

Evaluating ERK inhibitor sensitivity in HRAS-mutant head and neck squamous cell carcinoma

Head and neck squamous cell carcinoma (HNSCC) is a significant public health problem and the prognosis is very poor. There are limited treatments. RAS is a membrane-associated GTP binding protein that is a well-established driver for cancer progression. One approach to target RAS is to inhibit the activity of its downstream effectors. Of many pathways that is downstream of RAS, a critical pathway in other cancers is the MAPK pathway. Activated RAS binds to RAF which in turns activates MEK1 and MEK2 protein kinases. Ultimately, the MEK1/2 protein kinases phosphorylate ERK1/2 which control critical cell processes. SCH772984 is an allosteric and ATP-competitive ERK inhibitor (ERKi). We hypothesized that ERKi would inhibit the growth of HRAS-mutant HNSCC cells such as UMSCC43. I first made sure that SCH772984 inhibited ERK1/2 signaling, by immunoblotting for loss of activity of ERK and its substrates. I then evaluated the effect of ERK inhibition upon both anchorage-dependent and independent cell growth. In addition, I analyzed the cell cycle distribution upon treatment with ERK inhibitor using flow cytometry. The results showed that the doses I used did inhibit the growth in anchorage-dependent and –independent conditions. This study was limited to one cell line. Further studies in additional cell lines and at lower doses of ERK inhibitor are needed to evaluate the consequences of inhibition of ERK activity in HNSCC.