

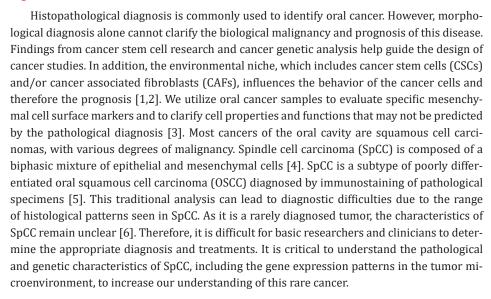


Targeting the Tumor Stroma for Oral Cancer Therapy

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Opinion

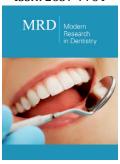


Current oral cancer treatments are organ specific and mainly use reagents that target squamous cell carcinoma in the head and neck regions. For example, the EGFR-targeting reagent cetuximab is well known for its application in malignant disease of the head and neck. However, prior research demonstrated that cetuximab is not effective in cases of recurrent or advanced SpCC [6]. This underscores the necessity of identifying other cell components that can be targeted. Our group demonstrated that a cetuximab-resistant recurrent SpCC sample expressed the mesenchymal stem cells (MSCs) markers platelet-derived growth factor receptor α (PDGFR α) and Nestin. Prospective cell analysis by using a flow cytometer revealed that recurrent SpCC cells expressed the CSC marker CD44v, which was identified in both EpCAM positive epithelial cells and PDGFRα positive mesenchymal cells. These results indicate that CSCs survived in both parenchymal and mesenchymal tissues. Cultured cells expressed legacy MSC markers such as CD73, CD90, and CD105, and they showed features such as colony forming, migration, and differentiation abilities. Our group demonstrated the utility of imatinib, which is known to inhibit the protein tyrosine kinase activity of Bcr-Abl and PDGFR α , in targeting PDGFR α -expressing stromal cells. Imatinib had a more potent inhibitory effect on the cultured cells and was more effective in inducing cell death relative to the cetuximab-treated group.

Perspectives

In our previous study, we evaluated the characteristics of cancer cells obtained from tissues in addition to conventional pathological diagnosis. By using a flow cytometer, it was possible to analyze the expression of markers several hours later. This strategy enables early prediction of the possible effects of chemotherapy and is expected to identify new markers and help develop drugs aimed at specific molecular targets. Analysis of the proliferation and migration abilities of the cancer cells, as well as drug response tests, can be used to further determine specific patient characteristics. This information, in combination with pathological analysis, helps inform diagnostic and treatment decisions and makes it possible to further

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elucidate the biological malignancy and prognosis of cancers as compared with pathological diagnosis alone. Our approach can contribute to the development of disease-specific individualized treatments that are essential for rare cancers with histologic types.

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