UCSD Scientists Sequence Genome of Marine Organism Producing Promising Disease-Fighting Agents

June 13, 2007 |

Bacteria discovered in Bahamian mud has potential as producer of natural antibiotics and anticancer products

Scientists at UC San Diego's Skaggs School of Pharmacy and Pharmaceutical Sciences and the Scripps Institution of Oceanography have solved the genomic puzzle of an ocean-dwelling organism with the potential to produce compounds that potentially treat diseases such as cancer.

Daniel Udwary, Ph.D., and Bradley Moore joined colleagues at Scripps and the Department of Energy's (DOE) Joint Genome Institute in successfully sequencing the genome of *Salinispora tropica*. The decoding opens the door to a range of possibilities for isolating and adapting potent molecules employed by the marine organism for chemical defense, communication and to scavenge for nutrients.

The results were released this week in the early online edition of the *Proceedings of the National Academy of Sciences*.

Salinispora was discovered in 1991 by Scripps Oceanography's Paul Jensen and William Fenical in shallow ocean sediment off the Bahamas. The bacterium produces compounds that have shown promising signs for treating cancers. Its product, "salinosporamide A," is currently in human clinical trials with Nereus Pharmaceuticals of San Diego for treatment of multiple myeloma, a cancer of plasma cells in bone marrow, as well as solid tumors.

"By sequencing *Salinispora tropica* we are now able to look in greater detail at this organism and potentially pull out some of the other compounds from the gene clusters that may make highly potent anticancer agents," said Moore, a professor with UC San Diego's Skaggs School of Pharmacy and Pharmaceutical Sciences and the Scripps' Center for Marine Biotechnology and Biomedicine. "It's exciting to be able to use this genomic information to maximize the discoveries from this prolific organism."

Much of the anticipation of producing new medicines from *Salinispora* comes from its potential to augment the current arsenal of antibiotics, many of which are ineffective against increasing

numbers of drug-resistant bacteria. More than half of the natural antibiotics now used clinically are derived from the *Streptomyces* genus, the land-based relatives of *Salinispora* that are considered the kings of antibiotic-producing organisms.

Having achieved genome sequencing success, Moore and his colleagues can now move into genetic engineering research, such as manipulating the machinery inside the bacterium to potentially yield new derivatives of compounds such as salinosporamide A. Other possibilities include using the information to increase compound manufacturing capabilities and generating new structures based on genomic designs.

"With the genome information in hand, we now understand the molecular basis for how nature synthesizes (salinosporamide A), which is allowing us to re-engineer its biosynthetic pathway," said Moore.

Sequencing the genome revealed several previously unknown aspects of *Salinispora tropica.* For example, while observations in similar bacteria revealed that typically 6- to 8-percent of the organism's genome is dedicated to producing molecules for antibiotics and anticancer agents, *Salinispora tropica's* genome showed an impressive 10 percent, much to the researchers' delight. The scientists pinpointed 17 gene clusters scattered throughout the organism's genome as responsible for producing the 10 percent.

"If we know the genetic roadmap of their potential, we can read the sequence and the DNA to predict what chemicals are being made," said Moore. "This is a way to mine the genomes for new chemical structures and new biology, with potential in a human health context."

Advances by Fenical's laboratory in deciphering the chemical structures of natural *Salinispora* products were key for Moore and the Joint Genome Institute (JGI) in solving the genome structure of *Salinispora tropica*. Indeed, the traditional "shotgun" approach, in which pieces of the genome are scrambled into small sections and rebuilt, failed to solve the genome puzzle. Instead, information about the natural chemistry of the organism helped close the sequencing gap, believed to be a first.

Current studies are concentrating on solving the genome of *Salinispora arenicola,* a related species also found in tropical sea sediment.

In addition to Udwary, Moore, Fenical and Jensen, co-authors of the research paper include Lisa Zeigler and Ratnakar Asolkar of Scripps Oceanography and Vasanth Singan and Alla Lapidus of JGI. The research was supported by the National Oceanic and Atmospheric Administration, the National Institutes of Health and JGI.

# # #

Media Contact: Debra Kain, 619-543-6163, ddkain@ucsd.edu

Share This Article

Related News

UC San Diego Health Begins Treating Multiple Myeloma with CAR T-cell Therapy
6/3/2021

Social Justice as Part of the Remedy for What Ails Us
6/3/2021

Diet Plays Critical Role in NASH Progressing to Liver Cancer in Mouse Model
6/1/2021

Noted Researcher and Scientific Leader Jack E. Dixon Retires
5/27/2021

View All News >

Follow Us

Follow @ucsdhealth