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# CAR-T–INSPIRED IMMUNOMODULATORY NANOVESICLES FOR TARGETED ELIMINATION OF ORAL SQUAMOUS CELL CARCINOMA CELLS

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***Abstract***

***Introduction:*** *Oral squamous cell carcinoma is associated with high morbidity and limited response to conventional chemoradiotherapy. Although chimeric antigen receptor T-cell therapy has shown remarkable success in hematological malignancies, its application in solid tumors is constrained by the tumor microenvironment and therapy-related toxicities. Recent advances suggest that chimeric antigen receptor T-cell - derived nanovesicles may replicate tumor-targeting properties while improving safety and tissue penetration.*

***Procedures:*** *Human Jurkat T-cells were engineered to express a second-generation anti-epidermal growth factor receptor chimeric antigen receptor. Chimeric antigen receptor T-cell–derived nanovesicles were generated using a serial extrusion method and characterized by dynamic light scattering, transmission electron microscopy, and Western blotting. Cellular uptake and cytotoxicity were evaluated in epidermal growth factor receptor-positive oral squamous cell carcinoma cell lines (HSC-3 and CAL-27) and compared with normal human gingival fibroblasts.*

***Results:*** *The engineered chimeric antigen receptor- nanovesicles exhibited a mean diameter of approximately 135 nm and retained key T-cell and chimeric antigen receptor-associated surface markers. Preferential internalization was observed in epidermal growth factor receptor expressing Oral squamous cell carcinoma cells, with minimal uptake in normal fibroblasts. Chimeric antigen receptor - nanovesicles induced significant, dose-dependent apoptosis in oral squamous cell carcinomacell lines while demonstrating negligible cytotoxicity toward normal gingival fibroblasts.*

***Conclusion:*** *Chimeric antigen receptor T-cell-inspired nanovesicles preserve the specificity and cytotoxic efficacy of their parental T-cells while overcoming key limitations of live-cell therapy. These findings highlight chimeric antigen receptor nanovesicles as a promising, safe, and off-the-shelf immunotherapeutic strategy for targeted treatment of oral squamous cell carcinoma.*

***Keywords:*** . Oral squamous cell carcinoma; CAR-T; Nanovesicles; Immunotherapy; EGFR; Targeted drug delivery

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