

Potential etiology of peri-implantitis and improved epithelial adhesion

Hidemitsu Harada¹, Shojiro Ikezaki¹, Shindo Yoshiko^{1,2}, Yuma Kido^{1,2}, Kae Kakura², Keishi Otsu¹, Hirofumi Kido

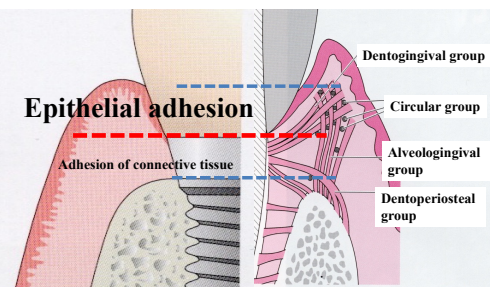
1. Division of Developmental Biology & Regenerative Medicine, Department of Anatomy, Iwate Medical University, Japan

2. Section of Oral Implantology, Department of Oral Rehabilitation, Fukuoka Dental College, Japan



Purpose and Background

Difference between Implant and periodontium

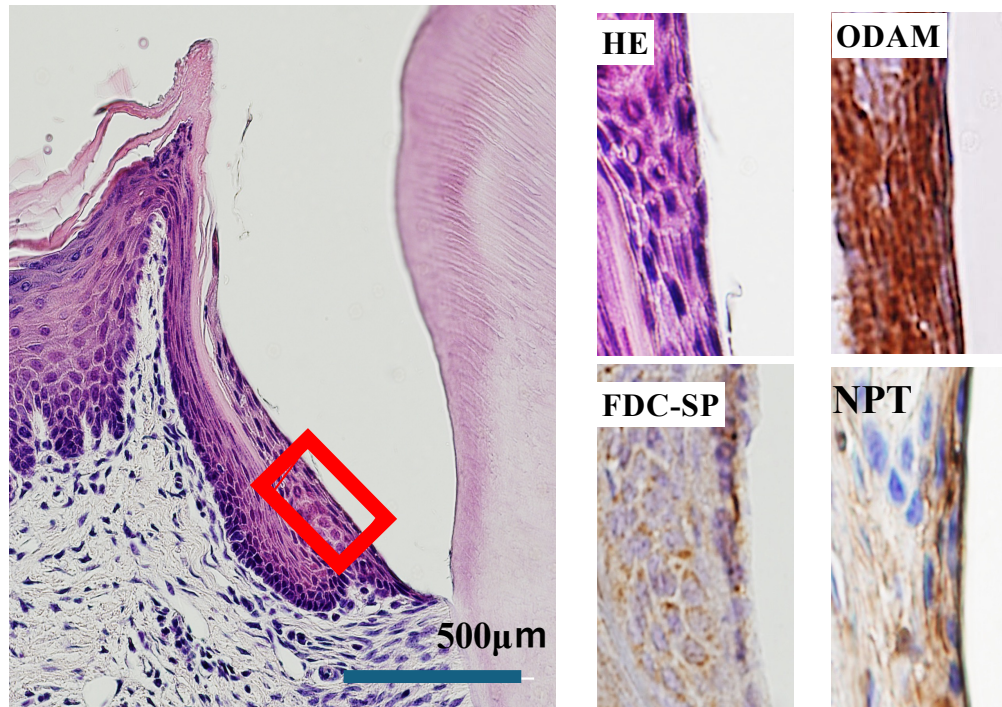


One of the reasons for the incidence of peri-implantitis may be the poor adhesion of the surrounding epithelial cells to the titanium. Insufficient sealing by adhesion between the epithelium and titanium can lead to bacterial infection. Accordingly, we developed junctional epithelial (JE) and gingival epithelial (GE) cell lines, and investigated the difference in adhesion to hydroxyapatite and titanium between JE and GE. Finally, we examined the effect of JE secretion protein on the adhesion of GE cells against titanium.

