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Ripple Marks

The Story Behind the Story

BY CHERYL LYN DYBAS

IT'S CATCHING

Leukemia, Third Known Transmissible Cancer, Infects Soft-Shell Clams

It sounds like the plot of a summer horror flick: malignant cells floating in the sea, ferrying infectious cancer everywhere they go.

The story is all too true, say scientists who've made a discovery they call "beyond surprising."

Outbreaks of leukemia that have devastated populations of soft-shell clams (*Mya arenaria*) along the east coast of the United States and Canada are the result of cancerous tumor cells making their way from one clam to another. The finding was reported in 2015 in the journal *Cell*.

"The evidence indicates that the tumor cells themselves are contagious—that they can spread from one clam to another in the ocean," says biochemist and immunologist Stephen Goff of Columbia University, a co-author of the *Cell* paper along with Michael Metzger of Columbia, and Carol Reinisch and James Sherry, both of Environment Canada. "The genotypes of the tumor cells do not match those of the host animals that acquire the disease," Goff says. "Instead, they are all derived from a single lineage of tumor cells."

THE PLOT THICKENS: THE CLAM

Soft-shell clams—also called steamers, longnecks, and Ipswich clams—are popular in seafood markets and on restaurant menus.

For those who favor clams on the half shell, the researchers believe that clam leukemia can't be contracted by eating potentially infected clams—nor by swimming in the ocean.

In the western Atlantic Ocean, *Mya arenaria*'s range extends from the Canadian to the US southeastern coastline. The species is also found in the eastern Atlantic along the UK coast, as well as in the North Sea's Wadden Sea, where it's the dominant large clam.

Mya arenaria originated in the Pacific Ocean during the Miocene 23.03 to 5.33 million years ago. In the early Pliocene from 5.33 million to 2.58 million years ago, it extended its range to the Atlantic, including European waters. The Pacific and European populations then went extinct between 2.58 million and 11,700 years ago in the Pleistocene, leaving only the Atlantic population.

Mya arenaria's shell is made of calcium carbonate and is thin and easily broken, hence the name soft shell. The clam lives buried in tidal mudflats, some 15 to 25 cm under the surface. It extends its paired siphons up through the mud to filter seawater for food. Water often spurts from the siphons, a tip-off for clam diggers.

MEANS AND OPPORTUNITY: THE DISEASE

Where clam diggers don't wipe out a mudflat's soft shells, clam leukemia may. The cancer, it's believed, originated in one unfortunate clam. It's astounding, Goff says, that a cancer that has killed so many clams traces to one incidence of the disease.

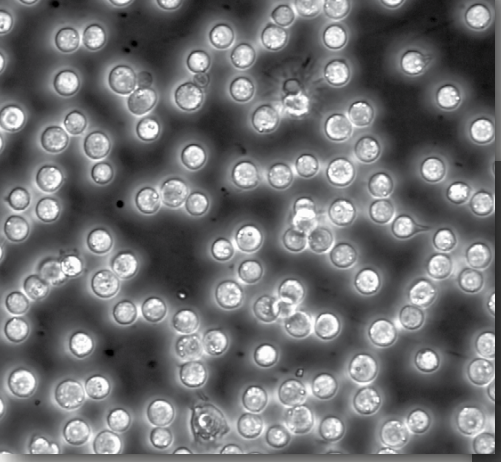
As the cancer cells divide, break free, and make their way into other clams, the leukemia has infected soft shells along 1,000 km of coastline. It's now found from northern Newfoundland to the Chesapeake Bay, nearly the entire range of *Mya arenaria*. "The prospects for disease control therefore aren't very promising," says Goff.

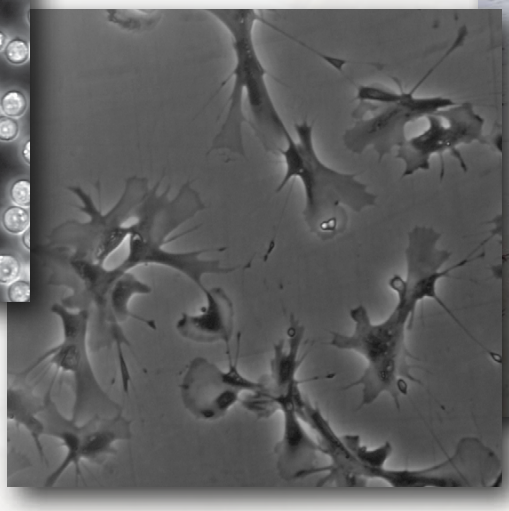
Only two other transmissible cancers are known in the wild: canine venereal disease and Tasmanian devil facial tumor disease (DTFD), spread when one Tasmanian devil bites another.

