Photo: Peter Northcote

Aquaculture

Anti-cancer sponge: the race is on for aquaculture supply

A consortium of science and industry is attempting a world first in culturing a native New Zealand sea sponge to supply a potentially valuable anti-cancer drug. Sean Handley, Mike Page, and Peter Northcote explain the race.

Scientists at Victoria University and NIWA first collected the encrusting sponge *Mycale hentscheli* from Pelorus Sound in 2000. Researchers at Victoria University and the Malaghan Institute found that extracts from the sponge were active against some cancer cells in laboratory tests. The extracts contained a novel chemical – peloruside A – that operates in a similar way to the cancer drug Taxol®, which is used to treat ovarian and breast cancer. Current gross sales of Taxol® are over US$2 billion a year; the drug also has potential in the treatment of chronic inflammation. To further prove the effectiveness of peloruside A, Victoria University and their commercial company VicLink have licensed pre-clinical trials of this compound with United States drug firm Reata Pharmaceuticals Inc.

First, get your sea sponge

A key obstacle for the clinical trials is supplying sufficient peloruside A. The chemical can either be extracted from sea sponges, or it can be manufactured through industrial chemical synthesis. Reata Pharmaceuticals Inc. have indicated they want to keep both options open. They see the marketing benefits of sourcing a potential drug from farmed sea sponges, as the leading anti-cancer drugs Taxol® and Taxotere® are extracted from another natural source, the yew tree. Consequently, scientists from Victoria University have been working with NIWA's aquaculture experts to develop a method of efficiently farming enough sea sponges to provide a supply of the potential drug. While some types of sea sponge have been farmed overseas for the bath sponge market, culturing a sea sponge successfully on a large scale to supply active chemicals is without precedent.

But the challenge is even more difficult: although *Mycale* sponges are found around most of New Zealand, it appears that only sponges in a small population in a short stretch of Pelorus Sound in Marlborough produce peloruside A. Fortunately, sea sponges are capable of growing from living fragments taken from established sponges. Therefore, to preserve the potentially precious wild sponge stocks in Pelorus Sound, we can take small pieces of sponge for culture, leaving the wild parent sponges in place. The 'donor' sponges rapidly heal over and continue to grow quickly, unharmed.

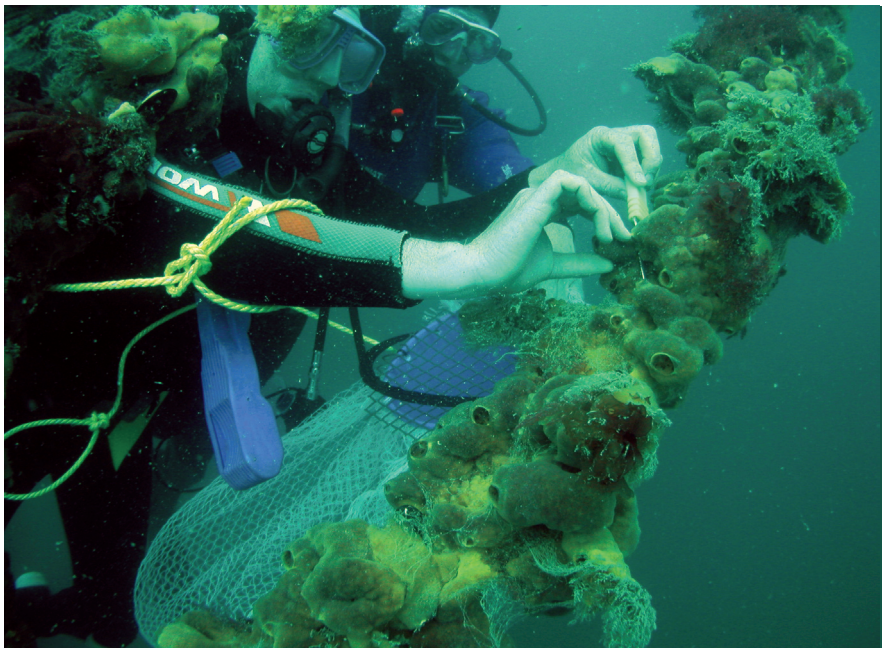
Fighting cancer with sponges

- Peloruside A, a potential anti-cancer chemical, can be extracted from a sponge that grows in New Zealand.
- Large quantities of the sponge must be cultured to provide enough peloruside A for testing in clinical cancer trials.
- At the same time, there are plans to try and synthesise peloruside A on an industrial scale.

