

Search for Unexplored Natural Products Targeting on Signaling Molecules

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Natural products continue to play an important role in the discovery of low-molecular weight lead compounds for new-drug developments. During our studies on search for bioactive natural products from unexplored natural resources targeting on signaling molecules, here we describe two subjects: 1) Isolation of natural products from myxomycetes; and 2) Search for natural products with TRAIL-receptor inducing effects.

1) Natural products from myxomycetes: The Myxomycetes (true slime molds) are an unusual group of primitive organisms that may be assigned to one of the lowest classes of eukaryotes. Spore germination experiments were studied of hundreds of field-collected myxomycetes collected in Japan and succeeded in laboratory culture of plasmodia of several myxomycetes in a practical scale for natural products chemistry studies. Pyrroloiminoquinones, polyene yellow pigments, and a peptide lactone were isolated from cultured plasmodia of myxomycetes, while new naphthoquinone pigments, cycloanthranilylprolines, tyrosine-kinase inhibitory bisindoles, and a cytotoxic triterpenoid aldehyde lactone were also isolated from field-collected fruit bodies of myxomycetes.

2) Natural products with TRAIL-receptor inducing effects: A series of cytotoxic sesquiterpene-dimers, parviflorenes A - J, were isolated from *Curcuma parviflora* (Zingiberaceae). The major constituent, parviflorene F, was revealed to enhance the gene expression and protein production of TRAIL-R2 and augment the activity of caspase 8 and 3 on the basis of DNA microarray, real time PCR, and Western blotting studies. TRAIL-R2 is one of death receptors involved in signaling mechanisms inducing apoptosis. Parviflorenes may be expected as a useful compound related to TRAIL signaling pathways and apoptosis inducement.