釉器表面，前磨牙正常萌出。牙囊是牙齿萌出所必需的，围绕着牙釉质器官和牙，并调节牙槽骨的形成和吸收[32]。牙囊细胞信号丢失或改变会抑制破骨细胞分化，影响成骨细胞和牙骨质母细胞分化，并抑制牙囊细胞增殖，从而导致牙齿萌出失败[33-34]。可见，牙囊在牙齿萌出中是必要的条件。

2.1.1　PTH和PTHrP调控牙囊激活单核细胞形成破骨细胞　学者们发现[35]，在大鼠牙囊细胞中可表达PTHrP，而牙囊细胞中也可表达PTH1R，猜测PTHrP可能通过与PTH1R结合而对牙囊产生旁分泌的作用。在牙齿发育期间，在牙胚周围发现有PTHrP的表达。Zhang等[36]通过将PTHrP与牙囊细胞共培养后，牙囊细胞中增加了RANKL/OPG比值的表达，从而促进破骨细胞的活性，同时，体内实验出现PTHrP使得牙齿萌出加速的情况。PTHrP通过激活核因子κ-B配体受体激活剂（receptor activator ofnuclear factor kappa-B，RANK）/骨保护素（osteoprotegerin，OPG）/核因子κ-B配体受体激活剂（receptor activator ofnuclear factor kappa-B ligand，RANKL）通路来促进破骨细胞的形成。

2.1.2　PTH和PTHrP调控牙囊调节成骨分化和骨吸收　牙囊间充质细胞可分化形成成牙骨质细胞、牙周膜细胞和牙槽骨细胞等以形成功能性牙根和牙周附着结构（即牙骨质、牙周膜和固有牙槽骨）[37]。Takahashi等[38]使用他莫昔芬诱导PTHrP-creER小鼠发现，$PTHrP^{+}$牙囊（dental follicle，DF）细胞分化成无细胞牙骨质，牙周韧带细胞和牙槽隐窝骨成骨细胞上的成牙骨质细胞；而PTHrP-PPR缺陷诱导$PTHrP^{+}$ DF细胞向非生理性成牙骨质样细胞的细胞转变，成为形成细胞骨质的成骨细胞样细胞，而不能成为建立牙周附着组织的韧带细胞和隐窝成骨细胞，导致牙周正常附着结构丧失从而引起牙齿萌出失败。可见，PTHrP在牙齿萌出中牙根与牙周正常组织形成发挥重要作用，证明其在牙齿正常萌出中必不可少的地位。赵迪芳等[27]通过建立特发性甲状旁腺功能减退症（idiopathic hypoparathyroidism，IHP）动物模型，发现下颌第三磨牙牙根定向牙槽骨的总体积以上骨量和小梁数降低，并检测到血清钙浓度降低，血清磷浓度升高，血清甲状旁腺素浓度明显降低，PTH/PTH1R信号传导的减弱降低了牙囊干细胞的增殖活性，抑制其对成骨细胞和破骨细胞分化和功能的调节，从而干扰牙胚周围牙槽骨的骨重塑，最终导致牙齿萌发延迟。以上研究证明PTH/PTHrP通过对牙囊的作用来调控成骨分化和骨吸收。尽管目前

多项研究证明PTH/PTHrP会通过影响牙囊的发育从而影响牙齿的萌出，但其背后的具体调控机制仍未完全明确，有待于进一步的研究。

2.2 PTH和PTHrP对牙槽骨的调节作用

2.2.1 PTH和PTHrP对破骨细胞的作用 学者们发现[39-40]，PTH过度表达会引起骨吸收，在牙齿发育及萌出过程中，通过调控破骨细胞的数量，PTH加速了局部牙槽骨吸收。研究表明[40-41]，PTH可通过RANKL/OPG/RANK通路调节骨细胞和成骨细胞中RANKL的表达、成骨细胞中OPG的表达以及骨吸收。RANKL可与破骨细胞前体细胞表面RANK结合，促进破骨细胞的分化与存活，并与成熟破骨细胞结合，增强其活性。而OPG是RANKL的诱导受体，可与RANK结合，阻止RANK对破骨前提细胞和破骨细胞发挥作用[6]。学者们发现[42]，PTH通过蛋白激酶A（protein kinase A，PKA）-cAMP反应元件结合蛋白（cAMP-response element binding protein，CREB）通路下调OPG表达。PTH的作用增加RANK与RANKL结合，激活破骨细胞，引起骨吸收。PTH通过cAMP-PKA途径抑制盐诱导激酶2（salt-inducible kinase 2，SIK2）对CREB的转录激活因子2（CREB-regulated transcription coactivator 2，CRTC2）的磷酸化，脱磷相关的CRTC2可以进入细胞核，作为CREB的共激活因子[43]。PTH（1-34）及其类似物除了通过上述途径外，还通过PKA-SIK2-SIK3和蛋白磷酸酶1（protein phosphatase 1，PP1）-蛋白磷酸酶2A（protein phosphatase 2A，PP2A）-CREB的转录激活因子3（CREB-regulated transcription coactivator 3，CRTC3）信号调节成骨细胞RANKL的表达[44]。

