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**PS-28 Translation Inhibiting Steroids from the Gorgonian *Isis hippuris***

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In our collaborative project for discovering new translation inhibitors, we could identify hippuristanol as a selective inhibitor against translation machinery.

On screening for translation inhibitors using bicistronic mRNA encoding firefly and *Renilla* luciferases, we found that a lipophilic extract of the gorgonian *I. hippuris* showed selective inhibition against cap-dependent translation. Biochemical studies by JP and coworkers identified that hippuristanol is the first selective inhibitor of eIF4A (RNA helicase),<sup>1</sup> a member of DEAD box family of RNA helicases. Hippuristanol was originally isolated as an antitumor constituent from the gorgonian *Isis hippuris*.<sup>2</sup> For our interest on structure-activity relationship, we tested totally 19 natural and synthetic analogs. As a result, stereochemistry at 22*R* spiroketal, secondary hydroxyl groups at C-3 and C-11 are indispensable for the activity. To examine the true producer of hippuristanol, we compared the extracts of the gorgonian and of symbiotic algae with LCMS. It is likely that hippuristanol is produced by the algae.

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2. Higa, T.; Tanaka, J.; Tsukitani, Y.; Kikuchi, H. *Chem. Lett.* **1981**, 1647-1650.