SLUGGING
IT OUT WITH CHEMISTRY

For most of us, an encounter with a slug begins and ends with the common garden variety – you know, the slimy slitherers that contentedly munch at your lettuce. But for marine ecologists, slug sightings can be far more flamboyant. Amongst coral reefs and sandy ocean floors, sea slugs boast brilliant colouring and exotic shapes. What lies beneath their mesmerising hues is even more astounding: a complex chemical defence strategy that enables these seemingly helpless creatures to protect themselves against a plethora of predators. In turn, sea slugs might just be able to help us ward off one of our biggest predators: cancer.

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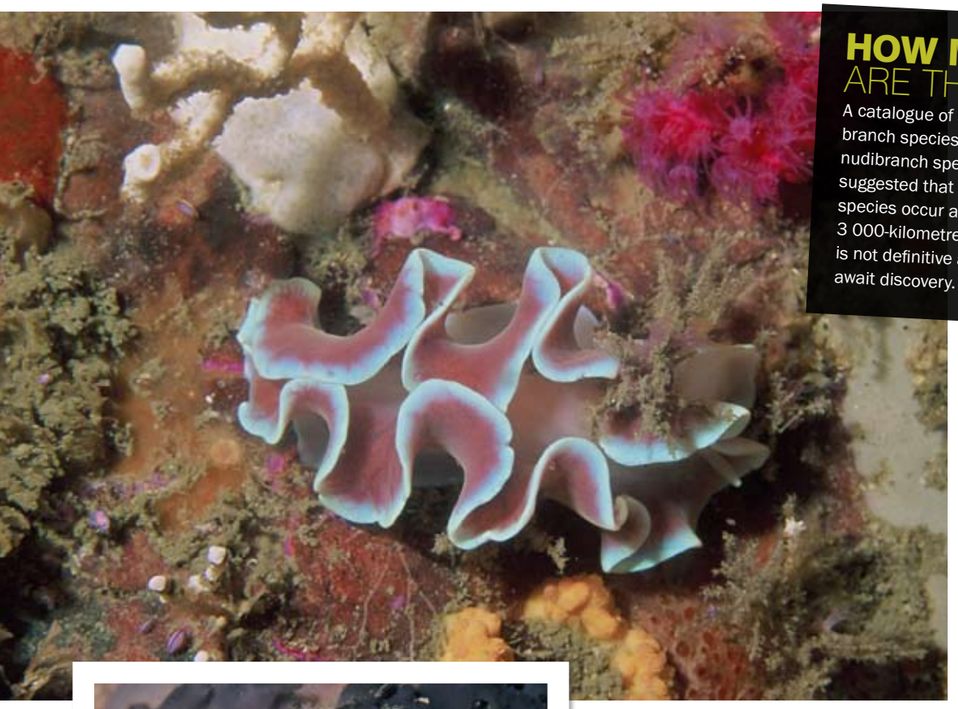
Like the garden slug, the sea slug is a gastropod mollusc and moves as slowly as its terrestrial counterpart by contracting the muscles of its foot-like body. The similarities, however, stop there. The sea slug is more formally known as a nudibranch, named for the naked gills that protrude from the dorsal posterior of the animal and enable it to breathe by extracting oxygen from the surrounding ocean. At its opposite end, just above the mouth, are two sensory antennae called rhinophores, which the animal uses to interpret its environment.

While the garden slug is more than happy with a diet of leafy vegetables, the nudibranch has more daring tastes. Using the toothed plate in its mouth (a radulla), it feeds on other invertebrates such as the sponges, soft corals, sea fans and sea squirts that live alongside it in the rock pools and on the reefs that line South Africa's coast. It is a menu that is not without risk. Corals and sea anemones contain poisonous stinging cells that help to protect them against predators, while humble sponges and many other immobile invertebrates have evolved finely tuned biological machinery that produces complex toxic chemicals.

In a wondrous feat of evolution, nudibranchs have developed not only an immunity to such poison, but an ability to 'recycle' the toxic molecules for use in their own chemical defence. Some nudibranchs are so specialised that they feed on a single species



HOW MANY ARE THERE?

A catalogue of southern African nudibranch species, compiled 25 years ago by nudibranch specialist Dr Terry Gosliner, suggested that at least 268 different species occur around South Africa's 3 000-kilometre-long coastline. This list is not definitive and many new species await discovery.

MARINE BIODISCOVERY:
Finding value in marine resources over and above fishing

gag-reflex, ensuring that the nudibranch is spat out before any real damage is done. If it is eaten, the predator often pays with its life.