2.2.2 PTH和PTHrP对成骨细胞的作用 PTH可通过直接作用于成骨细胞和骨细胞等而发挥成骨作用。PTH可刺激成骨特异性转录因子的表达，促进成骨细胞的增殖和分化，抑制成骨细胞的成脂分化[45-46]。PTH经上述一系列细胞作用，在成骨细胞的介导下实现成骨作用。而抑制成骨细胞凋亡是PTH在成骨过程中的重要作用。学者们发现[12, 47]，PTH使促凋亡因子Bad失活；下调凋亡诱导因子CARP-1的表达；促进骨形态发生蛋白（bone morphogenetic proteins，BMP）信号，增加Runx的表达，从而减少成骨细胞凋亡，促进成骨细胞的存活、增殖和分化。PTH和PTHrP在骨合成代谢和再吸收中发挥重要作用，线粒体代谢通过底物利用、骨细胞在骨皮层中的位置和线粒体生物发生在骨细胞生物能量学中发挥作用[48]。PTH可以触发成骨细胞释放ATP，作用与PTH结合的PTH1R的一种自分泌机制可能充当骨细胞中PTH1R信号传导的正反馈回路[20]。

2.2.3 PTH和PTHrP对牙槽骨的作用 牙槽窝底部的骨髓间充质干细胞（bone marrow mesenchymal stem cells，BMSCs）可分化为成骨细胞，形成新生骨质弥补牙齿向冠方萌出时的根方骨质缺损并成为推动牙齿萌出的动力[49]。PTH可以调节骨髓间充质干细胞的分化途径，促进其成骨分化，抑制其成脂分化[50]。在骨髓间充质干细胞中缺乏PTH1R的小鼠中，骨髓间充质干细胞的成骨分化减少，成脂分化增加，导致骨髓脂肪组织（bone marrow adipose tissue，BMAT））的形成增加。PTH受体信号传导的遗传丢失，BMAT快速增加，表达RANKL，刺激晚期破骨细胞分化，引起骨吸收[51]。间歇给药PTH可通过激活PKA途径抑制人骨髓间充质干细胞的成脂分化，同时刺激骨髓间充质干细胞的增殖、成骨分化和矿化。PTH通过激活cAMP-PKA信号通路指导BMSCs的命运，加速BMSCs的成骨分化，抑制BMSCs的成脂分化[50]。PTH/PTHrP结合诱导或稳定活性PTH1R构象，从而促进异三聚体G蛋白的偶联和激活。Gαs激活腺苷酸环化酶（adenylate cyclase，AC），导致cAMP合成和PKA的激活。Gαq激活磷脂酶C（phospholipase C，PC），将磷脂酰肌醇（4，5）-二磷酸（phosphatidylinositol 4，5-bisphosphate，PIP2）裂解为二酰基甘油（diacylglycerol，DAG）和肌醇（1，4，5）-三磷酸（inositol 1，4，5-trisphosphate，IP3）。然后IP3通过细胞质扩散并激活位于内质网膜上的IP3门控Ca^{2+}通道，将储存的Ca^{2+}释放到细胞质中。胞质内Ca^{2+}的增加促进蛋白激酶C（protein kinase C，PKC）易位到质膜，然后被DAG激活。另一种cAMP信号传导模式，内化的PTH1R也延长了cAMP的产生，并扩散到细胞核中直接激活核PKA[16]。Shen等[52]在对BMSCs持续用外源性PTHrP后，显著上调了p-PKA和p-CREB的磷酸化水平以及cAMP的合成，表明cAMP/PKA/CREB信号通路激活，并且，与经典Wnt/β-catenin信号通路相关的蛋白也显著上调。这说明PTHrP可同时调节cAMP/PKA/CREB和经典Wnt/β-catenin信号通路，从而影响BMSCs的成骨分化和增殖能力[52]。

