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**NSF-NIEHS Oceans & Human Health Center Role: External Advisory  
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### **Education**

- B.A. in Chemistry (with Honors) University of California, Santa Cruz, CA
- Ph.D. in Organic Chemistry Columbia University, New York City, NY

### **Research Interests**

My research efforts over the past decade have evolved into several programs that are distinct in focus, yet coalesce into an overriding theme that include molecular genetic, biochemical and bioorganic chemical studies of microbial natural product biosynthesis. Metabolic engineering and combinatorial biosynthesis are powerful approaches for harnessing the tremendous metabolic capabilities of microorganisms, including primary and secondary pathways. New genomic-based technologies are enhancing considerably our ability to understand and manipulate complex biosynthetic systems and will enable vast new opportunities in medicine and industry. My laboratory is exploring fundamental aspects of the systems described below, as well as pursuing drug discovery opportunities in the area of infectious diseases and cancer.

**Molecular genetic analysis** of terrestrial and marine natural products biosynthesis. A large number of novel natural products are being discovered from terrestrial and novel marine microbes. These exciting sources of new chemical entities will provide a wealth of unique information about the organization,

structure, and regulation of genes involved in secondary metabolism. The focus over the past five decades has been entirely on secondary metabolite pathways of terrestrial microorganisms. Since novel classes of microorganisms that produce important secondary metabolites are being discovered from marine sources, it is clear that there will be exciting new information to be learned from these novel organisms at the genetic level. Our focus currently includes marine cyanobacteria, actinomycetes and myxobacteria.

**Biochemistry, enzymology, and bioorganic chemistry** of proteins involved in biosynthesis of terrestrial and marine natural products. The unique chemistry operating to construct complex terrestrial and marine natural products provides a certain and virtually limitless source of novel enzymes and resistance proteins. The genes that specify the biosynthesis of these compounds will provide a readily accessible source of novel biocatalysts that perform interesting and potentially novel chemical reactions. As new classes of marine natural products are elucidated, the corresponding organisms identified and the gene clusters characterized, it will be possible to use the versatile tools of genetic engineering to over-express, purify and characterize fully the unique chemical catalysts that have evolved in the terrestrial and marine environments.

**Combinatorial biology** of marine natural product biosynthetic genes. Over the past few years it has become evident that powerful new molecular methods exist for the reconfiguration and expression of genes involved in natural product biosynthesis. There is huge potential to create novel organic molecules through deliberate in vivo and in vitro engineering of these pathways for production of human and veterinary pharmaceuticals, specialty chemicals, and high value biomaterials. Relatively few systems exist that can be readily tapped to provide the needed metabolic diversity for the creation of new pathways. Perhaps the single most important new source of this metabolic potential will be provided by natural product biosynthetic genes derived from marine microorganisms. We will continue to pursue aggressively novel metabolic pathways from micro- and macro-organisms, including sponge symbionts and other invertebrates.

## Representative Publications

Podust, L.M., Bach, H., Kim, Y., Lamb, D.C., Arase, M., **Sherman, D.H.**, Kelly, S.L. and Waterman, M.R. 2004. Comparison of the 1.85 Å structure of CYP154A1 from *Streptomyces coelicolor* A3(2) with the closely related CYP154C1 and CYPs from antibiotic biosynthetic pathways. *Prot. Sci.* 13:255-68. [Pub Med Link](#)

Salomon, C. E., Magarvey, N.A. and **Sherman, D.H.** 2004. Merging the potential of microbial genetics with biological and chemical diversity: An even brighter future for marine natural product drug discovery. *Natural Product Reports* 2004 21:105-121. [Pub Med Link](#)

Kim, B.S., Reynolds, K.A. and **Sherman, D.H.** 2004. An efficient method for creation and functional analysis of libraries of hybrid type I polyketide synthases.

*Prot. Eng. Des. Sel.* 17:277-284. [Pub Med Link](#)

Chang, Z., Sitachitta, N., Rossi, J.V., Roberts, M.A., Flatt, P.M., Jia, J., Gerwick, W.H. and **Sherman, D.H.** 2004. Biosynthetic pathway and gene cluster analysis of curacin A, an anti-tubulin natural product from the tropical marine cyanobacterium *Lyngbya majuscula*. *J. Nat. Prod.* 67:1356-1367. [Pub Med Link](#)

Srinivasan A., Bach H., **Sherman, D.H.** and Dordick, J.S. 2004. Bacterial P450-catalyzed polyketide hydroxylation on a microfluidic platform. *Biotechnol. Bioeng.* 88(4):528-535. [Pub Med Link](#)

Magarvey, N.A., Keller, J.M., Bernan, V., Dworkin, M., and **Sherman, D.H.** 2004. Isolation and characterization of novel marine actinomycete taxa rich in secondary metabolites. *Appl. Env. Microbiol.* 70(12):7520-7529. [Pub Med Link](#)

Hildebrand, M., Waggoner, L.E., Liu, H., Sudek, S., Allen, S., Anderson, C., **Sherman, D.H.** and M. Haygood. 2004. *bryA*: an unusual modular polyketide synthase gene from the uncultivated bacterial symbiont of the marine bryozoan *Bugula neritina*. *Chem. Biol.* 11(11): 1543-1552. [Pub Med Link](#)

Jeong, J.C., Srinivasan, A., Grünschow, S., Bach, H., **Sherman, D.H.**, and Dordick, J.S. 2005. Exploiting the reaction flexibility of a type III polyketide synthase through in vitro pathway manipulation. *J. Am. Chem. Soc.* 127(1):64-5. [Pub Med Link](#)

Nishizawa, T., Aldrich, C.C., and **Sherman, D.H.** 2005. Molecular Analysis of the Rebeccamycin L-Amino Acid Oxidase from *Lechevalieria aerocolonigenes* ATCC 39243. *J. Bacteriol.* 187(6):2084-92. [Pub Med Link](#)

Fortman, J.L., **Sherman, D.H.** 2005. Utilizing the Power of Microbial Genetics to Bridge the Gap Between the Promise and the Application of Marine Natural Products. *Chembiochem.* 2005 May 6;

More Info:

Diving for Drugs-Discovery Channel Interview

<http://www.exn.ca/dailyplanet/view.asp?date=2/8/2005%20>

[http://sitemaker.umich.edu/medchem/medchemfaculty/david\\_h.sherman](http://sitemaker.umich.edu/medchem/medchemfaculty/david_h.sherman)

<http://www.sitemaker.umich.edu/shermangroup>

<http://www.lifesciences.umich.edu/institute/labs/sherman/people.html>