

## Bankhead-Coley Cancer Research Program

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*2008 Program  
Bridge (1-year project)*

**Project Title:** Discovery of Novel Antitumor Agents Effective Against Pancreatic Cancer

**Project Summary:** The overall objective of this grant is to discover marine natural products that will contribute to the development of novel therapeutic agents for the treatment of pancreatic cancer. Although eleventh in occurrence, pancreatic cancer is the fourth cause of cancer death in the U.S., with over 33,000 deaths predicted for 2008. Less than 5 percent of patients diagnosed with pancreatic cancer survive five years post diagnosis.

Natural products have proven to be useful in the development of cancer therapeutics, with over 78 percent of the drugs approved for use against cancer being either natural products themselves or compounds based upon natural products. Examples include: the Vinca alkaloids, Taxol, irinotecan, topotecan, and doxorubicin. Gemcitabine, the treatment of choice for pancreatic cancer, is a simple analog of a sponge-derived nucleoside. The research group at Harbor Branch Oceanographic has pioneered the discovery of agents useful in the treatment of cancer from organisms living in deep-water habitats. They have contributed significantly to the discovery and development of marine natural product drug candidates including discodermolide, dictyostatin, ecteinascidin 743, and leiodermatolide.

In the current grant, we will continue our research program aimed at the discovery and development of new natural products with potential in the treatment of pancreatic cancer. The various components of this research include:

- 1) Screening of the HBOI collection of marine extracts against a panel of pancreatic tumor cell lines and in assays targeting aberrant signaling associated with pancreatic cancer.
- 2) Bioassay-guided fractionation, spectroscopic identification, and pharmacological studies on the purified natural products, with the final goal of identifying lead structures for development as cancer therapeutics. The compounds discovered will also have utility in other cancers where similar changes in signaling and cell cycle control are in play.