PTH和PTHrP作为破骨细胞介导的骨吸收的内分泌刺激因子，有助于牙槽骨的重塑[53]。Me-

kaapiruk等[54]发现，在PTHrP敲除小鼠的牙胚周围很少见到破骨细胞，且被周围的牙槽骨穿透或压缩，引起局部损伤，造成牙齿萌出障碍，而野生小鼠牙胚周围排列着整齐的破骨细胞。Wnt信号通路在牙齿发育，牙槽骨再生中发挥重要作用[55]。学者们[36]发现，PTHrP（1-34）通过失活Wnt/β-catenin途径来加速牙齿的萌出。可见，PTHrP对于破骨细胞的形成和活化中起重要作用，在牙胚发育与牙萌出中是不可或缺的。赵迪芳等[27]通过IHP动物模型，发现IHP组大鼠RANKL/OPG比值、RUNX2、OSX等成骨相关基因的表达水平和PTH1R表达量均显著降低。

瘦素受体（leptin receptor，LepR）是一种骨骼干细胞标志物，LepR细胞在拔牙后被迅速激活分化为成骨细胞，在拔牙窝中产生了大部分新形成的骨，这一过程受PTH/PTH1R信号轴调控。Lepr+OMSC中PTH/PTH1R信号传导出现问题的小鼠拔牙窝牙槽骨修复发现受阻[56-57]。学者们发现[58-59]，PTH可通过激活Hedgehog通路影响骨折愈合，参与下颌骨发育。以上研究说明PTH/PTHrP调控着颌骨（牙槽骨）的生长发育，参与牙槽骨的生长发育与牙齿的萌出。

2.3　PTH和PTHrP对牙根的作用

牙齿萌出是一个独特的生物过程，高度的矿化组织进入外部世界，它的发生与牙根形成同时进行。这两个过程以往被认为是独立的现象，然而，最近的研究支持的理论，他们其实是交织在一起，相互影响的[60]。牙囊中的牙髓间充质祖细胞位于这两个过程耦合的核心，为支持高功能牙根和牙周附着装置形成的不同间充质细胞提供了来源，同时促进了破骨细胞的形成。在牙根形成过程中，PTHrP（+）DF细胞分化为成骨细胞、牙周韧带细胞和牙槽隐骨成骨细胞，形成根尖部牙周组织及牙槽骨，而缺乏该信号的DF间充质细胞在根表面过早形成细胞牙骨质，导致牙周附着组织丧失，造成牙齿萌出障碍。这些细胞受PTHrP及PTH/PTHrP受体PPR的自分泌信号调节[38，60]。Tokavanich等[61]发现，PTH/PTHrP/PTH1R的功能丧失突变的小鼠磨牙的萌出速度要慢的多，并伴有牙根缩短和扩张以及根间骨缺损。这说明牙根形成及根尖牙槽骨形成受影响的牙齿萌出动力不足影响了牙齿的萌出。学者们[62]在研究PTH在被吸收的根部治疗效果时发现间歇性PTH显著促进根吸收的再生，且可促进OCCM-30小鼠成牙骨质细胞EPHB4和ephrinB2的表达，PTH可能通过ephrinB2-EPHB4正向信号通路促进根吸收再生。在牙根形成过程中，PTH是否可能也通过调节OCCM-30细胞活性从而调控牙根的形成。这需要更多的实验研究来进一步验证。