The first official case of DTFD was reported in 1996. Since then, Tasmania's devil population has declined by 70%, with 80% of the remaining devils affected.

There's a ray of light, however, in this dark day for Tasmanian devils. Some devils have been found with partial immunity to the disease. Breeding in captivity is underway to try to save the species.

Soft-shell clams with syphons extended. *This and background photo credit: Michael Metzger*





Microscope images of normal clam hemocytes (right) and neoplastic cells (above). *Photo credit: Michael Metzger*

(above) Biologist Anne Boettger digging for clams. *Photo courtesy of Anne Boettger*

ON THE LOOSE: FROM NEW YORK TO MAINE TO PRINCE EDWARD ISLAND

Will soft-shell clams go the way of Tasmanian devils, now listed as Endangered on the International Union for Conservation of Nature (IUCN) Red List of Threatened Species? No one knows.

In their studies of clam cancer, Goff and colleagues found that a particular sequence of DNA, which they appropriately named Steamer, was found at high levels in leukemia-ridden clam cells. While normal soft-shell cells contain only two to five copies of Steamer, cancer cells may have 150 copies.

The researchers at first thought this difference was the result of a genetic amplification process within each individual clam. But when Metzger analyzed the genomes of cancer cells from soft shells collected in Port Jefferson, New York; St. George, Maine; Larrabee Cove, Maine; and Dunk Estuary, Prince Edward Island, he was astounded. The cancer cells were identical to one another at the genetic level. "They were clones," says Metzger.

Adds Goff, "We were astonished to realize that the tumors did not arise from the cells of their diseased host animals, but rather from a rogue clonal cell line spreading over large geographic distances."

The cells can survive in seawater long enough to reach and infect a new host, the scientists found. They aren't sure, however, whether the leukemia can spread to other mollusks, or if there are cellular mechanisms in other species that would recognize the malignant cells as foreign invaders and halt them.

"We don't know what role Steamer played in the cancer's origin, if any," Goff says. "And we don't know how often these sorts of cancers might arise in mollusks or in other marine animals."

The findings suggest that transmissible cancers are more common than scientists suspected.

"Natural horizontal transmission of cancer between individuals has been considered a rare phenomenon, restricted to two exceptional cases in mammals," the researchers wrote in their paper. "Our finding of the horizontal transmission of a clonal clam leukemia extends the phenomenon to the marine environment, and demonstrates that this mechanism is more widespread than previously supposed."

WHERE'S THE TRIGGER?

Biologist Anne Boettger of West Chester University in Pennsylvania believes environmental contaminants may be the sparks that set off clam leukemia. She and colleagues studied soft-shell clams in three coastal New England locales: New Bedford Harbor, Massachusetts; Hampton Harbor, New Hampshire; and Ogunquit, Maine.

"Frequencies of terminal clam neoplasia are correlated with chronic environmental contamination," Boettger and colleagues reported in a 2013 paper in the journal *Northeastern Naturalist*. "That is likely involved in disease transmission by compromising their [the clams'] innate immune systems and making them more susceptible to infectious agents."

Boettger found the most clam leukemia in New Bedford Harbor. Of the three research sites, New Bedford Harbor has the highest levels of contaminants, including metals, PCBs, and PAHs (polycyclic aromatic hydrocarbons).

Once the leukemia is established in a soft-shell population, it kills 40% to 100% of the clams.

Ominously, Goff says, "we're working on a similar disease in additional species, but it's too soon for us to report on."

Stay tuned for the sequel...

AUTHOR'S NOTE: As *Oceanography* went to press, Goff and Metzger were reporting new findings in the journal *Nature*. The transmissible cancer has been discovered in three additional bivalve species—mussels (*Mytilus trossulus*) in West Vancouver, Canada; cockles (*Cerastoderma edule*) in Spain; and golden carpet shell clams (*Polititapes aureus*), also in Spain. *Mytilus trossulus* is the main native intertidal mussel in the northern Pacific. In North America, it is found from California to Alaska. *Cerastoderma edule* is widely distributed from Norway to the coast of West Africa; *Polititapes aureus* is common in the coastal waters of Spain and nearby nations. And there may well be a sequel to the sequel, the biologists say.

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