常见骨代谢机械敏感离子通道及其相关疾病的研究进展

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摘要 骨骼对于机械刺激的适应性对维持骨代谢平衡非常重要。这种适应性依赖于骨骼中的机械敏感细胞(成骨细胞、破骨细胞、骨细胞和间充质干细胞等)的机械敏感离子通道将细胞外的机械刺激转化为细胞内可传递的化学信号。TRP和Piezo是参与调控骨代谢的重要机械敏感通道。目前已有研究证明, 成骨细胞(Piezo1、TRPM3、TRPV4、TRPV2和TRPML1)、破骨细胞(TRPV6、TRPV1和TRPA1)、破骨前体细胞(Piezo1、TRPC3和TRPC6)、骨细胞(TRPV4和Piezo1)和间充质干细胞(TRPM7、Piezo1和Piezo2)的离子通道具有机械敏感性。但是上述机械敏感性离子通道调控骨代谢的具体功能和下游效应物仍存在很多的未知和争议。该研究通过综述主要的骨代谢相关的机械敏感离子通道类型及其功能, 为骨重建和骨性疾病的治疗提供可靠的理论依据和新的方法。

关键词 骨代谢; 机械刺激敏感细胞; TRP; Piezo; 疾病

Research Progress of Common Mechanically Sensitive Ion Channels in Bone Metabolism and Related Diseases

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Abstract Skeletal adaptation to mechanical stimulation is important for maintaining bone metabolic homeostasis. This adaptation relies on mechanically sensitive ion channels in bone's mechanically sensitive cells (osteoblasts, osteoclasts, osteocytes, mesenchymal stem cells, etc.) to convert extracellular mechanical stimuli into intracellular chemical signals. TRP and PIEZO are important mechanically sensitive channels involved in the regulation of bone metabolism. Studies have shown that the ion channels are mechanically sensitive, such as osteoblasts (PIEZO1, TRPM3, TRPV4, TRPV2 and TRPML1), osteoclasts (TRPV6, TRPV1 and TRPA1), osteoclast precursors (PIEZO1, TRPC3 and TRPC6), osteocytes (TRPV4 and PIEZO1) and mesenchymal stem cells (TRPM7, PIEZO1 and PIEZO2). However, the functions and downstream effectors of some mechanically sensitive ion channels are still unknown and controversial. The main types and functions of mechanically sensitive ion channels related to bone metabolism are reviewed to provide a reliable theoretical basis and a new method for bone remodeling and the treatment of bone diseases.

Keywords bone metabolic; mechanically sensitive cells; TRP; Piezo; diseases

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骨重建对维持骨骼结构完整性、骨再生能力和骨代谢稳态非常重要，而机械刺激对于骨重建过程起着至关重要的调控作用[1]。适宜的身体活动产生的机械刺激可以促进骨形成和骨重建，进而改善骨量和骨生物力学性能[2]。机械刺激通过改变细胞形态、突起数量、细胞间隙及细胞骨架构等，产生变化的机械信号。这些机械信号通过细胞表面的机械敏感通道被转换为化学信号，进而调控骨代谢相关机械敏感细胞的生理反应[3-4]。骨代谢相关的机械敏感细胞主要包括成骨细胞、破骨细胞、骨细胞、具有多能分化功能的间充质干细胞及破骨细胞前体细胞等[5]。多能的间充质干细胞在多种因素调控下发展成为骨祖细胞，最后由骨祖细胞定向分化为成骨细胞。破骨细胞是由骨髓中的髓系祖细胞分化而成的单核巨噬细胞相互融合，所形成的多核巨细胞。骨细胞由成熟的成骨细胞分化形成，占总骨细胞的90%~95%，是骨中最丰富、最长寿的细胞类型[6]。机械载荷通过改变骨陷窝形状，使骨组织各细胞产生机械应答，进而增加核因子κB(nuclear factor kappa-B, NF-κB)蛋白、核因子κB受体活化因子配体(receptor activator of nuclear factor-κB ligand, RANKL)、前列腺素E2(prostaglandin E2, PGE2)、NO、胰岛素样生长因子-1(insulin-likegrowthfactor-1, IGF-1)、成纤维细胞生长因子23(fibroblast growth factor 23, FGF23)、骨保护蛋白(osteoprotegerin, OPG)和葡萄糖-6-磷酸脱氢酶(glucose-6-phosphate dehydrogenase, G6PD)等分泌活动[7-9]，调控骨吸收和骨形成过程[10-14]，使其有可能成为治疗骨代谢紊乱疾病的潜在靶点[15]。

