Table S1 Examples of extracellular vesicle nanoparticles for oral cancer therapy.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Categories | Source | Isolation method of EVs | Cancer model | Functions | Drug-loading | Refs |
| EVs | HSC3 | The polymer-based precipitation (PBP) method and the ultracentrifugation method | HSC3 | Reduce the survival of the metastatic OSCC cells | HSP90α and HSP90β | [32] |
| EVs | MSCs | GETTM Exosome Isolation Kit (for stem cells) | Buccal lesions in dimethylbenzanthracene-induced OPMDs model | Attenuate inflammation severity and decrease the incidence and the amount of dysplasia in the OPMDs tissue | miR-185 | [35] |
| EVs | γδT cell | ExoQuick | CAL27 and SCC-VII; nude mice; immunocompetent C3H mice | Increased CD8+T cell proliferation, IFN-gamma production, and cytotoxicity against OSCC cells. Decrease the CD8+T cell expression of PD-1 and CTLA-4 at both mRNA and protein levels | miR-138 | [37] |
| EVs | Hypoxic HNSCC cells | Ultracentrifugation | SCC9 and CAL27 | Indicate hypoxic and aggressive cancer stroma | miR-192/215 | [38] |
| EVs | SCC9 | Differential centrifugation steps; ExoQuick Plasma prep, and exosome precipitation kit | SCC9; nude mice | Induce cell apoptosis and inhibit tumour growth | Chrysin | [39] |
| Exosomes | CAFs | Ultracentrifugation | CAL27 and SCC15; BALB/c nude mice bearing SCC15 cells | Suppress OSCC cell proliferation and metastasis | miR-34a-5p | [48] |
| Exosomes | CAFs | Differential centrifugation steps; ExoQuick Plasma prep and Exosome precipitation kit | CAL 27, SCC25, and HN4 | Confer cisplatin resistance | miR-196a | [50] |
| Exosomes | MSCs of human bone marrow | Centrifugation | CAL27, SCC9, SCC25, HN4, and NOK; athymic BALB/C nude mice bearing OSCC cells | Suppress the proliferation, invasion, and migration | miR-101-3p | [51] |
| Exosomes | CAL27 and SCC15 | The Total Exosome Isolation Reagent | CAL27 and SCC-15; normal gingival fibroblasts and cancer-associated fibroblasts | Prevent oncogenic  transformation of normal gingival fibroblasts | miR-21-5p | [53] |
| Exosomes | HOC313 | The Total Exosome Isolation Reagent and ultracentrifugation | HOC313 | Induce cell motility and invasion | miR-1246 | [55] |
| Exosomes | CAL27 and SCC25 | Ultracentrifugation and the ExoEasy Maxi Kit | CAL27 and SCC25 | Enhance cytotoxicity of natural killer cells | NAP1 | [56] |
| Exosomes | CAFs | Ultracentrifugation | HN4, HN30, CAL27, 293T, and MC3T3-E1 | Loss of miR-3188 in exosomes contributes to the malignant phenotypes of HNC cells | miR-3188 | [57] |
| Exosomes | CAL27, HUVECs | Ultracentrifugation | CAL27 | Target EFNA3 to promote oral cancer Angiogenesis | miR-210-3p | [59] |
| Exosomes | OSCC cells | Ultracentrifugation and the MagCapture™ Exosome Isolation Kit PS | A431, Ca9-22, HO-1-N-1 | Suppress squamous cell carcinoma cell growth | miR-6887-5p | [60] |
| Exosomes | SCC9 and HN12 | Ultracentrifugation and the ExoEasy Maxi Kit | SCC4, SCC9, SCC25, HN12, CAL27, and HOK | Knockdown of circ\_0000199 inhibited OSCC cell growth | circ\_0000199 | [61] |
| Exosomes | SCC90 | Ultracentrifugation | SCC90, THP1 | Induce macrophage M1 polarization and increases tumour radiosensitivity | miR-9 | [63] |
| Exosomes | NTECs | Ultracentrifugation | NTECs, Docetaxel resistant HSC-3DR, CAL27, HSC3, SAS, SCC15, and SCC9 | Suppress chemoresistance of docetaxel in tongue squamous cell carcinoma | miR-200c | [64] |
| Exosomes | OSCC cells | Ultracentrifugation | CAL27; 6-week-old female wide-type C57BL/6 mice drinking 4NQQ water for 10 weeks | Induce M2-like macrophages polarization | CMTM6 | [65] |
| Exosomes | OECM1 | Ultracentrifugation | OECM1, HUVECs; male nude C57BL/6 mice bearing OECM1 cells | Promote progression and tubular formation | miR-130b-3p | [66] |
| Exosomes | CAL27 | Ultracentrifugation | HUVECs, HOK, CAL27 | Promote human umbilical vein endothelial cells migration and tube formation | miR-221 | [67] |
| Exosomes | HSC3 | Polymer-based precipitation and centrifugation | HSC3; RT7 | Transform epithelial cells into a mesenchymal phenotype | EGFR | [68] |
| Microvesicles | CAL27 | Membrane biotinylation | CAL27 | Inhibit tumour growth and imaging | siRNA | [70] |
| Microvesicles | CAL27, SCC4, and SCC9 | Ultracentrifugation | CAL27, SCC4, SCC9 | Enhance endothelial cell angiogenesis | Shh | [71] |
| Microvesicles | CAL27 | Ultracentrifugation | CAL27 | High tumour-targeting to oral cancer due to the modified folate, as well as a synergistic anticancer impact, and in vivo imaging | Bcl-2 siRNA and paclitaxel | [72] |