The Effect of Erlotinib on Human Angiogenesis

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Introduction

Angiogenesis is the process of new blood vessels developing from pre-existing ones. Physiologic angiogenesis only occurs under very specific circumstances in healthy individuals, such as in wound healing and intestinal atrophy. In contrast, angiogenesis can occur in pathologic settings such as in cancer and some other diseases. The size of a developing tumor is limited by its ability to recruit blood vessels, and tumor growth and metastasis are associated with progression of many solid human tumors and poor prognosis. Erlotinib HCl has been shown to inhibit TK receptors of the c-erbB family, with the receptor EGFR being targeted. Erlotinib HCl is designed to inhibit activity of one of the tyrosine kinase (TK) receptors of the c-erbB family, the Epidermal Growth Factor Receptor (EGFR). Elevated EGFR expression has been associated with progression of many solid human tumors and poor prognosis. Erlotinib HCl has been shown to inhibit activity of one of the tyrosine kinase (TK) receptors of the c-erbB family, with the receptor EGFR being targeted.

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Hypothesis

Erlotinib HCl will inhibit both physiologic and pathologic angiogenesis in an in vitro angiogenesis model system.

Methods

The research protocols for this study were approved by Institutional Review Board of Louisiana State University Health New Orleans, LA, US. Erlotinib HCl was evaluated in an in vitro angiogenesis assay cited in the lab’s previous works.3 Human tissue samples used in the assay were harvested from various tissue (HPV and IVC) and liver NETs. For the purposes of the experiment, normal angiogenesis was modeled using venous tissue, while tumor samples modeled pathologic angiogenesis. The initial concentration of Erlotinib HCl treatment (10 µM) was selected based on previously reported effective concentrations for non-small cell lung cancer.4 For study purposes, each treatment group consisted of 30 tissue fragments. Using an unpaired t-test at p<0.05 (Primer of Biostatistics), we found that the Erlotinib HCl treated specimen had statistically significant inhibition of Angiogenic Growth and Combined Response values for the 10µM and 100µM groups compared to the control. The effect of the highest dose of Erlotinib HCl on percent initiation in the liver NET group had statistically significant inhibition of Angiogenic Growth and Combined Response values for all three Erlotinib HCl concentrations compared to the control. The trend of supernatant protein concentrations in treated and untreated IVC and liver NET samples with increasing concentration of Erlotinib HCl, highlighted elements representative ligand-receptor pairs.

Results

Table 1. Human Placental Vein Angiogenesis Model Data

Table 2. Human Inferior Vena Cava Angiogenesis Model Data

Table 3. Human Tumor Angiogenesis Model Data

Conclusions

In liver metastases of neuroendocrine origin, Erlotinib HCl effectively decreased angiogenic growth and percent initiation. Therefore, Erlotinib HCl also inhibited pathologic angiogenesis in a dose response manner in our in vitro model system.

Future Research

Perform cell survival and proliferation assays in human umbilical vein endothelial cells (HUVEC) and human umbilical vein endothelial cells (HUVEC) using Erlotinib HCl.

References