Baden shares saga of translation — from toxin to treatment and prevention

By Audrey Pinto

For veteran NIEHS grantee Daniel Baden, Ph.D., a William R. Kenan Jr. distinguished professor of marine sciences and director of the Center for Marine Science *(http://uncw.edu/cms/)* at the University of North Carolina Wilmington, Aug. 31 was a noteworthy day. He presented the inaugural lecture in Duke Environment Hall, the new home of the Duke University Nicholas School of the Environment, opening the 2014 Integrated Toxicology and Environmental Health Program (ITEHP *(http://sites.nicholas.duke.edu/envhealth/)*) lecture series with an inspiring account of research translation from bench to bedside to public health.

"Translational science is inherently interdisciplinary," Baden told the audience. He also observed that with climate change, the oceans are getting warmer and algal blooms thrive and multiply in warm waters. (Photo courtesy of Steve McCaw)

In his presentation, Baden *(http://uncw.edu/bio/faculty_baden.html)* shared the progress his team and collaborators worldwide have made to isolate new chemicals from *Karenia brevis (K. brevis)*, the dinoflagellate that produces the brevetoxins responsible for Florida red tide. He explained that nontoxic compounds isolated from the organism hold promise for countering the effects of red tide exposure, for treating cystic fibrosis, chronic obstructive pulmonary disease, and other forms of respiratory illness, as well as serving as a potential agent for drug delivery.

Duke University professor Edward Levin, Ph.D., who directs the lecture series, introduced Baden and moderated the question-and-answer session following his talk. (Photo courtesy of Steve McCaw)

In many ways, Baden, with his long and productive relationship with NIEHS, reflects the vision and goals outlined in the NIEHS 2012-2017 strategic plan for innovative cross-disciplinary translational research.

Serendipity at the bench

To illustrate how his team found this new therapeutic agent, Baden took the audience on a journey through scientific discovery, exploration, and the translation of research findings. He shared his belief that scientists must be open to new possibilities and that scientific discoveries should be applied to improving public health.

NIEHS health scientist administrator Annette Kirshner, Ph.D., center, was part of an audience that nearly filled the new auditorium. She was the program administrator for much of Baden's NIEHS-funded work when he was at the University of Miami. (Photo courtesy of Steve McCaw)

"We had a serendipitous moment when we found that one natural product from *K. brevis*, called brevenal, prevented, reduced, or reversed bronchoconstriction caused by other toxins from the same organism," he explained. "This was a baffling finding, but after several experiments, we confirmed that brevenal did indeed act as an antitoxin that also promoted mucociliary clearance, increased anti-inflammatory response, and promoted whole lung clearance."

In a public-private partnership, the team is now working with a pharmaceutical company to begin phase I trials, to move this new therapeutic into the Cystic Fibrosis Therapeutics pipeline, because of its potential to restore ion transport and to regulate mucus.

Transforming the mysteries of the ocean into marketplace miracles

"As our research progressed," Baden continued, "we found other therapeutic applications that have now been licensed. For example, brevisin –– another polycyclic ether isolated from the dinoflagellate *K. brevis* –– has no apparent

toxicity and moves rapidly across membranes, including the blood-brain barrier. This compound, trademarked Escortin, has huge importance for carrier-mediated chemotherapy, targeted drug delivery, and brain cancer."

Baden noted that brevenal has many more potential applications, including therapeutic and preventive agents that could be used in rescue packs for people at beaches, during red tide outbreaks, and for pretreatment. Through a compassionate use permit from the U.S. Food and Drug Administration, the Mote Marine Laboratory in Florida used brevenal to counter the toxic effects of red tide in manatees. The U.S. Department of Defense has also expressed interest in its inhaled mucociliary clearance properties.

The team continues its research into structure activity of the brevenal receptor, as reported in an NIEHS-funded paper published in March by the journal Marine Drugs. Work is also ongoing to streamline production of brevenal and brevisin, for trials of safety and efficacy, as well as clinical trials.

Environment Hall (http://nicholas.duke.edu/news/duke-open-new-40-million-environment-hall-april-10) was designed to meet or exceed the criteria for the U.S. Green Building Council's LEED platinum certification — the highest level of sustainability. (Photo courtesy of Steve McCaw)

Baden concluded his presentation by reiterating the importance of opening our minds to new possibilities. "Our oceans are filled with scientific potential, renewable resources, and treasures yet to be tapped," he said.

Citation: Goodman A, McCall JR, Jacocks HM, Thompson A, Baden D, Abraham WM, Bourdelais A. *(http://www.ncbi.nlm.nih.gov/pubmed/24686558)*
2014. Structure activity relationship of brevenal hydrazide derivatives. Mar Drugs 12(4):1839-1858.

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The Environmental Factor is produced monthly by the National Institute of Environmental Health Sciences (NIEHS) *(http://www.niehs.nih.gov/)*
, Office of Communications and Public Liaison.

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