Exosomes are nanoscale membrane-derived vesicles that are secreted by cells and play a critical role in modulating the tumor microenvironment and therapeutic drug resistance. Dsg2 is a desmocollin that is expressed in cancer cells and secreted as exosomes. Dsg2 overexpression increases exosome release and enhances EGFR/c-Src content. This work demonstrates that Dsg2 can regulate exosome biogenesis and protein loading to elicit a mitogenic effect in recipient mesenchymal cells.

**ABSTRACT**

Exosomes are nanoscale membrane-derived vesicles that are secreted by cancer cells and play a critical role in modulating the tumor microenvironment and therapeutic drug resistance. Dsg2 is a desmocollin that is expressed in cancer cells and secreted as exosomes. Dsg2 overexpression increases exosome release and enhances EGFR/c-Src content. This work demonstrates that Dsg2 can regulate exosome biogenesis and protein loading to elicit a mitogenic effect in recipient mesenchymal cells.

**RESULTS**

**Dsg2 is Overexpressed in HNSCCs and Detected in Serum Exosomes**

**Exosomes isolated from SCC-derived Cells are Enriched with Dsg2**

**Dsg2 Modulates Exosome Biogenesis and Stimulates Fibroblast Proliferation**

**SUMMARY & CONCLUSIONS**

Overexpression of Dsg2 is commonly observed in cutaneous skin cancers and can drive activation of EGFR-mediated signaling. Proteolytically-processed Dsg2 is exported in cell-derived and circulating exosomes. Dsg2 decreases Cav1 level in cells, potentially by promoting the endocytosis of caveolae and enhancing release of lipid-rich enriched exosomes. Dsg2 overexpression drives release of more EGFR/c-Src that can be taken up by recipient fibroblasts, enhancing proliferation. This work demonstrates that Dsg2 can regulate exosome biogenesis and protein loading to elicit a mitogenic effect in recipient mesenchymal cells.

**REFERENCES**


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