

Quantitative Immunohistochemistry Evaluating APE1 Expression in a Mouse Pancreatic Adenocarcinoma Model

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High levels of APE1 expression have been reported in numerous malignant tumors (brain, ovarian, pancreatic, and prostate). APE1 is an emerging target for a variety of novel anticancer drugs. Human apurinic endonuclease/redox factor 1 (APE1/Ref-1) mediates the repair of baseless sites in DNA caused by alkylation and oxidative DNA damage. Compound E3330 targets the redox signaling function of APE1. A pancreatic cancer mouse model was used to evaluate the drug effects of E3330 and Gemcitabine. The following doses were used across eight mice groups: E3330 at 12.5mg/kg, 25mg/kg, and 50mg/kg), Gemcitabine (35mg/kg), a combination of E3330 and Gemcitabine at 12.5mg/kg, 25mg/kg, and 50mg/kg), and an untreated vehicle control group. Mice were dosed i.p. 3 times weekly (MWF) and the study was completed at day 39. At termination, tumors were harvested and cross-sections were processed into a Paraffin block. Tissue sections were prepared and stained for H&E and an immunostain for CD31 (angiogenesis marker). Slides were imaged via Aperio whole slide digital system. The immunostains were evaluated to predict the effectiveness of treatment for pancreatic adenocarcinoma. IHC slides were quantitated using an Aperio positive pixel algorithm to determine the percent of angiogenesis in the various drug treatment groups. A biologically significant correlation was seen amongst the low and middle dose E3330 drug groups in comparison to the vehicle control. The (12.5 & 25) E3330 groups had an anti-angiogenic effect (shown by decreased CD31 positivity). These were slightly lower than the combinations of E3330 and Gemcitabine at the same dose treatment groups (possibly due to blunting of E3330). These results support previous studies demonstrating the anti-angiogenic activity of E3330.

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