Selective Detection of Cancer Cells Using a Dual-Targeting Fluorogenic Probe

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Cancer is the second leading cause of global death and has now become one of the biggest health threats to humanity. Much effort has been devoted to the discovery of efficacious anticancer drugs that can be employed to treat cancer. However, a prerequisite for effective treatment of this disease is the precise detection of tumors. In this regard, selective and sensitive imaging of tumors is invaluable for early diagnosis. Although numerous fluorescent probes targeting cancer cells have been developed for diagnosis of cancer, a majority of present fluorescence imaging agents have been designed based on mono-targeting of cancer cells and, as a result, they have poor tumor selectivity. Thus, target-selective fluorescent probes are needed, particularly those that respond to two enzymes that are overexpressed in spatially separated organelles of cancer cells. We developed a novel fluorogenic probe targeting both histone deacetylases (HDACs) and cathepsin L, which are located in different subcellular organelles and are aberrantly upregulated in cancer cells.[1] The new probe was composed of coumarin-fused fluorescein (FC) as a fluorescent dye, Boc-Lys(Ac) as a substrate for histone deacetylases (HDACs) in the nucleus, an amide linkage for selective cleavage by lysosomal cathepsin L, and an aminobenzyl group as a self-immolative linker. The fluorogenic probe was found to be useful for selective cancer cell imaging without interference arising from normal cells. The present study provides a new avenue for generation of fluorescent imaging agents with high selectivity toward cancer cells.

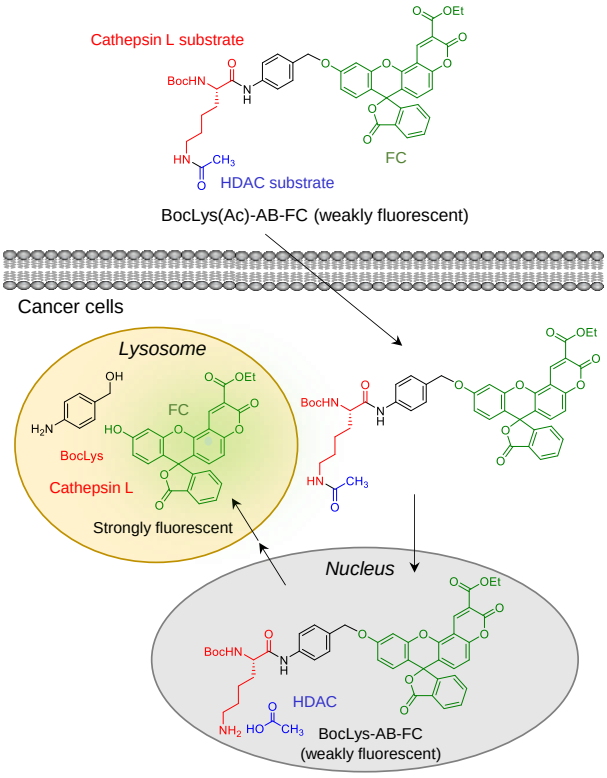

Figure 1. Schematic for fluorescence imaging of cancer cells using the dual enzyme-targeting fluorogenic probe.

References

[1] Sang-Hyun Park, Hyoje Jung, Yujun Kim, and Injae Shin, *Chem. Commun.* **2022**, *58*, 4079-4082.