目前，常见相关机械敏感通道为退化蛋白/上皮钠离子通道(degenerin/epithelial sodium channel, DEG/ENaC)、瞬态受体电位(transient receptor potential, TRP)通道、双孔钾通道(two-pore-domain potassium channel, K2P)、Piezo通道等[5]。其中TRP和Piezo通道是目前研究较多的机械敏感离子通道，这些离子通道可以对重力、流体剪切力、压应力、牵拉力等多种机械刺激产生响应[16]。

有研究发现，敲除小肠上皮中的*Piezo1*可促进骨形成，减少血清素的产生[17]。而敲除成骨祖细胞中的*Piezo1*和*Piezo2*时，发现成骨分化被抑制，骨吸收程度加强，进而导致新生小鼠自发性骨折[18]。但另一项研究表明，敲除成骨细胞或软骨细胞中的Piezo2对骨量无任何影响，而本体感受神经元细胞中Piezo2缺失反而会导致脊柱和髋关节发育不良[19]。也有研究发现，特发性脊柱侧凸患者成骨细胞中的机械敏感通道蛋白表达上调[20]，椎间盘退行性患者软骨细胞中的ASIC2表达增加[21]。由此可见，机械敏感通道蛋白的异常表达有可能涉及多种骨性疾病的发生。因此，本文通过综述骨代谢相关的机械敏感离子通道类型和功能，及机械敏感离子通道异常导致的骨性疾病，为疾病的治疗寻求新的策略和治疗方法。

1 常见骨代谢机械敏感离子通道类型和功能

目前有关TRP和Piezo通道调控骨代谢的研究较多，它们对Ca^{2+}都有通透性，进而改变下游的基因表达，引起细胞形态和功能的改变，调控骨代谢稳态[22]。*TRP*基因于1975年首次被发现，属于选择性机械敏感通道，目前包含7个亚型：TRPC、TRPV、TRPM、TRPN、TRPA、TRPP和TRPML，在多种骨细胞中均有所分布[23-25]。TRP通道由6个跨膜结构域，及胞内的N-端和C-端组成[26]。之前的研究表示，TRPV(2-4)、TRPA2、TRPM3、TRPM7、TRPC1和TRPC6不属于机械敏感离子通道[27]，而TRPM7、TRPM3、TRPV4、TRPV2、TRPML1、TRPV6、TRPV1和TRPA1等离子通道的机械敏感性仍需要进一步探究[28]。

2010年科学家首次发现Piezo通道，它允许钠、钾和Ca^{2+}通过，属于非选择性离子通道，有Piezo1和Piezo2两种类型[29]，包含24~36个跨膜区，由2 500个氨基酸组成。Piezo在成骨祖细胞、软骨细胞和间充质干细胞等多种细胞中表达，对机械拉伸和流体剪切力产生响应[18,30]。高强度的机械刺激会通过Piezo1和Piezo2诱导细胞死亡[31]。研究发现，敲除成骨细胞中*Piezo1*后，新生小鼠发生自发性骨折[32]。本体感受神经元细胞中*Piezo2*缺失导致脊柱和髋关节发育不良[19]。但是敲除成骨祖细胞中的*Piezo1*和*Piezo1/2*时，成骨分化被抑制，骨吸收程度加强；激活*Piezo1*和*Piezo1/2*表达后，因负重减少而导致的骨量减少的情况被逆转[18]。因此，Piezo1和Piezo2调控骨形成和骨重塑的具体机制仍存在很多争议和困惑。

