Role of *Fusobacterium nucleatum* and Multispecies Interactions in Endothelial Damage

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Abstract

Objectives: Periodontal pathogens and their virulence factors are linked with endothelial damage. Most research has focused on the oral pathogen *P.gingivalis (Pg)*, at the exclusion of other microorganisms identified in the circulation and atherosclerotic plaques, including *Fusobacterium nucleatum (Fn)* and *Tanerella forsythia (Tf)*. Here we use *in vitro* endothelial monolayer cultures and a zebrafish systemic infection model to identify mechanisms of bacterial-induced vascular damage.

Methods: Platelet-endothelial cell adhesion molecule-1 (PECAM-1) cell surface abundance and permeability of endothelial monolayers infected with wild-type *Pg* (W83 or gingipain-deficient mutant ΔK/R-ab), *Fn* or *Tf* as single and multispecies cultures were assessed by flow cytometry and dextran assay, respectively. Systemic effects of *Fn* were assessed using zebrafish embryos following systemic injection.

Results: In single species infections, W83 *Pg* and *Fn* induced a decrease in PECAM-1 abundance and an increase in endothelium permeability. In multispecies infections, PECAM-1 reduction and increased endothelium permeability were mediated by *Fn,* but not *Tf,* in both single and mixed species infection.

Conclusion: These data implicate *Pg* and *Fn* but not *Tf* in mediating disturbance of endothelium integrity through decreased PECAM-1 expression and highlight the need for further research on the role of *Fn* and multispecies interactions in cardiovascular disease.