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インドネシア産海綿 Spongia ceylonensis から得られた新規ジテルペンの構造と破骨細胞形成阻害活性
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【Objective】In our continuous search for inhibitors of osteoclastogenic differentiation of murine RAW264 cells from marine organisms, the marine sponge Spongia ceylonensis collected in Indonesia showed significant inhibition. The bioassay-guided purification afforded four new nitrogenous spongian diterpenes 1-4, along with 8 known spongian diterpenes and one known norscopalane diterpene. 1,2)

【Results and discussion】The structures of 1-4 were established by 2D NMR spectra. Compounds 1-4 contain amide nitrogen replacing the oxygen of classical spongian diterpenes. The amide carbonyl groups of 1 and 2 occupy position 15 whereas those of 3 and 4 occupy position 16. The nitrogens of 2 and 4 are substituted with isopentyl residue mostly derived from the decarboxylated amino acid leucine. However the nitrogens of 1 and 3 are substituted with isobutyl residue mostly derived from the decarboxylated amino acid valine. Structure activity relationship of the isolated compounds revealed characteristic regioselective inhibition of RANK-RANKL interaction based on the position of ring D carbonyl group. A computational docking study against RANKL was exploited to predict a hypothetical mechanism for the inhibitory activity and explain regioselective inhibition.