2 骨组织细胞机械敏感离子通道类型及功能

2.1 成骨细胞中机械敏感离子通道参与调控骨形成早期阶段

外界机械刺激可以通过机械敏感离子通道，将

细胞外力学信号转导为细胞内生物反应, 促进成骨细胞增殖和细胞外基质的分泌[33]。因此, 成骨细胞的机械敏感离子通道可能参与调控早期成骨细胞主导的骨形成阶段。成骨细胞中有多种TRP通道蛋白(如TRPML1、TRPM3、TRPV1、TRPA1、TRPV2和TRPV4等)表达。小鼠成骨细胞*TRPML1*被敲除后, 成骨细胞分化无明显的改变[34]。低强度牵拉成骨细胞后, Ca^{2+}可以通过TRPM3和TRPV4通道进而改变细胞内外Ca^{2+}浓度, 导致NF-Kb、RANKL和NFATc1活性增强, 骨吸收进程加快[35]。研究显示, 失去活性后的环氧合酶(cyclooxygenase, COX)可以通过TRPV4通道, 进而抑制成骨细胞分化, 而TRPV1、TRPA1通道则没有参与该过程[36]。然而另一项通过分别抑制成骨细胞中TRPV2和TRPV4通道的实验证明, 只有抑制TRPV2表达后钙内流才可被阻止, 而TRPV4通道被阻滞后细胞内外Ca^{2+}浓度无变化[37]。体外培养成骨细胞, 分别使用微重力和压应力刺激, 发现微重力环境抑制*Piezo1*表达, 成骨分化标志基因表达降低; 而压应力环境下*Piezo1*表达增加, 成骨分化能力增强; 敲除小鼠成骨细胞中*Piezo1*后骨形成被抑制, 骨量减少[38]。另一项研究同样证明了敲除成骨细胞中的*Piezo1*会导致骨量和骨强度降低[39]。

由此可见, 成骨细胞中的Piezo1对变化的机械负荷产生感知和响应; 而成骨细胞中TRPML1无机械敏感性, TRPV2和TRPM3可能具有机械敏感性, 研究最多的TRPV4的机械敏感性仍需要继续探究。

2.2 参与破骨细胞生成的机械敏感离子通道

多核的破骨细胞由巨噬细胞集落刺激因子(macrophage colony-stimulating factor, M-CSF)和RANKL诱导骨髓前体细胞分化而来。

前期研究表明, 破骨细胞中TRPC1、TRPV1、TRPV2、TRPV4和TRPV5参与调节细胞内外Ca^{2+}浓度[25,40-41]。当敲除*TRPV6*后, 股骨的破骨细胞数量增加, 股骨干骺端面积增加[42]。而*TRPC6*缺失将导致小鼠骨体积、骨小梁厚度降低和数量减少, 骨小梁面积升高和破骨数量增加; 同时体外实验表明, 外源性补充*TRPC3*后, 细胞内Ca^{2+}浓度增加, 减弱因*TRPC6*缺失对骨形成的影响, 但破骨细胞分化能力及骨吸收程度未发生显著改变[43]。当*TRPV1/TRPA1*被敲除后, 降钙素基因相关肽(calcitonin gene-related peptide, CGRP)表达降低, 抑制*Jdp2*转录和NF-kB活性, 延缓破骨细胞的成熟[44]。当敲除小鼠的*TRPML1*基因后, RANKL诱导的Ca^{2+}活动减弱, 成熟的破骨细胞分泌酸性磷酸酶(tartrate-resistant acid phosphatase, TRAP)能力减弱, 骨吸收减少, 骨硬度增加; 当敲除成骨细胞中的*TRPM3*和*TRPV4*基因时, 骨髓源性巨噬细胞的*NFATc1*和破骨细胞分化基因表达会降低, 从而导致骨吸收进程被抑制[34]。此外使用机械牵拉诱导单核巨噬细胞向破骨细胞分化时, Piezo1被激活并释放环氧化酶2(cyclooxygenase-2, COX2)和PGE2, 进而激活NF-κB信号通路, 加速破骨细胞的形成[45]。因此, 机械敏感离子通道TRPV6、TRPC6、TRPC3、TRPML1、TRPV1、TRPA1和Piezo1参与调控破骨细胞的生成, 增加骨吸收。

