Cyclic stretch force induces periodontal ligament cells to secrete exosomes that suppress IL-1β production through the inhibition of the NF-κB signaling pathway in macrophages

論 文 内 容 要 旨

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Background: In the oral mechanical environment, periodontal ligament cells (PDL cells) contribute to maintaining periodontal tissue homeostasis. Recent studies showed that exosomes, small vesicles secreted by a number of cell types, play a pivotal role in cell-to-cell communication in biological processes.

Method: The supernatants from human PDL cells (PDL-sup) stimulated with cyclic stretch were prepared first. The secretion of exosomes from PDL cells stimulated with cyclic stretch was then examined by the western blot, transmission electron microscopy analysis and immunofluorescence microscopy analysis. After that, the role of exosomes in the inflammatory response of macrophages using the human macrophage cell line THP-1 was detected by real-time PCR, ELISA, immunocytochemistry assay.

Results: The treatment of macrophages with PDL-sup, but not PDL-sup from unstimulated PDL cells, inhibited the production of IL-1β in LPS/nigericin-stimulated macrophages. The pretreatment of PDL cells with GW4869, an inhibitor of exosome secretion, or siRNA for Rab27B, which controls exosome secretion, abrogated the inhibitory effects of PDL-sup. A transmission electron microscopy analysis demonstrated the existence of exosomes with diameters ranging between 30 and 100 nm in PDL-sup, suggesting that exosomes in PDL-sup contribute to this inhibition. An immunofluorescence microscopy analysis revealed that exosomes labeled with PKH67, a fluorescent dye, were incorporated by macrophages as early as 2 h after the addition of exosomes. Purified exosomes inhibited IL-1β production in LPS/nigericin-stimulated macrophages and the nuclear translocation of NF-κB as well as NF-κB p65 DNA-binding activity in LPS-stimulated macrophages, suggesting that exosomes suppress IL-1β production by inhibiting the NF-κB signaling pathway.

Conclusion: These results indicate that PDL cells in mechanical environments contribute to the maintenance of periodontal immune/inflammatory homeostasis by releasing exosomes.