Bacterial Challenge Shifts E-Cadherin Localization and Compromises Gingival Barrier Integrity

Noor Fatima[1]; Styliani Alimperti[2]; Hamideh Afzali[1]; Yu Jung Heo[1]; and Dana T. Graves[1]

[1]University of Pennsylvania, School of Dental Medicine, Department of Periodontics, Philadelphia, Pennsylvania, United States.
[2]Georgetown University, Department of Molecular and Cell Biology, Washington, DC, United States

INTRODUCTION

- Oral mucosal wound healing depends on efficient epithelial restitution and restoration of barrier integrity, processes that require dynamic regulation of cell–cell adhesion
- E-cadherin is an integral component of epithelial junctions and undergoes context-dependent remodeling during repair, where its dysregulation can impair both barrier function and wound closure.
- As inflammatory or microbial challenges are known to disrupt epithelial homeostasis, we examined whether such conditions alter E-cadherin distribution in oral keratinocytes by comparing non-inflamed and inflamed conditions.

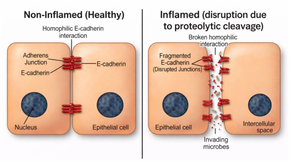
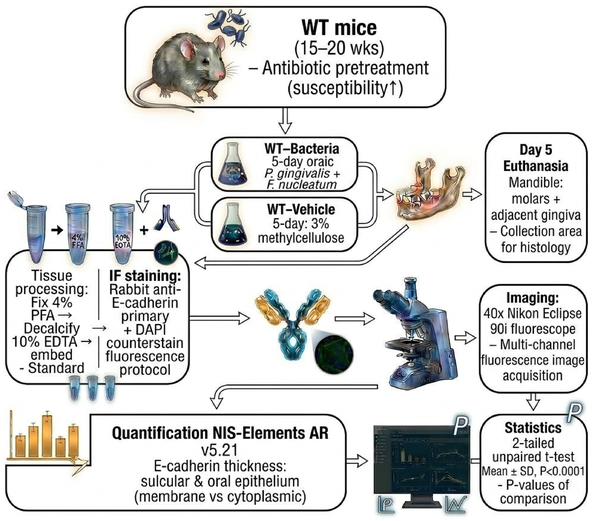


Figure 1. Schematic of E-cadherin junctions in non-inflamed vs. inflamed states.

METHODS



WT: Wild Type; PFA: Paraformaldehyde; EDTA: Ethylenediaminetetraacetic acid.

RESULTS

E-cadherin was predominantly localized at the cell membrane in the vehicle group. Bacterial challenge induced redistribution of E-cadherin from the membrane to both membrane and adjacent cytoplasm.

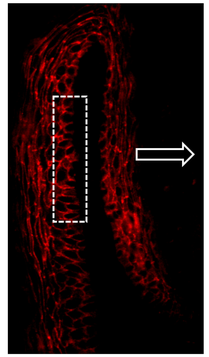


Figure 2A. Single-channel Cy5 view of Cre−vehicle−treated gingival epithelium immunofluorescence. E-cadherin (red) localizes exclusively to thin plasma membranes, confirming intact junctional distribution without cytoplasmic translocation in control conditions. White box inset indicates zoomed region shown in Figure 2B.

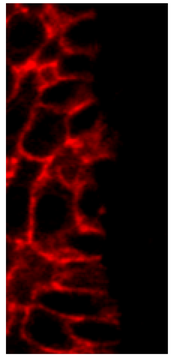


Figure 2B. Zoomed single-channel Cy5 view of basal layer in Cre−vehicle−treated gingival epithelium. E-cadherin (red) localizes exclusively to thin plasma membranes, evident in the basal layer with continuous junctional distribution and no cytoplasmic translocation in control conditions.

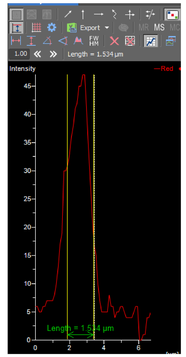


Figure 2C. Intensity profile across plasma membrane in Cre−vehicle control gingival epithelium demonstrates E-cadherin localization exclusively in the membrane. A single sharp peak in mean fluorescence intensity occurs when the profile line traverses the cell membrane, rapidly dropping to background levels with a measured membrane thickness of 1.53 µm, confirming thin, junctional distribution without cytoplasmic extension.

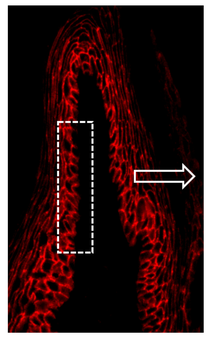


Figure 3A. Single-channel Cy5 view of Cre−bacteria−challenged gingival epithelium immunofluorescence. E-cadherin (red) localizes to thickened plasma membranes with cytoplasmic translocation, confirming disrupted junctional distribution in bacterial-challenged conditions. White box inset indicates zoomed region shown in Figure 3B.