2.3 骨细胞相关机械刺激感受器

有研究发现, 骨细胞中*Caspase-9*和*Caspase-3*表达上调, 可激活MAPKs和Erk1/2信号通路, 进而增加*ATF4*的表达, 增加骨形成[46]; 而骨细胞中β-catenin和ERK入核水平增加, 可抑制骨细胞凋亡[47]; 骨细胞分泌的破骨因子参与调控破骨细胞的凋亡, 进而调节骨重建进程[48]; 而骨细胞中OPG/RANKL/RANK(receptor activator of nuclear factor κ)和Wnt/β-catenin信号等[49-52]也参与调控骨重建过程; 此外有研究表明, 骨细胞通过分泌骨硬化蛋白加速骨吸收速度, 进而降低骨量, 而骨细胞数量未发生改变[53], 因此有关骨细胞参与骨重建调控的问题, 仍需要进一步探究。

骨细胞对流体剪切力刺激产生最大的响应[8]。有研究发现流体剪切力可激活骨细胞TRPV4通道, 加速增加细胞内Ca^{2+}浓度, 进而激活钙调蛋白依赖性激酶II(calmodulin-dependent kinase II, CaMK II), 抑制硬化蛋白的分泌[54]; 此外也可激活骨细胞中的Piezo1通道, 使YAP1和TAZ活性增强, 抑制Wnt1的表达[39]。骨细胞被机械牵拉后, 细胞中的Piezo1-Akt信号通路被激活, 细胞内Ca^{2+}浓度升高, *Sost*表达降低, 骨吸收增加[55]。骨细胞中的*Piezo1*被敲除后, 导致骨细胞机械敏感性降低, 骨形成减少, 骨量丢失[39]。研究发现, 骨细胞中TRPV5和TRPV6均有分布, 但是其机械敏感性未被证明[56-57]。因此, TRPV4和Piezo1是骨细胞响应机械刺激的关键敏感离子通道。

因此综上所述, 不同细胞中机械敏感通道对骨代谢的影响各不相同, 其中成骨细胞中Piezo1参与调控机械负荷诱导骨生成阶段, 而TRPV2、TRPM3和TRPV4的机械敏感性还需要进一步探究; 破骨

细胞中的TRPV6、TRPC6、TRPC3、TRPML1、TRPV1、TRPA1和Piezo1参与调控破骨细胞的生成，增加骨吸收；骨细胞中TRPV4和Piezo1作为调控骨代谢平衡的关键敏感离子通道。

3 MSCs中的机械敏感离子通道

间充质干细胞(mesenchymal stem cells, MSCs)是一种具有特定分化潜能及自我更新能力的细胞，可分化为成骨细胞、脂肪细胞、软骨细胞等，受到生物学和再生医学的广泛关注[58-59]。有研究表明，适宜的机械刺激可促进MSCs向成骨分化的转录及翻译水平，进而促进其成骨分化[60-61]，但长时间的机械牵拉，导致BMSCs(bone mesenchymal stem cells, BMSCs)死亡增加[62]。目前发现，MSCs有多种机械敏感通道：TRPP3、TRPM8、TRPM7、TRPC6和Piezo1等，但是对MSC中机械转导的反应尚未完全阐明。

