Heterogeneity of Human Gingival Fibroblasts in Tobacco-stimulated Collagen Degradation

W. ZHANG,* M. FANG, F. SONG and L. J. WINDSOR

Department of Oral Biology, Indiana University School of Dentistry

Indiana University – Purdue University Indianapolis

Abstract

Matrix metalloproteinases (MMPs) are a large family of zinc-dependent endopeptidases and their activity is modulated by tissue inhibitors of metalloproteinases (TIMPs). Smoking is a risk factor for periodontal disease. Cigarette smoke condensate (CSC) is the particulate matter of cigarette smoke. Human gingival fibroblasts (HGFs) are one of major cellular components in periodontal tissue. CSC can increase collagen degradation of HGFs by enhancing and altering the localization of MMPs. Previous clinical studies also showed that some smoking people even with very high dental plaque index still had good periodontal status and did not develop periodontal disease. Objectives: The aim of this study was to investigate the heterogeneity of HGFs to CSC-stimulated collagen degradation and to start examining its mechanisms. Methods: Eleven HGF cell lines were established from healthy gingival tissue from patients undergoing crown-lengthening surgery. HGFs were seeded as single colony (75,000 cells/well) in 6-well Type I collagen coated plates and exposed to 100 µg/ml CSC (Murty Pharmaceuticals, Lexington, KY) diluted in serum-free media with/without a MMPs inhibitor (GM6001, 100 nM, Chemicon, Temecla, CA) for 3 days. HGFs were seeded with serum free media alone as controls. The mRNA levels of multiple MMPs/TIMPs were measured by reverse transcription-polymerase chain reaction. Results: CSC increased collagen degradation in 7 HGF cell lines (CSC-susceptible HGFs), but not in 4 HGF cell lines (CSC-unsusceptible HGFs). GM6001 inhibited CSC-stimulated collagen degradation in all of CSC-susceptible HGFs. The mRNA levels of MMP-1, MMP-2, MMP-3, MMP-14, TIMP-1, and TIMP-2 increased 2.5, 1.3, 3.9, 2.0, 1.6, and 1.3 fold, respectively, in the CSC-susceptible HGFs. However, expression of MMPs/TIMPs basically didn't change in the CSC-unsusceptible HGFs, except for MMP-3 which increased 1.4 fold. Conclusions: Heterogeneity of HGFs existed in regard to the CSC-stimulated collagen degradation and the altered expression of the MMPs/TIMPs may be responsible for this heterogeneity. This project was supported by the IUPUI Tobacco Cessation and Biobehavioral Center.