Porphyromonas gingivalis Fimbriae-Dependent Activation of Inflammatory Genes in Human Aortic Endothelial Cells

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Abstract

Epidemiological and pathological studies have suggested that infection with the oral pathogen Porphyromonas gingivalis can potentiate atherosclerosis and human coronary heart disease. Furthermore, infection with invasive, but not noninvasive P. gingivalis has been demonstrated to accelerate atherosclerosis in apolipoprotein E-deficient (ApoE(-/-)) mice and to accelerate local inflammatory responses in aortic tissue. In the present study, using high-density oligonucleotide microarrays, we have defined the gene expression profile of human aortic endothelial cells (HAEC) after infection with invasive and noninvasive P. gingivalis. After infection of HAEC with invasive P. gingivalis strain 381, we observed the upregulation of 68 genes. Genes coding for the cytokines Gro2 and Gro3; the adhesion molecules intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule (VCAM)-1, and ELAM-1 (E-selectin); the chemokine interleukin-8 (IL-8); and the proinflammatory molecules IL-6 and cyclooxygenase-2 were among the most highly upregulated genes in P. gingivalis 381-infected HAEC compared to uninfected HAEC control. Increased mRNA levels for signaling molecules, transcriptional regulators, and cell surface receptors were also observed. Of note, only 4 of these 68 genes were also upregulated in HAEC infected with the noninvasive P. gingivalis fimA mutant. Reverse transcription-PCR, enzyme-linked immunosorbent assay, and fluorescence-activated cell sorting analysis confirmed the expression of ICAM-1, VCAM-1, E-/P-selectins, IL-6, and IL-8 in HAEC infected with invasive P. gingivalis. We also demonstrated that increased expression of ICAM-1 and VCAM-1 in aortic tissue of ApoE(-/-) mice orally challenged with invasive P. gingivalis but not with the noninvasive P. gingivalis fimA mutant by immunohistochemical analysis. Taken together, these results demonstrate that P. gingivalis fimbria-mediated invasion upregulates inflammatory gene expression in HAEC and in aortic tissue and indicates that invasive P. gingivalis infection accelerates inflammatory responses directly in the aorta.