Development of Novel Anticancer Compounds Based on Metabolic Products of Marine Bioluminescent Systems

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Cancer is one of the major health problems worldwide, with several patients still not escaping therapy failure and serious side-effects. Moreover, the development of new anticancer drugs presents also high rates of failure due to problems with efficacy or toxicity. Thus, it is essential that more effective and safe therapeutic agents are developed, while also focusing on more detailed investigations of their mode of action at preclinical stages.

Bioluminescence is the emission of light due to a biochemical reaction [1], being widespread in nature with focus on marine organisms. Among these organisms, the most common bioluminescent substrate is marine Coelenterazine, or Clz [1]. Following our previous development of self-activating photosensitizers for photodynamic therapy based on Clz [2,3], we have recently focused on the metabolic product of this reaction, Coelenteramine or Clm [4,5]. More specifically, we have synthesized various Clm analogs and evaluated their anticancer activity [4,5]. Among the studied compounds, we identified a bromophenyl-substituted analog with the most promising activity toward different cancer cell lines, such as gastric and lung [4,5], while presenting an interesting profile of safety [4]. Furthermore, it was also able to enhance the activity of a known chemotherapeutic agent, when used in combination [5].

Further research showed that this analog can activate effector caspases [4]. Moreover, synchrotron radiation-based FTIR, or SR- FTIR, microspectroscopy was also used to investigate its mechanism of action [6]. SR-FTIR is an interesting approach that allows to probe the biochemical composition of biological systems, including cells, with single-cell resolution [6]. This analysis showed that the anticancer activity of this analog is closely connected with cellular lipids, by affecting their organization and composition due to oxidative stress [6]. Interestingly, this effect was not observed in noncancer cells, helping to explain its profile of safety [6].

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