Materials and Methods

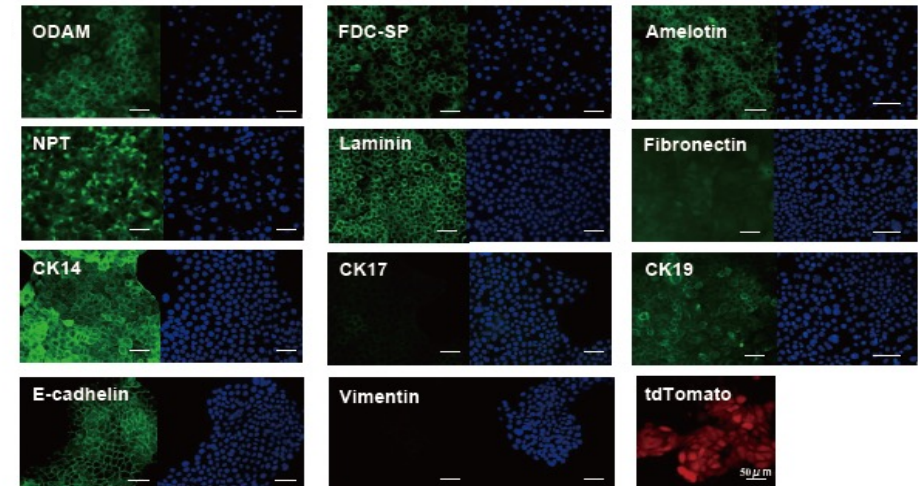
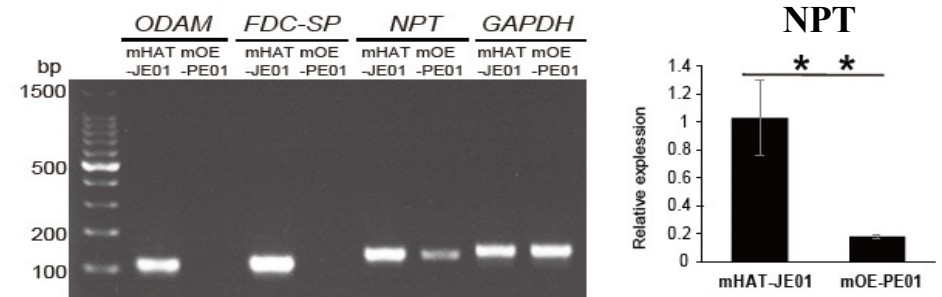
- Establishment cell lines; mHAT-JE01 cells: The cells were derived from labial cervical loop cells of mouse mandibular incisor germ at PN4d and differentiated into JE cells under apatite coated plate. OE-PE01 cells: the cells were originated from gingival and palatal epithelial cells (K14cre/tdTomato mice) (PN3d). (Ikezaki et al., J Oral Biosci. 2023 Mar;65(1):47-54.)
- Immunostaining; 4% PFA fixed tissue and cells were prepared and immuno-stained by the antibodies of JE marker proteins.
- Gene expression profiling; Expression of JE marker molecules were confirmed by RT-qPCR and immunohistochemistry.
- Cell adhesion assay; 1500/10 μ l cells were seeded on the apatite and titanium disk/plate, and after 1h were washed by culture medium.
- Data are expressed as means $\pm$ SD. * $p < 0.05$. ** $p < 0.01$.