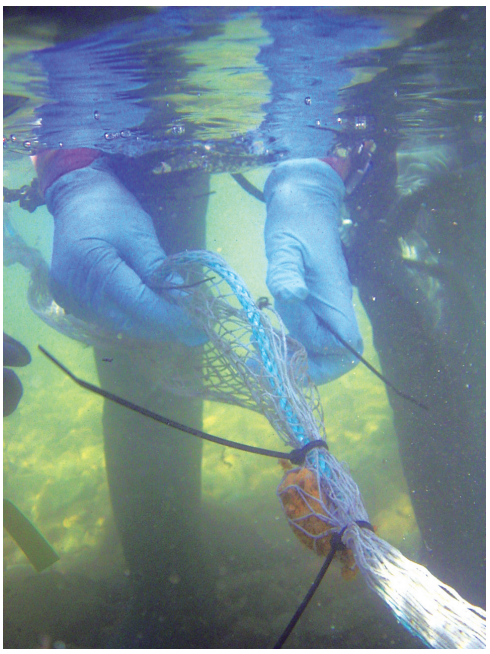
From small 'seeds', mighty sponges grow

Beginning with fragments from wild sponges, we have raised a collection of 'captive' *Mycale*. Now we are working with Marlborough Mussels Ltd to develop a simple but effective method for growing the sponge on existing mussel farms. Small cubes of sponge, about the size of an apricot (3 cm^3), are cut from a cultivated parent sponge and tied onto fishing mesh and then suspended at optimum depths under water. At present, we are growing the sponges on redundant mussel farm space beneath the anchor ropes at the ends of the farm lines, so they do not tangle with nearby ropes laden with farmed mussels. Luckily, we have found that *Mycale* is an ideal candidate for aquaculture, as it can grow an incredible 15-fold in size during winter and spring.

In 2006–07 we aim to grow over half a tonne of sponge from second-generation sponge stocks which started out from only a small quantity of seed material selectively removed from



Divers delicately harvest fragments from the second-generation donor sponges that have been grown on a mussel farm.



Photos: Mike Page

Standing in shallow water, a worker attaches the 'seed' sponge onto fishing mesh for on-growing.

wild sponges. To continue to increase the cultured sponge stocks each year, we harvest a proportion of the sponge to supply the raw material for peloruside A extraction for the pre-clinical trials, while retaining enough raw sponge material to re-seed the farm the following year.

Sponge aquaculture is not without its problems. As with any monoculture – on land or in the sea – as soon as you intensify the density of a species, the weeds turn up to make things difficult. Mussel farms are no different: the weeds are fouling organisms such as the colonial sea squirt *Aplydium*, which has been a particular problem. *Mycale* can outgrow and smother most things, but to control some of the ascidians we have resorted to using divers to 'weed' the farmed sponges. But this is time consuming: if commercial aquaculture of *Mycale* is to succeed, we will need to develop methods that minimise fouling competition and speed up bulk production of the sponge. Together with Marlborough Mussels Ltd's efficient marine farming experience, we are already developing ways to reduce labour costs, for example, by mechanising the seeding of sponges on to our ropes.

Research bottlenecks

The flip-side to the potential production of several tonnes of *Mycale* sponge is the large-scale technology needed to process such bulk quantities of material. We estimate that, after extraction and purification, the final yield from 200 kg of raw sponge will be a mere 2 g of pure peloruside A. Up until now, Victoria University has been able to cope with the volume of sponges NIWA researchers has supplied. However, industrial-scale processing technology will be needed for extracting clinical-scale quantities of peloruside A. Alongside this extraction effort, Reata Pharmaceuticals Inc. will be developing industrial synthesis technology, possibly overseas.

Marlborough Mussels have been very supportive of our research and development efforts because they are keen to diversify their marine farm production into potentially lucrative new aquaculture species. They can see the likely benefits of the development of a pharmaceutical drug from a sponge grown on their farms. They are also very aware that peloruside A may not make it through clinical trials, or that industrial synthesis of the drug may overtake an aquaculture supply. Reata Pharmaceuticals Inc. are supporting the push ahead with a two-pronged approach to provide sufficient peloruside A for clinical trials: aquaculture plus extraction, as well as industrial synthesis. Our aim is to use our research and industry partnership to provide an aquaculture supply of the drug to ensure the greatest benefits and financial returns for New Zealand. W&A

Further reading and useful link

Page, M.J. (2003). Aquaculture of a sponge for bioactives. *Fisheries and Aquaculture Update 8*: 2.

'Peloruside A' on the Marine Biotech website: www.marinebiotech.org/pelorusidea.html

Dr Sean Handley and Mike Page both work at NIWA in Nelson. Dr Peter Northcote is the programme leader of Victoria University of Wellington's FRST-funded Mycale *project (VICX0205).*

Photo: Mike Page

Mycale hentscheli growing in the wild.