

Title	Effects of single or combination therapy of teriparatide and anti-RANKL monoclonal antibody on bone defect regeneration in mice
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論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

Teriparatide (TPTD) と抗RANKL抗体の併用療法による骨再生 (海綿骨、皮質骨) への効果を検討した。マウスの大腿骨骨幹部 (皮質骨再生) と骨幹端部 (海綿骨再生) に骨欠損を作成し、(1)対象群 (C群) : 生理食塩水、(2)TPTD群(T群) : TPTD、(3)Ab群 : OYC-1、(4)併用群 (COMB群) : TPTD + OYC-1の4群に分けて検討した。術後 μ CTによる再生骨量と骨密度の評価、再生骨部の組織学的評価と力学試験を行った。海綿骨の再生骨量は、骨形成初期にCOMB群が他3群と比較し有意に増加した。一方、皮質骨の再生骨量はCOMB群で、Ab群より有意に再生骨量が増加したがT群と同程度であった。組織学的検討ではCOMB群で層板骨形成の遷延を認めたが、力学試験では強度低下は認めなかった。骨密度は、COMB群で他の3群と比較し有意に骨密度が増加した。TPTDと抗RANKL抗体の併用療法は、骨量増加と海綿骨再生を促進するが皮質骨には同様の効果を認めなかった。骨粗鬆症による骨折は、椎体や骨幹端部など海綿骨の多い部位であり、併用療法が有効となる可能性が示唆された。

論 文 内 容 の 要 旨
Synopsis of Thesis

氏 名 Name	北口 和真
論文題名 Title	Effects of single or combination therapy of teriparatide and anti-RANKL monoclonal antibody on bone defect regeneration in mice (マウスの骨欠損部骨再生に対するテリパラチドと抗RANKL抗体の単剤と併用療法による効果)
論文内容の要旨	
〔目的(Purpose)〕	
<p>The purpose of this study is to investigate the effects of a single or combination therapy of teriparatide (TPTD) and anti-RANKL Ab (anti-murine receptor activator of nuclear factor κB ligand monoclonal antibody) on the regeneration of both cancellous and cortical bone.</p>	
〔方法ならびに成績(Methods/Results)〕	
<p>Methods: Nine-week-old mice underwent bone defect surgery on the left femoral metaphysis (cancellous-bone healing model) and right femoral mid-diaphysis (cortical-bone healing model). After surgery, the mice were assigned to 1 of 4 groups to receive 1) saline (5 times a week; CNT group), 2) TPTD (40 μg/kg 5 times a week; TPTD group), 3) anti-RANKL Ab (5 mg/kg once; Ab group), or 4) a combination of TPTD and anti-RANKL Ab (COMB group). The following analyses were performed: Time-course microstructural analysis of healing in both cancellous and cortical bone in the bone defect, the volumetric bone mineral density of the tibia with micro-computed tomography, histological, histomorphometrical, and biomechanical analysis of regenerated bone.</p>	
<p>Results: Regeneration of cancellous bone volume in the COMB group was the highest among the 4 groups, and this combined administration prompted medullary callus formation in the early phase of bone regeneration. On the other hand, regeneration of cortical bone volume in the COMB group was significantly higher than in the Ab group and was almost same as in the TPTD group. Histological analysis showed remaining woven bones, cartilage matrix, and immature lamellar bone in the COMB and Ab groups. However, biomechanical analysis showed that hardness and Young's modulus of regenerated cortical bone in the COMB group was not lower than in both the CNT and TPTD groups. Volumetric bone mineral density in the tibia was significantly increased in the COMB group compared with the other 3 groups.</p>	
〔総括(Conclusion)〕	
<p>In the early phase of bone regeneration, the combination of TPTD and anti-RANKL Ab accelerates regeneration of cancellous bone in bone defects and increases cancellous bone mass in the tibia more effectively than either agent does individually, but these additive effects are not observed in the regeneration of cortical bone.</p>	