Results 1



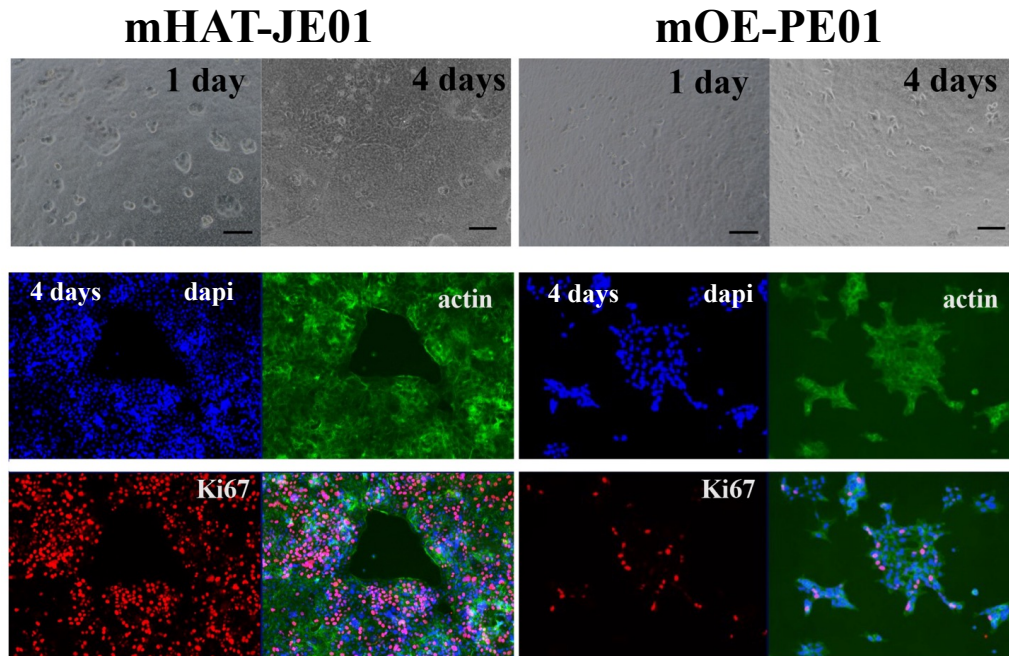
JE secretes enamel specific proteins (ODAM; odontogenic ameloblast-associated protein, FDC-SP; follicular dendritic cell secreted protein, NPT nephronectin) on the surface of enamel, because they are derived from the enamel epithelium. These proteins, called sibling proteins, have the ability to adhere to apatite and bind integrins. JE is thought to use these proteins to adhere to enamel, but loss of these protein may reduce adhesion to enamel.

Results 2



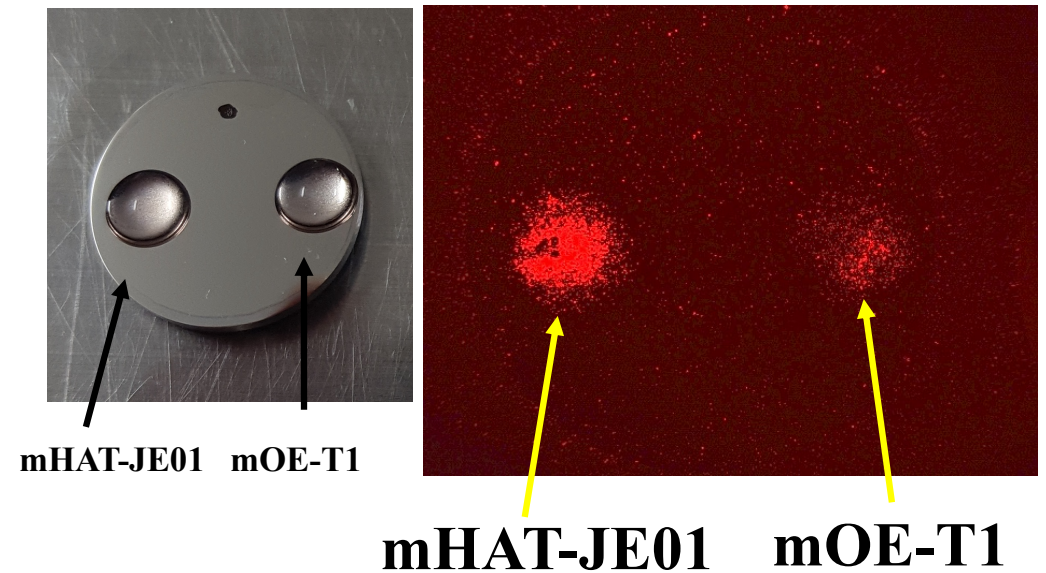
JE cell line (mHAT-JE01) secretes enamel proteins (ODAM and FDC-SP). These proteins are not expressed in GE cell line (mOE-PE01). mHAT-JE01 is thought to use these proteins to adhere to enamel.