有研究指出，TRPP3和TRPM8在MSCs都有表达，参与调控线粒体功能[63]，此外，TRPM8也参与调控MSCs成骨分化进程[64]。另一项研究发现，膜电位参与调控BMSCs的细胞周期，进而改变BMSCs增殖的数量[65]。TRPM7对MSCs的功能调控至关重要，XIAO等[66]发现，TRPM7可直接感受细胞张力，促使Ca^{2+}通过TRPM7通道流入膜内，触发内质网上肌醇三磷酸受体2(inositol trisphosphate receptor type 2, IP3R2)释放Ca^{2+}，促进NFATc1核定位及成骨分化；而LIU等[67]对MSC施加1.2 pa流体剪切力，发现TRPM7诱导的Ca^{2+}内流增多，且Osterix表达升高，但Runx2无变化；此外BMSCs在向成骨分化过程中，*TRPM7*表达上调，细胞磷脂酶C(phospholipase C, PLC)被激活，*Smad1*表达增加，使成骨分化标志物表达上调[68]；也有学者提出在机械刺激下，TRPM可能通过双层脂质模型和细胞骨架模型两种途径介导Ca^{2+}动员后，诱导NFATc1等转录因子向细胞核移位，成骨基因表达增加，促进MSCs向成骨分化[69]。

使用流体静水压激活MSCs中的Piezo1通道，发现ERK1/2、P38和MAPK信号通路表达上调，*BMP2*和成骨分化因子(*Runx2*、*Osterix*、*ALP*和*COL1A1*)表达增加，进而促进成骨分化[70]；同时该研究也证明了Piezo1蛋白介导的机械力学转导，成脂分化进程被抑制[70]。牙髓干细胞中的Piezo1/2通过感受超声刺激，ERK1/2和MAPK信号通路被激活，促进牙髓干细胞成骨分化[71]。使用Yoda1激活MSCs的Piezo1通道后，下游的PYK2和MEK/ERK信号通路也被进一步激活，加速MSCs迁移速度[72]。因此，机械刺激通过TRPM7和Piezo1诱导MSCs增殖和成骨分化，进而加速骨形成早期进程。

4 机械敏感离子通道障碍引发的骨性疾病

机械敏感通道参与调控多种生理功能，异常表达则导致不同的骨性疾病[20]。常见的骨性异常疾病为特发性脊柱侧凸、远端关节紊乱、骨痛、骨骼发育障碍、骨微血管发育障碍、骨肿瘤、骨密度降低等。

目前，有关TRP通道蛋白异常的相关疾病研究较多。使用TRP代替骨巨细胞瘤细胞中组蛋白Gly34，肿瘤细胞RANKL分泌增加，破骨细胞前体细胞招募增多，且向破骨细胞分化增加，骨吸收增加[73]。机体缺乏*TRPV1/TRPA1*时，骨骼中疼痛增加，并伴有多核破骨细胞数量增多，真菌性骨髓炎炎症反应增强[44]。分析骨髓瘤患者的骨髓微环境，发现其中Ca^{2+}浓度升高，破骨分化途径(TRPV2-钙调磷酸酶-NFAT信号通路-RANKL)表达增强，导致破骨细胞分化增加，骨溶现象进一步加重[74]。此外，通过分析骨密度降低的患者发现，老年性骨密度降低患者破骨细胞前体细胞中*TRPC3*表达上调[43]；成骨细胞和破骨细胞的*TRPV4*基因发生缺失后导致骨量降低或骨骼发育不全，当TRPV4通道活化后，*SOX9*转录水平增加，进而促进软骨形成[75]；然而通过分析动脉粥样硬化并发骨质疏松症患者的成骨细胞，发现Ca^{2+}通过TRPV2而非TRPV4进入细胞，引起溶血性磷脂酰胆碱毒性增强，导致成骨细胞凋亡，骨形成减少[37]。Piezo蛋白也参与调控骨性疾病的发生：*Piezo2*基因发生突变后将导致关节、眼肌、肺功能和骨骼发育障碍，诱发远端关节紊乱[76]；此外，通过机械拉伸激活Piezo1通道，可以促进血管分支的形成和血管的稳定，进而预防骨微血管异常[77]。此外有研究发现，敲除小鼠*Sost*后，小鼠颅骨再生速度加快，β-catenin表达上调，但BMP信号蛋白表达未发生改变[78]。

