LHRH-conjugated BinB pore-forming domain for specific targeting to breast cancer cells

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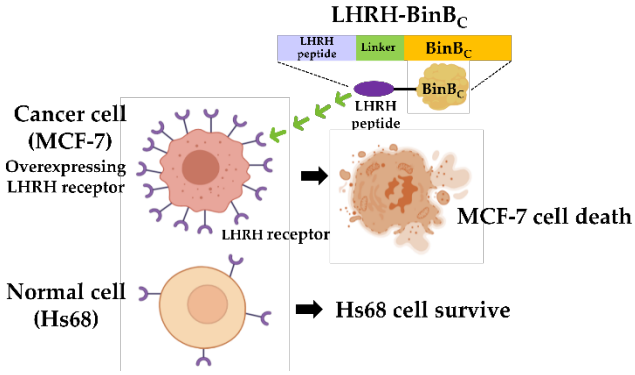
Abstract: Breast cancer has a high incidence in females around the world. Treatments of this cancer lack specificity and cause long-term side effects to the patients. As a result, pore-forming toxins from bacteria together with cell targeting peptides (CTPs) have been used as alternative anticancer agents. Here, we aim to increase the target specificity of BinB toxin derived from *Lysinibacillus sphaericus* by fusing a luteinizing hormone-releasing hormone (LHRH) peptide to its pore-forming domain (BinBc) to target MCF-7 (LHRH receptor positive) cells. Hs68 (LHRH receptor negative) cells were used for comparing the degree of LHRH-mediated target specificity. Parasporin-2 (PS2), a pore-forming toxin from *Bacillus thuringiensis* with strong cytotoxicity against human cancer cells, was also used as a positive control. The cytotoxic effects of BinB, PS2, BinBc, and LHRH-BinBc were monitored by MTT assay. We found that BinB at highest concentrations (16 μM) could reduce the viability of MCF-7 and Hs68 cells, whereas PS2 at 0.00125 to 0.08 μM and at 0.5 μM showed strong cytotoxic effects on MCF-7 and Hs68 cells, respectively. However, both BinBc and LHRH-BinBc caused no cytotoxic effects on Hs68 cells, but they could inhibit the proliferation of MCF-7 cells. Moreover, LHRH-BinBc was slightly more active to MCF-7 cells than free BinBc. Our results have suggested that BinBc represents an attractive biotoxin that can be engineered as a potential anti-cancer agent.

Graphical abstract:



Keywords: Binary toxin; C-terminal domain of BinB (BinBc); Parasporin-2 toxin; cell-targeting peptide; LHRH peptide

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