

**O-42: STRUCTURAL CHARACTERIZATION OF ENIGMAZOLE B, A SPONGE MACROLIDE WITH DIFFERENTIAL CYTOTOXIC ACTIVITY TOWARD CELLS WITH A MUTANT FORM OF c-KIT**

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c-KIT, a type III transmembrane receptor tyrosin kinase, mediates pleiotropic biological effects such as growth and development of mast cells, melanocytes, hematopoietic stem cells, and interstitial cells. Mutations in codon 816 of the catalytic domain of human c-KIT have been implicated in a verity of malignancies including leukemia, germ cell tumors, and mastocytosis. At present, no inhibitor has been identified that impairs the activity of this mutant c-KIT. A screen was developed to find compounds that differentially inhibited cells expressing a mutant form of c-KIT relative to wild-type c-KIT. During our study of an extract from the Papua New Guinea marine sponge *Cinachyrella enigmatica*, a new macrolide named enigmazole B was isolated, which exhibited significant activity in the c-KIT assay. The structure of enigmazole B was elucidated by spectral analyses to be a phosphate substituted 16-membered macrolide. To determine the absolute stereochemistry, the phosphate group was removed by treatment with an antarctic phosphatase, followed by chemical derivatization and application of the advanced Mosher method. In this presentation, details of the isolation, spectroscopic characterization, structure elucidation, and biological activities of enigmazole B will be described.