TRPV4作为一种关键的调节开关可调节骨代谢稳态，一旦骨代谢稳态遭到破坏，将导致骨吸收或者骨形成进程障碍。TRPC3通道异常促进骨吸收，导致骨密度降低，TRPV1/TRPA1促进破骨细胞增殖，加剧骨髓炎症。TRPV2和Piezo1可能通过调控成骨细胞凋亡，调节血液毒性和血管的分支情况，进而调节骨形成。因此，机械敏感通道蛋白参与维持骨代

谢稳态, 进而预防骨代谢稳态紊乱疾病的发生。

5 总结和展望

骨代谢相关的细胞为成骨细胞、破骨细胞、骨细胞、破骨前体细胞和间充质干细胞等。间充质干细胞可诱导分化为成骨细胞, 调控骨形成早期阶段, 成骨细胞进一步成熟后形成骨细胞。破骨细胞及破骨前体细胞参与调控骨吸收进程。流体剪切力、压应力、牵拉力、重力等机械刺激影响骨代谢平衡, 进而改变骨量和骨强度。通过综述相关文献发现, 骨代谢的机械敏感离子通道多数为TRP和Piezo通道蛋白(表1), 并根据这些文献整理了骨代谢相关的Piezo1和TRP家族的部分离子通道蛋白参与的细胞内机械转导途径(图1)。成骨细胞分布的机械敏感离子通道有: Piezo1、TRPM3、TRPV4、TRPV2和TRPML1; 破骨细胞分布的机械敏感离子通道有: TRPV6、TRPV1和TRPA1; Piezo1、TRPC3和TRPC6; 骨细胞中分布有TRPV4和Piezo1机械敏感离子通道; TRPM7、Piezo1和Piezo2分布在MSCs。机械刺激通过这些离子通道改变胞内的Ca^{2+}浓度, 调控下游效应因子(RANKL、NFATc1、NF-kB、Sost等), 进而调控骨代谢相关信号通路(BMP、MAPK和Wnt/β-catenin等)。此外, 研究发现机械敏感离子通道异常与多种骨性疾病发生有关: TRPC3、TRPV4和TRPV2可能与骨量减少有关, Piezo1可能与维持正常的骨微血管有关, Piezo2的异常表达将会导致远端关节紊乱, TRPV1和TRPA1与骨髓炎症痛觉相关。综上所述, 多种骨性疾病可能是由于机械敏感离子通道异常表达后, 导致的骨代谢平衡失调造成。因此, 对机械敏感离子通道调控骨代谢的

表1 多种骨代谢相关的机械敏感离子通道类型和功能

Table 1 Various types and functions of mechanically sensitive ion channels related to bone metabolism

