The salivary peptide histatin-1 promotes endothelial cell adhesion, migration, and angiogenesis

Por: Torres, P (Torres, Pedro)[1]; Diaz, J (Diaz, Jorge)[2]; Arce, M (Arce, Maximiliano)[2,4,5]; Silva, P (Silva, Patricio)[1,7]; Mendoza, P (Mendoza, Pablo)[1]; Lois, P (Lois, Pablo)[3]; Molina-Berrios, A (Molina-Berrios, Alfredo)[1]; Owen, GI (Owen, Gareth I.)[2,4,5,6]; Palma, V (Palma, Veronica)[3]; Torres, VA (Torres, Vicente A.)[1,2]

FASEB JOURNAL
Volumen: 31
Número: 11
Páginas: 4946-4958
DOI: 10.1096/fj.201700085R
Fecha de publicación: NOV 2017
Tipo de documento: Article
Ver impacto de la revista

Resumen

Saliva is a key factor that contributes to the high efficiency of wound healing in the oral mucosa. This is not only attributed to physical cues but also to the presence of specific peptides in the saliva, such as histatins. Histatin-1 is a 38 aa antimicrobial peptide, highly enriched in human saliva, which has been previously reported to promote the migration of oral keratinocytes and fibroblasts in vitro. However, the participation of histatin-1 in other crucial events required for wound healing, such as angiogenesis, is unknown. Here we demonstrate that histatin-1 promotes angiogenesis, as shown in vivo, using the chick chorioallantoic membrane model, and by an in vitro tube formation assay, using both human primary cultured endothelial cells (HUVECs) and the EA. hy926 cell line. Specifically, histatin-1 promoted endothelial cell adhesion and spreading onto fibronectin, as well as endothelial cell migration in the wound closure and Boyden chamber assays. These actions required the activation of the Ras and Rab interactor 2 (RIN2)/Rab5/Rac1 signaling axis, as histatin-1 increased the recruitment of RIN2, a Rab5-guanine nucleotide exchange factor (GEF) to early endosomes, leading to sequential Rab5/Rac1 activation. Accordingly, interfering with either Rab5 or Rac1 activities prevented histatin-1-dependent endothelial cell migration. Finally, by immunodepletion assays, we showed that salivary histatin-1 is required for the promigratory effects of saliva on endothelial cells. In conclusion, we report that salivary histatin-1 is a novel proangiogenic factor that may contribute to oral wound healing.-Torres, P., Diaz, J., Arce, M., Silva, P., Mendoza, P., Lois, P., Molina-Berrios, A., Owen, G. I., Palma, V., Torres, V. A. The salivary peptide histatin-1 promotes endothelial cell adhesion, migration, and angiogénesis.

Palabras clave

Palabras clave de autor:signaling; GTPase; saliva; Rab5; wound healing
KeyWords Plus:WOUND-HEALING PROPERTIES; HUMAN-PAROTID SECRETION; RICH PROTEINS; GROWTH-FACTOR; RAC; MORPHOGENESIS; MUCOSAL; CLOSURE; RAB5

Información del autor

Dirección para petición de copias: Torres, VA (autor para petición de copias)

+ Univ Chile, Fac Dent, Inst Res Dent Sci, Calle Sergio Livingstone 943, Santiago 8380492, Chile.

Direcciones:

+ [1] Univ Chile, Fac Dent, Inst Res Dent Sci, Calle Sergio Livingstone 943, Santiago 8380492, Chile
+ [2] Univ Chile, Adv Ctr Chron Dis ACCDiS, Santiago, Chile
+ [3] Univ Chile, Fac Sci, Lab Stem Cells & Dev Biol, Santiago, Chile
+ [4] Pontificia Univ Catolica Chile, Fac Biol Sci, Santiago, Chile
+ [5] Pontificia Univ Catolica Chile, Fac Med, Santiago, Chile
+ [6] Pontificia Univ Catolica Chile, Millennium Inst Immunol & Immunotherapy, Santiago, Chile
+ [7] Univ Cent Chile, Fac Hlth Sci, Santiago, Chile

Direcciones de correo electrónico:vatorres@med.uchile.cl

Financiación

Entidad financiadora	Número de concesión
Fondo Nacional de Desarrollo Cientifico y Tecnologico (FONDECYT)	1140907 1140970 1140697 11140227
Comision Nacional de Investigacion Cientifica y Tecnologica-Fondo de Financiamiento de Centros de Investigacion en Areas Prioritarias (CONICYT-FONDAP)	15130011
Fondo de Fomento al Desarrollo Cientifico y Tecnologico (Fondef)	D09E1047
Biomedical Research Consortium of Chile (BMRC)	13CTI-21526-P6
Instituto Milenio en Inmunologia e Inmunoterapia (IMII)	P09/016-F

Ver texto de financiación

Editorial

FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA

Información de la revista

- **Impact Factor:** Journal Citation Reports

Categorías / Clasificación

Áreas de investigación: Biochemistry & Molecular Biology; Life Sciences & Biomedicine - Other Topics; Cell Biology

Categorías de Web of Science: Biochemistry & Molecular Biology; Biology; Cell Biology

Información del documento

Idioma: English

Número de acceso: WOS:000413398500025

ID de PubMed: 28751526

ISSN: 0892-6638

eISSN: 1530-6860