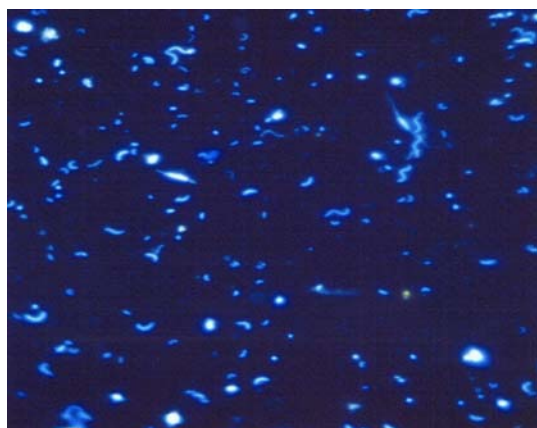


Research Project 3: Pharmaceutical Lead and Pharmacological Probe Discovery

Investigation several years ago of a phenomenon called “swimmers itch” among local watermen, led to the discovery of a set of potent tumor promoters, the lyngbyatoxins, produced by the marine cyanobacterium *Lyngbya majuscula*. Prompted by this discovery, a systematic investigation of a representative cross section of cyanobacteria has yielded a plethora of biologically active compounds in the intervening years. Some of these unique compounds, e.g. curacin A, the dolastatins and the cryptophycins, are under development as chemotherapeutic agents for the treatment of various cancers, while others have been identified as potent environmental toxins, e.g. the microcystins, the anatoxins and cylindrospermopsin.



Microbial diversity in a drop of seawater. (Hawai'i Institute of Marine Biology)

During the past decade genomic studies have revealed a previously unimagined diversity of microbes in ocean waters, ocean sediments and as symbionts in marine invertebrates. Bringing to bear modern genomic tools, contemporary isolation and cultivation techniques as well as state-of-the-chemistry tools, this project seeks to characterize biologically active small molecules from marine microbes and microalgae. Less than 1% of all microbes have been brought into laboratory culture thus far and the bulk of known of known microbial chemistry stems from that same fraction. It is our hypothesis that by applying these new techniques, we can expand the taxonomic range of organisms that can be cultured and discover significant new chemistry as it applies to human health.

One area of emphasis within this project is the search for new antibacterials and antifungals. In this therapeutic area, the urgency and need appear to be the most immediate in view of the global spread of multi-drug resistant human pathogens on the one hand and the waning private sector research investment in antibiotics discovery on the other.

In collaboration with other members of the Natural Products Program at the Cancer Research Center of Hawaii, a second area of emphasis within this project is the discovery of new agents effective in modulating signal transduction pathways important for tumor development and metastasis, with the goal of discovering new biologically active small molecules as tools for use in pharmacology and as leads for cancer treatment.

For more information about the Pacific Research Center for Marine Biomedicine, visit our website at <http://www.prcmb.hawaii.edu/index.asp>.