国際セッション口演

（C会場）

5月30日（土） C会場  9：00～10：20
Autophagy promotes MSC-mediated vascularization in cutaneous wound healing via regulation of VEGF secretion

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Keywords: MSCs, autophagy, paracrine, VEGF

Vascularization deficiency caused a lot of diseases, such as diabetes ulcer and myocardial infarction. Mesenchymal stem cells (MSCs), with the self-renewal and multipotent differentiation capacities, have been used for many diseases treatment through regulation microenvironment. Numerous studies reported that MSCs transplantation could largely improve cutaneous wound healing via paracrine secretion of growth factors. However, whether MSCs take part in the angiogenesis process directly remains elusive. Previous study proved that autophagy inhibited immunosuppressive function of MSCs and prevented the degradation of MSCs function in inflammatory and senescent microenvironment. Here, we proved that autophagy determines the therapeutic effect of MSCs in cutaneous wound healing through promoting endothelial cells angiogenesis and demonstrated that the paracrine of vascular endothelial growth factor (VEGF) in MSCs was required in wound site. We further revealed that autophagy enhanced the VEGF secretion from MSCs through ERK phosphorylation directly. Collectively, we put forward that autophagy-mediated paracrine of VEGF plays a central role in MSCs cured cutaneous wound healing and may provide a new therapeutic method for angiogenesis-related diseases.
Methods

Keywords: periodontal ligament cell, Peroxisome proliferator-activated receptor gamma, Hard-tissue formation

Background: Peroxisome proliferator-activated receptor γ (PPARG) is known as a key nuclear receptor for adipocyte differentiation and glucose homeostasis. Many researches illustrate that PPARG acts as an inhibitor of osteogenesis. However, neither functions of PPARG in periodontal tissue homeostasis nor periodontal ligament (PDL) cell differentiation have been investigated. In this study we focus on investigating the effects of PPARG for periodontal homeostasis and regeneration.

Methods: 1) PDL cells were transected with PPARG specific siRNA then cultured with mineralization medium. 2) PDL cells were cultured in mineralization medium with thiazolidines, PPARG exogenous activator or inhibitors of lipooxygenase (an endogenous enzyme catalyzing the synthesis of PPARG endogenous ligands, which have ability to bind allosteric side of PPARG). Cell differentiation ability was reflected by Alkaline activity and Alizarin red staining. 3) Paraffin sections of mice maxillula molars and surrounding periodontal tissue were used for hematoxylin and eosin (HE) staining or performed immunohistochemistry (IHC) with anti-PPARG and anti-phospho-PPARG.

Results: 1) Inhibition of PPARG resulted in suppressed differentiation of PDL cell in contrast to MSC cells in which osteogenic ability was increased. 2) Thiazolidines showed variety effects on PDL cell differentiation, mineralization and proliferation. The inhibitors of lipooxygenase significantly suppressed PDL cell differentiation. 3) PPARG and phospho-PPARG were identified in PDL cell by IHC.

Conclusion: PPARG is critical for PDL cell differentiation for hard-tissue forming cells. Endogenous ligands binding to allosteric site of PPARG may shift PPARG regulated-transcription during PDL cell differentiation.

Long-term follow-up of successful therapeutic measures for a peri-implantitis patient with a history of generalized chronic periodontitis: A case report

Eiji Ichimaru

Keywords: peri-implantitis, implant therapy, risk factor, long term follow up, successful therapy

Introduction: The aim of this case report is to assess therapeutic measures of peri-implantitis in the long term.

Case Presentation: 62 years old, female patient with generalized chronic periodontitis (stage 3, grade B) received regular implant therapy, including placement at 47, 46, 44, 35 and 37 sites and inter-prostheses with cementation and definitive prostheses with screw retention, after periodontitis was stabilized with periodontal initial therapy. Supportive periodontal and implant therapy (SPIT) was then initiated. Peri-implantitis was developed in 47, 46 and 37 sites two years after the initiation. Since she was periodontally healthy at that time, preventive measures were continued. Therapies for peri-implantitis were performed: reinforcing self-oral hygiene measure, nonsurgical debridement for implant, removing residual luting cement, modifying prosthesis to improve hygiene and resective surgery. SPIT was then resumed. Peri-implant inflammatory symptoms improved. The progressive bone loss has ceased, with some recovery, at 47, 46 and 37 sites, for 4 years and 7 months after SPIT had resumed, although small amount of suppuration/exudate was occasionally observed at 37.

Conclusion: Those consecutive therapies to reduce risk factors were effective to resolve peri-implantitis. Small amount of suppuration/exudate observed even after ceasing progressive bone loss indicated that the goal for therapy of peri-implantitis should be established with definitive diagnostic criteria.