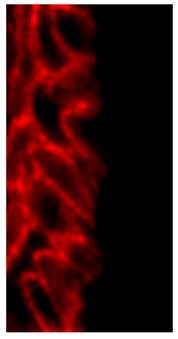


Figure 3B. Zoomed single-channel Cy5 view of basal layer in Cre−bacteria−challenged gingival epithelium. E-cadherin (red) shows thickened plasma membranes with prominent cytoplasmic translocation, confirming disrupted junctional distribution in bacterial-challenged conditions.

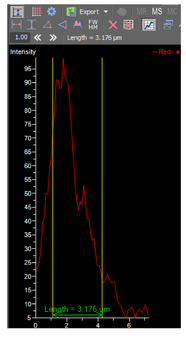


Figure 3C. Intensity profile across plasma membrane in Cre−bacteria−challenged gingival epithelium demonstrates E-cadherin localization in both membrane and cytoplasm. A broad, elevated peak in mean fluorescence intensity reflects thickened distribution when the profile line traverses the cell membrane/cytoplasm, with measured thickness of 3.17 µm confirming disrupted junctional extension versus controls.

RESULTS

Quantification revealed significantly increased E-cadherin thickness in bacteria vs. vehicle groups (*P*<0.001): oral basal epithelium, 3.88 ± 0.33 µm vs. 1.88 ± 0.25 µm; sulcular epithelium, 3.63 ± 0.32 µm vs. 1.70 ± 0.31 µm.

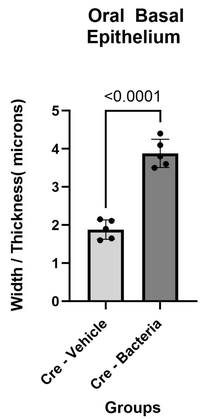


Figure 4A. Quantification of E-cadherin membrane width/thickness in the oral basal epithelium of Cre− vehicle- and Cre − bacteria-treated mice. Bacterial challenge significantly increased E-cadherin thickness compared with vehicle control, consistent with redistribution of E-cadherin from the membrane toward the adjacent cytoplasm. Individual data points represent separate samples (n=5*n*=5 per group), and bars indicate mean ± SEM. P<0.0001..

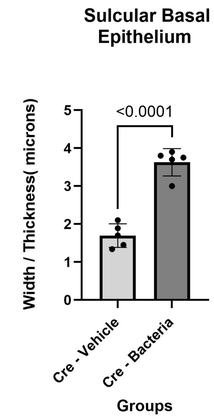


Figure 4B. Quantification of E-cadherin membrane width/thickness in the sulcular basal epithelium of Cre− vehicle- and Cre− bacteria-treated mice. Bacterial challenge significantly increased E-cadherin thickness compared with vehicle control, consistent with redistribution of E-cadherin from the membrane toward the adjacent cytoplasm. Individual data points represent separate samples (n=5n=5 per group), and bars indicate mean ± SEM. P<0.0001.

These changes in E-cadherin distribution caused by bacteria are consistent with a loss of barrier membrane function and a shift from the membrane to both the membrane and adjacent cytoplasm following bacterial stimulation in vitro (data not shown). Together, these findings support the idea that bacterial exposure weakens epithelial junctional organization and promotes redistribution of E-cadherin away from its normal membrane-restricted pattern.

CONCLUSION

- **Bacterial challenge shifts E-cadherin localization from predominantly membrane-bound in vehicle controls to a mixed pattern of membrane and adjacent cytoplasmic distribution. This redistribution compromises epithelial barrier integrity [1,2] and can delay in-vitro "wound" scratch closure by oral keratinocytes** [3].
- As E-cadherin dynamics can modulate epithelial restitution and barrier repair in a context-dependent manner, altered E-cadherin localization/expression is a plausible contributing mechanism linking pathogen exposure to impaired mucosal healing, but direct causality in oral wound models requires specific demonstration.

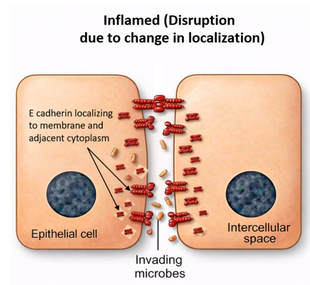


Figure 5. Schematic of inflamed epithelium with E-cadherin redistribution from the membrane to both membrane and adjacent cytoplasm post-bacterial challenge.

REFERENCES

1. Katz J, Sambandam V, Wu JH, Michalek SM, Balkovetz DF. Characterization of Porphyromonas gingivalis-induced degradation of epithelial cell junctional complexes. Infection and Immunity. 2000;68(3):1441–1449. doi:10.1128/IAI.68.3.1441-1449.2000.

2. Abe-Yutori M, Chikazawa T, Shibasaki K, Murakami S. Decreased expression of E-cadherin by Porphyromonas gingivalis-lipopolysaccharide attenuates epithelial barrier function. Journal of Periodontal Research. 2017;52(1):42–50. doi:10.1111/jre.12367.

3. Bhattacharya R, Xu F, Dong G, Li S, Tian C, et al. Effect of Bacteria on the Wound Healing Behaviour of Oral Epithelial Cells. PLOS ONE. 2014;9(2):e89475. doi: 10.1371/journal.pone.0089475.

Created with BioRender Poster Builder