

Dolphin mouths house ‘the dark matter of the biological world’

By Nicoletta Lanese

Researchers have identified two deep lineages of bacteria that have never been characterized before — and they found them in a dolphin’s toothy grin.

These deep lineages are known as phyla. A phylum is a broad taxonomic rank that groups together organisms that share a set of common characteristics due to common ancestry. The discovery of two bacterial phyla, as well as additional novel genes and predicted products, provides new insights into bacterial diversity, dolphin health and the unique nature of marine mammals in general, said David Relman, MD, professor of medicine and of microbiology and immunology at the School of Medicine.

A paper describing the research was published Nov. 16 in *Current Biology*. Relman, who holds the Thomas C. and Joan M. Merigan Professorship, is the senior author. The lead author is Natasha Dudek, a graduate student at UC-Santa Cruz.

The U.S. Navy’s Marine Mammal Program reached out to Relman more than 10 years ago for help in keeping its dolphins healthy. The animals are highly trained and perform missions at sea.

Previous research by Relman’s group, in collabora-

tion with the Marine Mammal Program, revealed a surprising number of never-before-seen bacteria in dolphin and other marine mammal samples, particularly those swabbed from the dolphins’ mouths, said Relman, who is also chief of infectious diseases at the Veterans Affairs Palo Alto Health Care System. Some of the bacteria found in the current study are affiliated with poorly understood branches of the bacterial tree.

Striking gold

“These organisms, about which we have known just a tiny bit, are basically the dark matter of the biological world,” he said. “We knew there was gold in those dolphin mouths, and we decided it was time to go after it with more comprehensive methods.”

In the new study, the researchers identified bacterial lineages by reconstructing their genomes from short bits of DNA. The genome of a given cell serves as its blueprint and contains all its operating instructions, encoded in DNA. The researchers named one of the newly identified lineages Delphibacteria, in honor of the dolphins (Delphinidae is the Latin name for oceanic dolphins).

By looking at the genes encoded in the genomes of Delphibacteria representatives, the researchers gained insight into the bacteria’s lifestyle. The bacteria are predicted to express a property called denitrification that may affect dolphins’ oral health: The chemical process can cause inflammation and could be connected to gum disease. Denitrification also occurs in plaque on human teeth, suggesting that something about mammalian mouths selects for this process.

Putting puzzle together

The researchers differentiated between bacteria and predicted their behavior by looking broadly at their genomes. “What we do first is shear the DNA

into a bunch of little bits and pieces, the mix of DNA is sequenced and we then try to figure out how the genomes were originally assembled,” said Dudek. If a gene is one piece of a puzzle, the researchers put together the whole puzzle. This approach has been spearheaded by collaborator and study co-author Jillian Banfield, PhD, at UC-Berkeley.



David Relman

By taking this approach, the researchers spotted bacteria that had long eluded characterization. They also identified a number of unusual proteins, including previously unknown forms of Cas9. Cas9 proteins are part of a bacterial immune system called CRISPR-Cas, a system well-known for its use in gene-editing technology. Scientists can use this system to modify genomes and control how cells function. It can be used to turn genes on or off, replicate human diseases in animals and possibly prevent disease in humans.

“Typically, people are interested in small Cas9 proteins that might be easy to manipulate and deliver into cells,” said Relman. “These are the opposite — they’re enormously big.” Different structures in the genes that encode these proteins account for the size difference, and the researchers suggest these large Cas9 proteins have different properties from those known before. Dudek plans to pursue this line of research further.

The study also feeds nicely into ongoing work in Relman’s lab. A large, comparative study is underway to investigate how adaptation to life in the sea might affect marine mammal microbiomes. Beyond discovering and characterizing novel bacteria, Relman wants to apply his research to conservation.

“Marine mammals are becoming increasingly endangered,” he said. “They are sentinel species for the health of the sea, and the more we can understand their biology, the better we can anticipate changes in the health of their environment.”

