ADAMTSL4 improves microfibril of Marfan syndrome derived cells

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Abstract

Marfan syndrome (MFS) is a systemic disorder affecting connective tissues that is caused by mutations of the FBN1 gene encoding fibrillin-1, a major microfibril component. Prior observation suggested that MFS is associated with increasing susceptibility to severe periodontitis which associated with irreversible damage of periodontal ligament (PDL). However, the molecular mechanisms of microfibrils assembly in PDL formation remain largely unknown. Here, we report that ADAMTSL-4β, a novel microfibril binding protein, not only promotes fibrillin-1 microfibril assembly in PDL but also improves microfibril disorganization in cultured PDL cells obtained from MFS patient (M-HPDL). Expression patterning analysis revealed that adamtls1/4β mRNA is strongly expressed in the dental follicle, the origin of the PDL, and ADAMTSL-4β protein is colocalized with the fibrillin-1 microfibril in the course of microfibril maturation during PDL development. In contrast, mice homozygous for a targeted hypomorphic allele (mgR1mgR) of FbnI, which served as a mice model of MFS, showed disorganization of PDL in association with progressive fragmentation of ADAMTSL-4β microfibrils. M-HPDL able to form insufficient fibrillin-1 microfibril, nevertheless overexpression of ADAMTSL-4β in M-HPDL markedly improved fibrillin-1 microfibril assembly. Our results suggest that ADAMTSL-4β regulates microfibril assembly of fibrillin-1 during PDL development, and could be a novel therapeutic target for the damaged PDL tissue in patients with MFS.

Workshop I-B

Optimal Spaces for Bone Regeneration created by artificial ECM of Titanium Web

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Objective: To create a new dental implant system with biologically self-curing ability, we aimed improvement from the conventional 2-D bone-titanium connection into 3-D one, by which the osteoblast activity is able to extend into the spaces created by 3-D collaboration zone of fibrous titanium and active bone tissue.

Methods: The new device is composed of a titanium web layer of about 1 mm thickness that was vacuum-sintered with the rod of titanium bulk, named TWT (titanium web–equipped titanium rod). The web is an unwoven 3-D fibrous structure made of thin titanium fibers, whose cross-sections are square form of 50 microns in side. The web structure was designed to create the optimal spaces for bone ingrowth. Artificial roots of tooth of TWT (4 x 8 mm) were implanted into the created sockets of premolars region of Beagle mandibles, 2 months after the tooth extraction. As a control, commercial artificial roots (Astra Tech Co., USA, 8 mm in length and 4 mm) were implanted.

Results: After 20, 32 and 80 weeks, histological observations revealed that the bone ingrowth into web layers started at 20 weeks, and completed at 80 weeks, in the every areas where bone tissue contacted to the TWT implants.

Conclusions: TWT works as 3D living connection between bone and implants.