Targeting NIR Fluorescent Dyes for Intraoperative Lung Cancer Visualization

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Fluorescence-guided surgery (FGS) is an emerging field that allows surgeons to intraoperatively enhance the visualization of solid tumors, delineate tumor margins, identify synchronous lesions and micrometastases. FGS employs near-infrared (NIR) fluorophores in the 700-900 nm range, where the absorption coefficients of water, oxyhemoglobin, and deoxyhemoglobin are minimal and autofluorescence and scattering are significantly reduced. This results in tissue becoming more transparent, allowing for better resolution and depth penetration. Our lab develops and translates targeted NIR fluorophores for non-small cell lung cancer (NSCLC) surgery. We have focused on fluorophores that target dysregulated pathways in lipid metabolism that are common to a number of tumor types. We employ a translational paradigm that includes veterinary clinical trials as an intermediate to human patient studies. Our most advanced probe, targeting choline kinase (ChoKα), a critical enzyme in lipid biosynthesis, has completed veterinary clinical trials, and is undergoing IND-enabling studies prior to a Phase-I human clinical trial. A second class of activatable fluorophores that target cytosolic phospholipase A2 (cPLA2) is entering veterinary clinical trials in canine patients. Recent studies involve the development of short-wave infrared (SWIR) fluorophores with emissions >1000 nm. SWIR dyes show superior tissue penetration and resolution in phantoms and in mice, allowing for high-resolution vascular imaging and clearer imaging of internal organs. In animal tumor models and tissues SWIR dyes show low autofluorescence and high tumor to background (TBR) ratios. The ability of SWIRs to provide high-resolution, high TBR images with enhanced depth penetration positions them as promising candidates for surgical imaging.