Modeling Therapy Response and Spatial Tissue Distribution of Erlotinib in Pancreatic Cancer.

Pancreatic ductal adenocarcinoma (PDAC) is likely the most aggressive and therapy-resistant of all cancers. The aim of this study was to investigate the emerging technology of matrix-assisted laser desorption/ionization imaging mass spectrometry (MALDI IMS) as a powerful tool to study drug delivery and spatial tissue distribution in PDAC. We utilized an established genetically engineered mouse model of spontaneous PDAC to examine the distribution of the small-molecule inhibitor erlotinib in healthy pancreas and PDAC. MALDI IMS was utilized on sections of single-dose or long-term-treated mice to measure drug tissue distribution. Histologic and statistical analyses were performed to correlate morphology, drug distribution, and survival. We found that erlotinib levels were significantly lower in PDAC compared with healthy tissue ($P = 0.0078$). Survival of long-term-treated mice did not correlate with overall levels of erlotinib or with overall histologic tumor grade but did correlate both with the percentage of atypical glands in the cancer ($P = 0.021$, $rs = 0.59$) and the level of erlotinib in those atypical glands ($P = 0.019$, $rs = 0.60$). The results of this pilot study present MALDI IMS as a reliable technology to
study drug delivery and spatial distribution of compounds in a preclinical setting and support drug imaging-based translational approaches. Mol Cancer Ther; 15(5); 1145-52. ©2016 AACR.