

Extended abstract

Dr. Edouard Delcroix research grant 2025

This extended abstract is part of the full report. Data of this specific final report are under embargo and are therefore not yet published online.

1. General information

Title of the idea	Yessotoxins in marine sea spray aerosols as anticancer agents due to their lysosome targeting: a comparative study in cancerous and non-cancerous human alveolar epithelial cell lines
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2. Dr. Edouard Delcroix research grant

Extended abstract

Oceans are a rich source of bioactive compounds, making them valuable for marine biodiscovery and pharmaceutical applications. Microalgae play a crucial role in this context by producing a variety of molecules, including phycotoxins. The cost-effective and environmentally sustainable cultivation of microalgae makes them highly promising for medical and industrial applications. In vitro and in vivo screenings have demonstrated that several compounds from microalgae possess significant bioactivities, including antioxidant, anti-inflammatory, anticancer, and antimicrobial properties.

Of particular interest in this research is yessotoxin (YTX), a phycotoxin with potential therapeutic applications. YTX has already shown potential for its use as anti-cancer drug using the in vivo B16F10 melanoma mouse model. Following local YTX application, YTX revealed a significant reduction in tumor growth, without any significant toxicity. In vitro studies have provided various insights into YTX's mode of action, but the exact mechanism still remains a mystery. In summary, cAMP, calcium, PDEs (phosphodiesterases), PKC and AKAP-149 as well as mitochondria, are involved. The role of each and the final effect depended on the cellular model studied. The in vitro evidence for YTX anti-cancer potential is poor and unclear, and the mechanistical cause for potential anti-cancer activity is unknown.

In our previous research, where we investigated YTX effect on human cells through various assays, we found that yessotoxins specifically and severely targeted the lysosomal membrane integrity. Cancer cells tend to have more fragile lysosomal membranes compared to healthy cells. Therefore, targeting lysosomes represents a novel approach for the induction of cancer-specific cell death, as cancer cells are more susceptible towards the lysosome damaging effects.

We hypothesized that the anti-cancer effect of YTX is due to its lysosome targeting. Thereby, cancer cells are more sensitive than non-cancerous cells, as cancer cells have weaker lysosomes. To validate the hypothesis, we carried out a comparative research in cancerous and non-cancerous human alveolar epithelial cell lines. A combination of various fluorescence and absorbance assays were applied, as well as RNA sequencing to gain insights into the mode of action.