
Despite numerous advances in treatment, the 5-year survival rate for head and neck squamous cell cancer (HNSCC) has remained largely unchanged for the past 50 years. This poor outcome is due to a number of variables, including the development of multiple primary tumors. Therefore, it is essential to supplement early detection with effective chemopreventive strategies. Using the carcinogenic agent 4-nitroquinoline 1-oxide (4-NQO) to produce HNSCC in a mouse model, we tested the hypothesis that ZD6474 is an effective chemopreventive agent in a preclinical animal model of HNSCC. CBA mice were treated with 4-NQO (100 µg/mL) in their drinking water for a period of 8 weeks. The mice were then randomized to either no treatment or oral lavage of ZD6474 (25 mg/kg/d) for 24 weeks (total time of experiment 32 weeks). At the completion of the study, the proportion of mice with dysplasia or HNSCC was significantly different between the 2 treatment groups (96% in the control and 28% in the ZD6474 group; Fisher exact test: P < .001). Similarly, the proportion of animals with HNSCC was significantly different between the 2 treatment groups (71% in the control and 12% in the ZD6474 group; Fisher exact test: P < .001). In addition, animals treated with ZD6474 displayed a lower proliferative index, a decrease in microvessel density, and the inhibition of phosphorylation of EGFR and VEGFR2 compared with the control mice. These data support the hypothesis that ZD6474 may be promising chemopreventive agent for individuals at risk for developing HNSCC.

ISOLATION OF COMPONENTS OF SQUAMOUS CELL CARCINOMA PARENCHYMA AND STROMA FOR FUNCTIONAL STUDIES. Z. Kurago, E. Wagner, L. Ramanathapuram, EL. Lamb, JH. Lee, NYU, New York, U South Dakota/Sanford Health, Vermillion.

Malignant cell success depends in part on the support of its microenvironment. The microenvironment of oral squamous cell carcinoma (SCC) is complex, and the interactions between the various components are poorly understood. Our long-term goal is to provide a system for ex vivo testing of treatments that target both the parenchyma and the stroma of SCC and potentially enable individualized approaches to patient treatment. The purpose of the present study was to develop an ex vivo approach to the analysis of the stromal composition of SCC and the interactions between the parenchyma and stroma. To do this, fragments of a human papilloma virus–negative SCC of the tongue were processed, sectioned, and stained by hematoxylin and eosin and immunohistochemistry. Several fragments were explanted in complex media to support various cell types. A variety of nutritional studies include responsiveness to microbial stimuli, migration assays, assessment of colony formation, and organotypic cultures to compare the functions of tumor-associated and normal mesenchymal counterparts and their effect on SCC cell survival and migration.


Dyskerin is a multifunctional protein that is commonly up-regulated in neoplasia, including oral squamous cell carcinoma (OSCC). Dyskerin binds to and stabilizes noncoding RNAs, including a subset of small nucleolar RNAs (snoRNAs), which are characterized by a common H/ACA secondary structure. Because dyskerin is a ubiquitous protein, we hypothesized that its loss of function would reduce the accumulation of all H/ACA snoRNA, regardless of cell type. To test this hypothesis, we transfected UM-SCC1 OSCC cells and U2OS osteosarcoma cells with dyskerin small interfering (siRNA); siRNAs directed against GAPDH and a nonspecific target served as negative controls. Forty-eight hours later, total RNA was extracted, reverse transcribed, and subjected to real-time polymerase chain reaction analysis. Loss of dyskerin function significantly reduced the levels of 3 randomly selected H/ACA snoRNA, including U17A, U19, and U66, by more than twofold in both cell lines relative to the controls. In contrast, the levels of C/D box snoRNA, snoRNA U5A, and miR-let-7g remained essentially unchanged; dyskerin is not known to bind to these RNA. However, dyskerin was recently shown to directly bind to micro-RNA (miRNA) sequences that are embedded within and processed from H/ACA snoRNA. miRNAs are a class of small noncoding RNA that regulate posttranscriptional gene expression. We have now shown for the first time that loss of dyskerin also significantly decreased the levels of the miRNA miR-664, miR-1248, and miR-1291, as well as their corresponding precursors. The roles of these dyskerin-regulated noncoding RNAs in tumorigenesis are not currently known. Nonetheless, these findings suggest new and novel avenues of investigation into the molecular mechanisms by which dyskerin may contribute to neoplasia.


Background. Spindle cell squamous cell carcinoma (SCSCC) is a rare bimorphic malignant neoplasm of the upper aerodigestive tract and skin. This tumor is composed of a squamous cell carcinoma (SCC) and a malignant spindled component; therefore, diagnosis on hematoxylin and eosin–stained sections alone presents a challenge. The present case had serendipitous findings of tissue-bound and serum autoantibodies on direct and indirect immunofluorescence (IF), respectively.

Objectives. The aim of this study was to report the immunohistochemistry (IHC) findings in a case of oral SCSCC and to further investigate the nature of the patient’s circulating autoantibodies by using an enzyme-linked immunosorbent assay (ELISA).

Results. IHC showed that the carcinoïdomatous portion of the tumor expressed pankeratin, epithelial membrane antigen, and E-cadherin; the sarcomatoid component expressed vimentin, smooth muscle antigen, and N-cadherin; both carcinoïdomatous and sarcomatoid portions of the tumor expressed p63 and CK34BE12. Direct and indirect IF showed autoantibodies in a stratified epithelial specific-antinuclear antibody pattern; ELISA