

# Logic-Gated Approach for Targeted Delivery and Site-Selective Activation of Photothermal Agents in Precision Cancer Treatment

## **Abstract:**

Logic-gated strategies represent a promising approach to achieving highly selective cancer therapies. In this work, we present LG-AB (Logic Gate Aza-BODIPY), an OFF-ON photothermal therapy (PTT) agent that exhibits a shift in its wavelength of maximum absorbance when activated within cancer cells. This shift enables the molecule to absorb light and generate heat specifically in the cancerous tissue. Unlike conventional activatable agents that rely on a single biomarker, LG-AB employs an AND logic-gated design, where glucose transporter 1 (GLUT1) overexpression directs the agent to the tumor site, followed by activation through elevated glutathione (GSH) levels. Beyond demonstrating photothermal efficacy in human lung cancer and murine breast cancer cells, we show that LG-AB effectively attenuates cancer progression through heat-induced apoptosis, with minimal off-target effects to surrounding tissues. The versatility of this strategy is further demonstrated through the development and application of LG-CPT (Logic Gate Camptothecin), which utilizes the same logic-gated design. Our results show that enhancing specificity and limiting collateral damage can be broadly applied across different therapeutic agents.