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Abstract
Palytoxin (PlTX), a large polyhydroxylated compound, is among the most potent non-peptide toxin in marine organisms known so far. The literature emphasizes the sodium/potassium pump (NaK) as the privileged target for PlTX when exerting its toxic effects. In this study, we focused on an undescribed species (Palythoa sp. Pc001), a coral species belonging to the genus Palythoa routinely cultivated in aquariums. We demonstrated that this species contains one of the highest yields of pure PlTX production ever found, 2.22 ± 0.41 mg PlTX per gram of wet Palythoa. Using molecular data combined with external morphology, we identified Palythoa sp. Pc001 as the sister species to Palythoa aff. clavata. Further, the clade of a symbiotic Symbiodinium sp. was characterised by DNA barcoding and pigment content. Molecular data showed that Palythoa sp. Pc001 contains generalist Symbiodinium belonging to clade C. This paper also describes for the first time the localisation of PlTX and Symbiodinium cells in tissues of a highly toxic Palythoa species. PlTX toxicity was assayed on 72 h-cultured murine and human cancer cells versus the normal human dermal fibroblast (NHDF ; PC C12300)cell line. Using MTT colorimetric assay and quantitative videomicroscopy, our results showed much higher in vitro cytotoxic activity on cancer cells (IC50 0.54 ± 0.05 x 10-12 M) than on non-cancerous ones (IC50 > 1 x 10-6 M). Such a strong differential effect has never been reported with respect to the most potent NaK ligands (cardiac glycosides) described so far. Moreover, PlTX displayed similar in vitro growth inhibitory activity in rodent and human cancer cells, although the NaK in rodents displays a double mutation in the ?1-subunit that usually decreases the sensitivity to others cardiac glycosides like ouabain, when compared to human cells. This work demonstrates, first, that picomolar concentrations of PlTX have significant higher cytotoxic effects on cancer cells than on non-cancerous ones, and secondly, that this in vitro antitumor effect would not be entirely relied onto its canonical targeting to the NaK ?-subunit. Thus, PlTX ranks amongst highly potent anti-cancer drugs as it targets cancers while potentially minimizing the drug's side effects on healthy cells.

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