**PIGF Overexpression in Head and Neck Squamous Cell Carcinoma**

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**ABSTRACT**

Head and neck cancers are a heterogeneous group of malignancies, with squamous cell carcinoma (HNSCC) comprising the most common type, and the 8th most common cancer cause of death worldwide. HNSCC are highly vascularized tumors; therefore, inhibitors of new blood vessel formation are postulated to have therapeutic effect in HNSCC, by choking off the blood supply to the tumor. Clinical trials have been undertaken using angiogenesis inhibitors targeting VEGF and its receptors in human cancers, including HNSCC. Because PIGF is crucially important to normal blood vessel development, VEGF inhibition therapy has been associated with a number of serious adverse effects, curtailing its use in some clinical trials. Also, resistance to VEGF therapy was common.

Because of these issues, we have turned our attention to another member of the VEGF family, Placenta Growth Factor (PIGF), which has a much more limited expression pattern, and is not essential for normal vascularization. PIGF overexpression has been demonstrated in a number of tumors, but is not reproducibly produced by many normal tissues. Thus, inhibiting PIGF as a cancer treatment is predicted to be less toxic than inhibiting VEGF.

Importantly, PIGF inhibition in various mouse cancer models was associated with decreased tumor growth, indicating that PIGF blockade might have therapeutic potential as a safer alternative to VEGF inhibition therapy.

The aim of this pilot study was to determine the level of expression of PIGF in HNSCC cell lines and frozen tissue samples compared with normal oropharyngeal samples by qRT-PCR and immunohistochemistry. The results indicated that PIGF inhibition might be a useful therapeutic strategy in HNSCC.

**METHODS AND MATERIALS**

PIGF was expressed at significantly higher levels in squamous cell carcinoma compared to normal oropharynx. Further testing of additional tumor specimens is currently underway.

**RESULTS**

All HNSCC cell lines expressed PIGF mRNA. Immunohistochemistry was performed on the cell lines with the highest expression: UM-SCC-1, UM-SCC-14a, UM-SCC-22a, and UM-SCC-40. Each stained positive with PIGF antibody compared with isotype control antibody.

Nineteen tumor samples and five uvula samples were obtained from the tissue biopsies for qRT-PCR. One tumor sample was basal cell carcinoma, and the histologic information for another was unavailable; therefore, these were excluded from analysis. Tumor subtypes included oral cavity (n=12, 70%), oropharynx (n=4, 24%), and supraglottis (n=1, 6%). Since variances are significantly different between groups (p<0.02, F-test), a 2 sample heteroskedastic T-test was used. qRT-PCR indicated that PIGF was overexpressed in the tumor samples compared with the benign uvula, with p=0.0035.

**REFERENCES**