The Effect of Wnt/Beta-Catenin Signaling Inhibition on Oral Squamous Cell Carcinoma

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Oral Squamous Cell Carcinoma (OSCC) is a cancer of the mouth epithelium with an annual incidence rate in the US of nearly 48,000 cases annually and a 5-year survival rate of only 65%. Cancer stem cells (CSCs) are believed to be responsible for progression of OSCC, possessing stem-cell qualities including pluripotency that drive tumor development and chemotherapy resistance. Within cancerous cells is a pathway called the Wnt/ß-catenin signaling pathway, known to play a pivotal role in OSCC and CSC survival. This pathway causes the degradation of cellular junctions and upregulation of cancer-driving genes through the binding to and activation of CREB binding protein (CBP), a transcriptional coactivator that drives tumor progression. One of the genes up-regulated by this pathway, DPAGT1, drives N-glycosylation of the cellular adhesion protein E-cadherin, thus facilitating tumor growth through epithelial-mesenchymal transition (EMT). This study aimed to inhibit CBP/Beta-catenin interaction through treatment with ICG-001, a Wnt pathway inhibitor. Western blot and tissue imaging revealed that in ICG-001-treated tumors, E-cadherin and Beta-catenin localized at cell membranes, while levels of EGFR, CTHRC1, GPT, and vimentin (all involved in EMT) were reduced. These results suggest that ICG-001 helps preserve adhesion proteins essential for maintenance of cell adherens junctions and prevent of cell proliferation. Because of the significance of Wnt signaling in CSC maintenance, ICG-001 may hold particular promise in preventing tumor growth and metastasis. Though further research is needed to determine optimal dosage and elucidate the full in vivo effects of ICG-001, it offers promising results in treating OSCC.

Awards Won:
ADA Foundation: Second Award of $1,000