MARINE CHEMILUMINESCENCE AS ANTI-TUMOR THERAPY WITH ENHANCED TUMOR-SELECTIVITY AND ACTIVITY

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Cancer is the second-highest cause of death worldwide, still being a challenging disease to treat. Thus, more efficient antitumor therapies are needed.

To this end, we have developed several single-molecule photosensitizers capable of intracellular and tumor-selective self-activation due to a chemiluminescence reaction triggered solely by a cancer marker [1,2]. Chemiluminescence consists in the conversion of thermal energy into excitation energy and subsequent light emission due to a chemical reaction [3]. This is a widespread phenomenon in nature, especially in the oceans, in which Coelenterazine is the most representative chemiluminescent substrate [3].

Herein, we developed Coelenterazine single-molecule derivatives which chemiluminescent reaction is triggered solely by a cancer marker [1,2]. Moreover, these compounds are directly chemiexcited to triplet excited states capable of generating the highly cytotoxic singlet oxygen, without requiring either a light source or any catalyst or co-factor (Figure 1).

Encouragingly, in vitro cytotoxicity assays demonstrated that these new compounds induced significant toxicity toward different tumor cell types [1,2]. In fact, this cytotoxic effect was better than the one induced by reference drugs. Furthermore, while these molecules were able to destroy tumor cells, they did not induce any toxicity toward non-cancer cells in the same concentration range [1,2].

Given this, our results indicate that the novel Coelenterazine derivatives have potential for anti-tumor therapy with enhanced tumor-selectivity and activity.

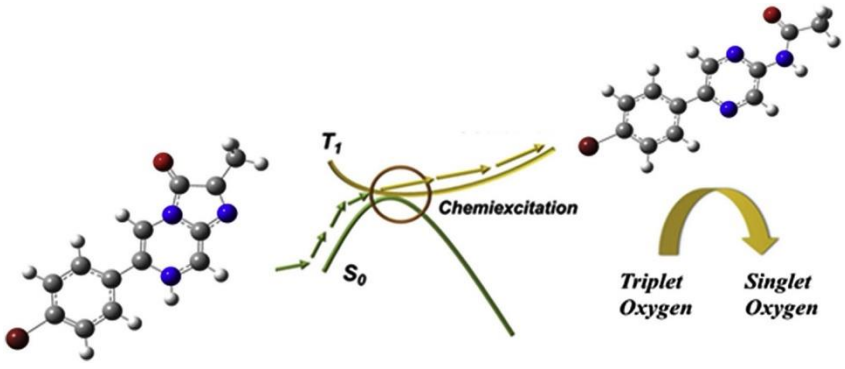

Fig.1. Proposed anti-tumor mechanism for the single-molecule Coelenterazine derivatives.

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References

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