Other Stanford co-authors are postdoctoral scholars Christine Sun, PhD, and Daniela Aliaga Goltzman, PhD, and former research associate Elisabeth Bik, PhD.

Researchers from UC-Berkeley also contributed to the study.

The Office of Naval Research supported the study. Stanford’s departments of Medicine and of Microbiology and Immunology also supported the work. **ISM**



Studying the bacteria found in the mouths of dolphins is giving researchers insight into dolphin health and the unique nature of marine mammals in general.

Stanford Medicine magazine showcases new approaches in pediatric care

By Patricia Hannon

There’s something special about children and how they approach their world — wide-eyed, curious, energetic, creative, playful and trusting. They’re also vulnerable, and that’s why they count on the adults in their lives to take good care of them.

But when they’re sick, that can be a challenge, especially for the medical professionals who are trying to make them better in an environment that’s traditionally been designed around adult care.

The new issue of *Stanford Medicine* magazine, which was produced in collaboration with Lucile Packard Children’s Hospital Stanford, shows how physicians, researchers and caregivers are transforming pediatric care to ensure that treatment puts children — and their families — at the center of their health care more than ever before.

Lloyd Minor, MD, dean of the School of Medicine, writes in his letter to readers that finding better and more precise medical options for children depends on a close “collaboration between Stanford Medicine researchers and clinicians who routinely bring medical advances from their laboratories to the benefit of our pediatric patients.” Caring for children, he said, calls for special tools and strategies.

“The risk-to-benefit relationship

is very different in children,” Pejman Ghanouni, MD, PhD, assistant professor of radiology, said in a story about how he and other physicians are reimagining an adult-focused ultrasound treatment to successfully shrink some bone tumors in children. The procedure prevents children from having to undergo invasive surgery or radiation treatments that can be more harmful to them than to adults. “Kids are not small adults, so we really need different treatment options,” he said.

Hospital expansion

Lucile Packard’s belief in the importance of family and nature in the healing process is reflected in every corner of the 521,000-square-foot addition to the children’s hospital that bears her name. The issue provides an inside look at the new facility, where every room has a planter box outside it and a view of a sweeping garden where children can play. The patient rooms are designed for families to use as gathering spaces, with extra sleeping space for two people. Animal sculptures and mosaics help families find their way around the hospital.

The facility includes the most advanced equipment and technologies to improve diagnostics and treatment with children and teens in mind.

Also featured in this pediatrics-

themed issue:

- A story about a promising immunotherapy treatment known as CAR T-cell therapy, which relies on the use of a patient’s own genetically modified immune cells to track down and attack leukemia cells.

- A look at how the shortage of affordable housing in the Bay Area puts the health care of children at risk, and how Stanford pediatricians are working with social service and housing agencies to help tackle the problem.

- An interview with Save the Children CEO Helle Thorning-Schmidt, who said that for her organization, “There is nothing more urgent than protecting children in armed conflict.”

- A story about how virtual reality is being used to calm anxieties in fearful children and teens undergoing sometimes frightening medical procedures, as well as to help them understand their illnesses and how their physicians plan to treat them.

The issue also includes a look at how Joseph Woo, MD, professor and chair of cardiothoracic surgery, and his colleagues are increasingly using a patient’s own tissues to repair, rather than replace, damaged aortic valves to give patients better long-term outcomes.

In addition, the issue includes an excerpt from a book by wilderness medicine experts Paul Auerbach, MD,



a professor of emergency medicine at Stanford, and Jay Lemery, MD, an associate professor of emergency medicine at University of Colorado. In *Enviromedics: The Impact of Climate Change on Human Health*, the authors lay out the adverse health effects linked to global warming and call on physicians to lead the way in raising awareness of the problem.

The magazine is available online at <http://stanmed.stanford.edu>. Print copies are being sent to subscribers. Others can request a copy at 723-6911 or by sending an email to medmag@stanford.edu. **ISM**