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New cytotoxic C11 cyclopentenones from Okinawan ascidians -why the ascidians have the C11 cyclopentenones in quantity?-

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**New cytotoxic C₁₁ cyclopentenones from Okinawan ascidians
-Why the ascidians have the C₁₁ cyclopentenones in quantity?-**

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It has been amply demonstrated that ascidians are prolific producers of novel bioactive metabolites, which include a diverse array of alkaloids and a small number of acetogenins. A significant number of ascidian-derived compounds have entered into preclinical and clinical trials as antitumor agents. Ascidians of the family Didemnidae, e.g. *Diplosoma* species and *Lissoclinum* species, contain numerous biologically active and structurally unique secondary metabolites. A series of *exo*-allylidene-lactones, didemnenones, were first isolated from Didemniid ascidians (*Didemnum voeltzkowi* and *Trididemnum cf. cyanophorum*) by Fenical and Lindquist. The didemnenones have antitumor activity against leukemia cells, antimicrobial activity and antifungal action.

In this study, we explored new biologically active compounds in okinawan marine ascidians, a *Lissoclinum* sp., a *Diplosoma* sp. and two unidentified spp. These ascidians contained C₁₁ cyclopentenones (acetogenins) in common. The ascidian *Lissoclinum* sp. collected from Tarama Island contained three didemnenones and a dimer of didemnenone. The extract of the ascidian *Diplosoma* sp. from Hateruma Island included four new didemnenones and a halogenated nucleoside, along with an inseparable mixture of two known compounds (didemnenones A and B) and artificial methylacetals of didemnenones A and B. Another unidentified ascidian collected from Hateruma island contained unstable C₁₁ cyclopentenones at high concentration. These compounds which comprise a large part of the extracts of each ascidian showed moderate toxicity against fertilized sea urchin eggs or HCT116 cancer cells.

The producers of the compounds and their roles in the ascidians are the subjects of interest. Ascidians commonly associate with the unicellular prokaryotic alga *Prochloron* and/or other cyanophytes, which should be origins for most of bioactive metabolites from ascidians. Biological study on the symbiotic algae in the ascidians is also in progress.

In the meeting, isolation, structures, activities of the metabolites along with biogenetic relationship between the C₁₁ cyclopentenones will be presented.