This is chemical warfare at its most efficient, where the enemy is repelled by deadly chemical ammunition stolen from dinner out on the reef. But our admiration for nudibranchs goes beyond their ingenious chemical defence.

sponge or other marine invertebrate, while others are able to modify and even intensify the defence chemicals extracted from their food.

(Several nudibranch species, such as the common Antarctic nudibranch *Austrodoris kerguelensis*, that lives in colder water where invertebrate prey is widely dispersed, are able to manufacture their own toxic chemicals using similar biochemical processes to those found in sponges and other marine invertebrates. Because these particular nudibranch species can defend themselves without relying on their diet to replenish their defence chemicals, they are widely regarded as the most evolutionarily advanced of all the gastropod molluscs.)

Molecules are absorbed through the gut and stored in glands in the skin, enabling each species to produce a unique chemical compound. Should a fish or any other nudibranch-eater not heed its prey's brightly coloured warning, these compounds are released and usually produce a

Over the course of history, nudibranchs have selected and preyed upon the most toxic invertebrates and have become crawling smorgasbords of the best in chemical defence. This has done researchers a huge favour, allowing them to forgo a slow and tedious analysis of the toxins of countless sponges, sea squirts and soft corals, and take advantage of the evolutionary work already done by nudibranchs.

For the past 20 years, scientists at Rhodes University in South Africa have employed sophisticated techniques to identify the chemical compounds and to map out the defence strategies employed by many sea slugs and other marine invertebrates occurring along the Eastern Cape coast. These procedures are so precise that a chemical blueprint can be obtained from a single nudibranch. Such research in South Africa and around the world has led to the discovery toxic chemicals with the capacity to kill cells. Could we use these chemicals to kill specific cells, like cancer? The answer to this question has great significance for the quest to find possible cures for the many forms of cancer that ravage human society.

GLOBAL **HITCHHIKERS**

Many marine invertebrate species, including nudibranchs, hitch rides on the bottom of the countless ships that sail around the world, so if you're looking for unusual nudibranchs, the walls of harbours are a good place to start. *Polycera capensis*, for instance, is a South African species, is also regularly found in Australia's Sydney harbour, where it first appeared in 1932.

Working from the template provided by nature, teams of chemists have set about recreating chemical compounds in the laboratory, as it is neither feasible nor environmentally favourable to accumulate the five grams of drugs needed for a clinical trial by harvesting nudibranchs and other marine invertebrates. (One nudibranch often provides only 1/1000th of a gram of a defence chemical.) Because of the structural complexity of the chemicals used by the sea slugs, their laboratory manufacture is back-breaking work and a major hurdle to their commercial manufacture for the global cancer drug market.

However, the research at Rhodes University on nudibranchs – the only work of its kind in Africa – has provided valuable information for the possible design of new anti-cancer compounds. Already, scientists here have isolated chemicals from *Leminda millecra*, the most common nudibranch in Algoa Bay off Port Elizabeth, that are able to kill oesophageal cancer cells at fairly low concentrations. Oesophageal cancer is particularly prevalent in the rural communities of the Eastern Cape and lab work to find synthetic analogues of the nudibranch natural products is ongoing.

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Similar international marine biodiscovery efforts focused on sea squirts have led to the commercial manufacture of a new anti-cancer drug called trabectedin (brand name Yondelis®), which was originally found in the Caribbean sea squirt *Ecteinascidia turbinata*. In the past two years Yondelis® has been used to treat soft tissue cancers and is one of the first commercialised anti-cancer drugs to come from the sea.

We can be certain that it will not be the last. The closer we look at the interaction between the nudibranch and its surroundings, the more intricate it appears. And as we learn more about the complex and fascinating chemical warfare that rages under the water, so might we improve our own battle readiness against cancer. **AG**

ABOVE The spectacular *Bonisa nakasa*, also known as the gas-flame nudibranch, for obvious reasons.

OPPOSITE A common resident of South Africa's Algoa Bay, *Leminda millecra* produces chemicals that are able to kill oesophageal cancer cells. Researchers here and around the world are compiling blueprints of nudibranchs' toxins, with a view to recreating them in the lab and, potentially, developing new anti-cancer drugs.

OPPOSITE, INSET Unlike the common garden slug varieties found on land, sea slugs prey on other invertebrates. Here two *Hypselodoris capensis* feast on a sponge.

PREVIOUS PAGE, RIGHT tba

PREVIOUS PAGE, LEFT A Chromodoris nudibranch at full stretch.