细胞 Cell	机械敏感离子通道 Mechanically sensitive ion channel	信号途径 Signaling pathway	干预 Intervention	影响 Functional	参考文献 References
Osteoblast	Piezo1	Piezo1-YAP1/TAZ-Wnt	Microgravity/ compressive	Expression of osteogenic differentiation factor	[38]
Osteoblast	Piezo1	Unclear	Knockout	Bone mass and bone strength	[39]
Osteoblast	TRPM3/TRPV4	TRPV4-Ca^{2+}-NF-κb,RANKL, NFATc1	Stress	Accelerates bone resorption	[35]
Osteoblast	TRPV4	NOX2/ROS-TRPV4-Ca^{2+} -CaMKII	FSS	Inhibits osteogenic differentiation	[36]
Osteoblast	TRPV2	TRPV2-Ca^{2+}	Antagonists of TRPV2 and TRPV4	Inhibition of Ca^{2+} flow	[37]
Osteoblast	TRPML1	Unclear	Knockout	No change	[34]
Osteoclast	TRPV6	Unclear	Knockout	The number of osteoclasts increases and the area of metaphysis increases	[42]
Osteoclast	TRPV1/TRPA1	TRPV1/TRPA1-CGRP-Jdp2-NF-κB	Knockout	Inhibits osteoclast maturation	[44]
Pro-Osteoclast	Piezo1	Piezo1-COX2-PGE2- NF-κB	Stress	Accelerates osteoclast differentiation	[45]
Pro-Osteoclast	TRPC	TRPC3/TRPC6 -Ca^{2+}-NF-κB, RANKL, NFATc1	Silent TRPC6 Expression	Promotes osteoclast differentiation and bone resorption activity	[43]
Osteocyte	TRPV4	TRPV4-Ca^{2+}-CaMK II	FSS	Inhibits sclerosin formation	[54]
Osteocyte	Piezo1	Piezo1-Akt-Sost	Stress	Regulation of bone remodeling	[55]
Osteocyte	Piezo1	Piezo1-YAP1/TAZ-Wnt	Compressive stress	Promotes osteogenic differentiation	[38]
MSCs	TRPM7	TRPM7-Ca^{2+}-IP3R2-Ca^{2+} -NFATc1	Stress	Promotes osteogenic differentiation	[66]
MSCs	TRPM7	TRPM7-Ca^{2+}-PLC -Smad-Osterix	FSS	Promotes osteogenic differentiation	[67-68]
MSCs	Piezo1	Piezo1- ERK1/2, P38, MAPK- BMP2-Runx2, Osterix- ALP, COL1A1	FSS	Promotes osteogenic differentiation	[79]
MSCs	Piezo1	Piezo1-BMP2	Mechanical force	Promotes osteogenic differentiation and inhibitory adipogenic differentiation	[70]
MSCs	Piezo1	Yoda1- Piezo1-PYK2, MEK/ERK	Agonists Yoda1	Facilitates migration of MSCs	[72]
Pulp stem cells	Piezo1/2	Piezo1/2-ERK1/2, MAPK	Ultrasonic	Promotes osteogenic differentiation	[71]

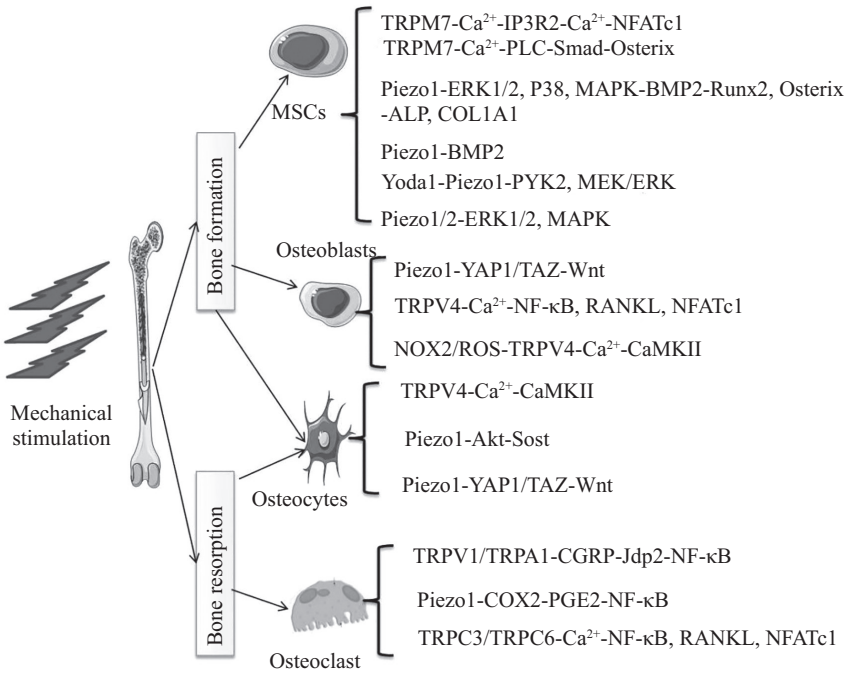

图1 骨代谢相关的Piezol和TRP家族的离子通道蛋白参与的细胞内机械转导途径

Fig.1 Bone metabolism-related ion channel proteins of the Piezol and TRP families are involved in intracellular mechanical transduction pathways

机制仍需要进一步的探究和挖掘, 其有望为治疗多种骨性疾病提供确切的治疗靶点和方法。

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