2.4　PTH和PTHrP对牙周膜的作用

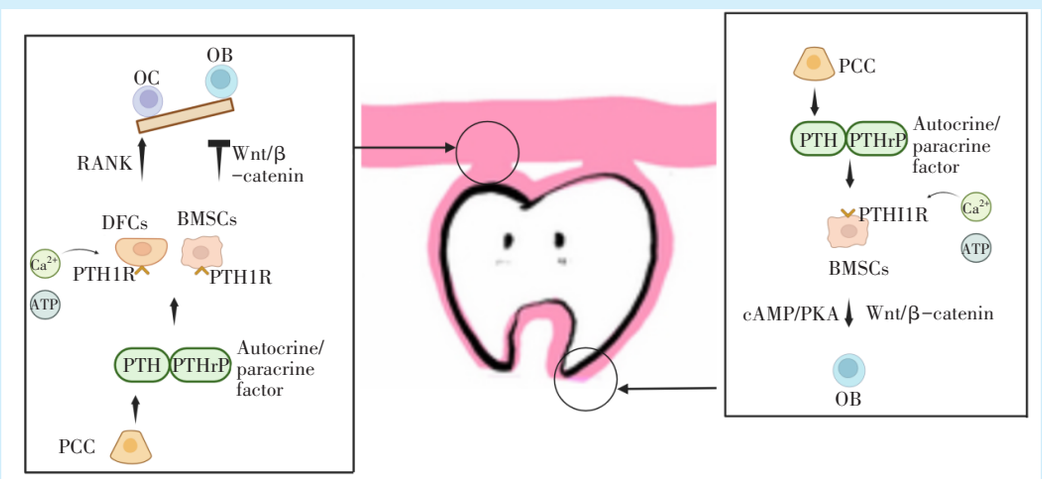
牙周膜细胞在牙齿萌出和牙槽骨代谢中起重要作用，牙周膜形成是牙齿萌出过程中的重要动力。牙周膜干细胞（periodontal stem ligament cells，PDLSCs）与牙骨质及牙周组织再生密切相关，具有未分化间充质干细胞的特点，能分化形成牙骨质、牙槽骨和牙周膜样组织[63]。PDLSCs有助于体内牙周组织的形成，并可在移植入小鼠体内后产生牙骨质/ PDL样结构[64]。使用动物模型研究中发现，PTH/PTHrP/PTH1R在调节PDL中的干细胞中具有重要意义。Cui等[65]发现，缺乏PTH1R表达导致信号转导出现问题的小鼠，出现牙周膜（PDL）变窄，胶原纤维排列不规则，骨膜蛋白表达下调，PDL中骨样组织的异常形成。PTH1R型fl/+小鼠和纯合基因敲除小鼠中具有强直根的PDL完全丧失。综上，PTH/PTHrP可调节牙周组织结构发育，参与牙齿萌出，表达失常可能会出现牙齿萌出障碍，但具体机制仍需进一步研究。

同时，牙周膜干细胞在生成破骨细胞，引起骨吸收中也起到作用。Nakao等[66]发现PTHrP以剂量和时间依赖的方式增加人PDL细胞中Notch1配体Jagged1的表达。PTHrP诱导的Jagged1上调是由PKA激活介导的。Jagged1促进了RANKL诱导的破骨细胞生成。这些结果表明，PTHrP诱导PDL细胞中Jagged1的表达，这2种信号的协同效应导致破骨细胞和牙本质细胞的形成，从而可能导致牙槽骨的吸收以促进牙齿萌出。

3　总结与展望

PTH主要生理作用是调节钙稳态，作用方式是体循环，而PTHrP对于骨重塑非常重要。牙萌出是一个独特的生物过程，由多方协作完成（图1）。其中，破骨细胞使牙槽骨吸收是牙萌出的关键，PTH/PTHrP与受体结合后，激活OPG/RANK/RANKL信号通路调控破骨细胞的分化、成熟及功能，通过失活Wnt/β-catenin途径来加速牙齿的萌出；并通过调控cAMP/PKA和Wnt/β-catenin信号通路来促进底部牙槽骨形成。PTH/PTHrP具有复杂的时空调控作用，对牙齿萌出至关重要。牙萌出需要在精

确的时间表达某些分子，以调节骨吸收和骨形成，从而形成牙萌出通道及萌出所需动力。在萌出时，牙囊接收信号刺激，破骨细胞侵入冠侧骨引起吸收，根尖部牙槽骨形成。目前在牙萌出中对于局部作用的PTHrP研究较多，而用药上PTH研究较多。PTH/PTHrP在口腔应用中有着非常重要的作用，不仅在牙萌出中占据重要地位，在正畸、种植、口外以及牙周治疗中都有着应用，但在使用频率及剂量上还需进一步探究。PTH/PTHrP在牙萌出中的作用还未完全明确，未来应进一步研究PTH/PTHrP作用背后的机制，以及给药方式、剂量、时间和频率，为临床应用提供进一步的理论支撑。



PCC: parathyroid chief cell. DFCs: dental follicle. BMSCs: bone marrow mesenchymal stem cells. OC: osteoclast. OB: osteoblast. PTH: parathyroid hormone. PTHrP: parathyroid hormone related peptide. PTH1R: type 1 PTH/PTHrP receptor. RANK: receptor activator of NF-κB. OPG: osteoprotegerin. RANKL: receptor activator ofnuclear factor kappa-B ligand. cAMP: cyclic adenosine monophosphate. PKA: protein kinase A

Figure 1　Roles of parathyroid hormone and parathyroid hormone-related peptide in regulating tooth eruption

图1　甲状旁腺激素与甲状旁腺激素相关肽在调节牙萌出中的作用

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