NATIONAL CANCER INSTITUTE

U.S. TO SCREEN MARINE ORGANISMS FOR DRUGS

BETHESDA, Md.—The National Cancer Institute (NCI) will soon award two important contracts directed toward the discovery of potential anti-tumor products from marine organisms. Although in the past NCI has tested many voluntarily submitted marine extracts, this represents the first time it will be sponsoring collection.

One of the two contracts will call for the screening of organisms from shallow water (under 100 feet). The other applies to deep water (over 100 feet). Both call for the acquisition of a total of 1,000 organisms a year for five years. The shallow-water contract will concentrate on the Indo-Pacific region; the geographic area to be covered by the deep-water contract will be less specified. According to Gordon Cragg of the Natural Products Branch of NCI's Developmental Therapeutics Program (DTP), by the beginning of this month DTP should choose which companies will fill the contracts. Actual collections should begin by the end of the year.

"The NCI has had an interest in marine natural products for 15 years," says Cragg. During that time the Institute has tested some 15,000 to 20,000 extracts.

According to NCI, compounds with anti-tumor activity have already been isolated from sponges, tunicates, bryozoans, nudibranch egg-masses, corals, and algae. Cragg says NCI's new collections will focus on these invertebrates, as well as mollusks. "We want to spread our net fairly widely," he concludes.

Cragg estimates that NCI will have preliminary results on crude extracts from the collections within a year or two; isolation of pure products from which to make potential drugs could take 5–10 years. Compounds will be tested at NCI's Frederick Cancer Research Facility near Bethesda on a "disease oriented" *in vitro* panel of more than 20 human cancer cell lines. Trials will initially focus on lung cancer, but will include other solid tumors like colon and breast cancers. The colorimetric, growth-inhibition assay, to be performed in microculture plates, is based on reduction of a tetrazolium salt to a colored formazan inside viable cells. When a substance is demonstrated effective on one or more cell types, *in vivo* animal studies will be done.

Currently, only one product derived from a marine organism is in U.S. clinical trials: didemnin B. Now in late stages of phase I testing, the

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Trididemnum, a colonial tunicate from which the anti-tumor extract didemnin B is isolated, appears as thin, leathery patches on rocks or coral in the lower left and upper right of this photograph.

drug is derived from an unclassified tunicate from the genus *Trididemnum*, originally collected in the Western Caribbean sea in 1978 by Kenneth Rinehart (University of Illinois, Urbana-Champaign). Didemnin B has shown anti-viral and immunosuppressant activity in addition to *in vitro* activity against leukemia and melanoma cells.

According to Rinehart, almost all the work in testing marine organisms for anti-cancer products occurs in the U.S. and Japan. SeaPharm (Princeton, NJ) in the U.S. specializes in this approach, while in Japan the Suntory Institute of Biomedical Research

(Osaka) and the Mitsubishi-Kasei Institute of Life Sciences (Tokyo) have the same focus.

NCI regards large-scale collection and screening as an important complementary strategy to "rational" drug development. Consequently, NCI's Developmental Therapeutics Program is not limited to scouring the sea for potential drugs. It plans to extract chemicals from some 20,000 plants that will be collected in rain forests over the next five years; over the same period it also intends to isolate and cultivate 1,000 blue-green algae from marine and terrestrial environments. —Arthur Klausner

TISSUE CULTURE ASSOCIATION

PROTEIN PHOSPHORYLATION: THEME & VARIATIONS

CHICAGO—A central theme at this year's meeting of the Tissue Culture Association was articulated by Paul Greengard (Rockefeller University, NY): "Protein phosphorylation must have arisen very early in the evolution of cells, since it has been adapted in a myriad of ways to mediate the action of a wide variety of regulatory substances."

Many growth factor receptors and viral oncogenes possess a protein phosphorylation activity. They are tyrosine-specific protein kinases (known as PTKs). Tony Hunter (Salk Institute, La Jolla, CA) discussed recent results from his laboratory that bear on the important question of the role of this activity in controlling cell growth. Normally, tyrosine phospho-