Results 3



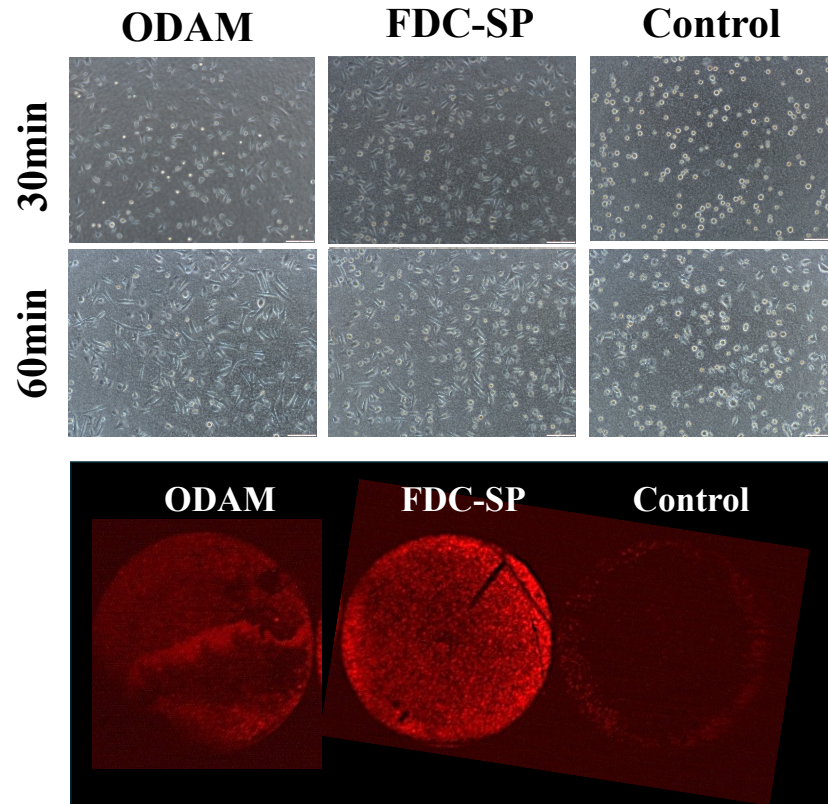
The cells were seeded on apatite-coated plates on days 1 and 4. mHAT-JE01 has higher initial adhesion and proliferates more actively than mOE-PE01.

Results 4



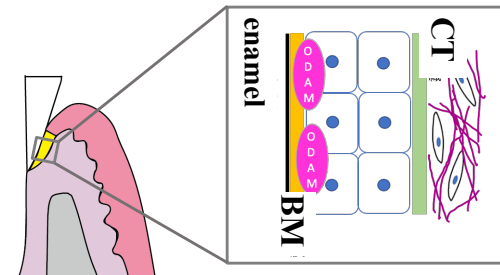
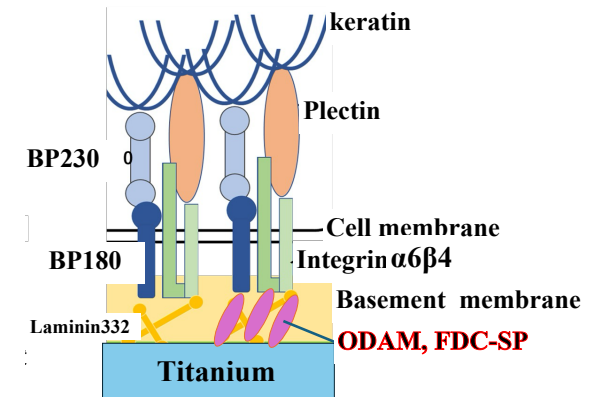
HAT-JE01 and mOE-T1 were seeded and washed 1 hr later. mHAT-JE01 had higher adhesion ability to titanium than mOE-T1

Results 5



The effects of ODAM and FDC-SP on the initial adhesion of mOE-T1 were examined. Coating apatite plates with ODAM and FDC-SP significantly improved cell adhesion and cell elongation after adhesion. In addition, when titanium discs were coated with these proteins, they showed higher adhesion.

Discussion



JE adheres to hydroxyapatite (enamel) via the sibling proteins ODAM and FDC-SP. Sibling proteins are known to adhere not only to apatite but also to titanium. However, because titanium implants have already lost their junctional epithelium, the peri-implant epithelium has a reduced ability to adhere to titanium. We speculate that this reduced adhesion is one of the etiological causes of peri-implantitis, and that coating titanium surface with ODAM or FDC-SP improves the epithelial cell adhesion. Therefore, ODAM and FDC-SP have potential as prophylactic or therapeutic agents for peri-implantitis.