

## An Activatable Prodrug for the Treatment of Metastatic Tumors

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**Abstract :** Metastatic cancers have historically been difficult to treat. However, metastatic tumors have been found to have high levels of reactive oxygen species such as hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), supporting the hypothesis that a prodrug could be activated by intracellular H<sub>2</sub>O<sub>2</sub> and lead to a potential anti-metastatic therapy. In this study, prodrug 7 was designed to be activated by H<sub>2</sub>O<sub>2</sub>-mediated boronate oxidation, resulting in activation of the fluorophore for detection and release of the therapeutic agent, SN-38. Drug release from prodrug 7 was investigated by monitoring fluorescence after addition of H<sub>2</sub>O<sub>2</sub> to the cancer cells. Prodrug 7 activated by H<sub>2</sub>O<sub>2</sub> selectively inhibited tumor cell growth. Furthermore, intratracheally administered prodrug 7 showed effective anti-tumor activity in a mouse model of metastatic lung disease. Thus, this H<sub>2</sub>O<sub>2</sub>-responsive prodrug has therapeutic potential as a novel treatment for metastatic cancer via cellular imaging with fluorescence as well as selective release of the anti-cancer drug, SN-38.

**Keywords :** hydrogen peroxide, prodrug, metastatic tumors, fluorescence

**Conference Title :** ICBS 2014 : International Conference on Bioimaging and Sensing

**Conference Location :** Barcelona, Spain

**Conference Dates :** October 27-28, 2014