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HEALTH SECURITY

Marine organisms enlisted in battle against bacterial sheets

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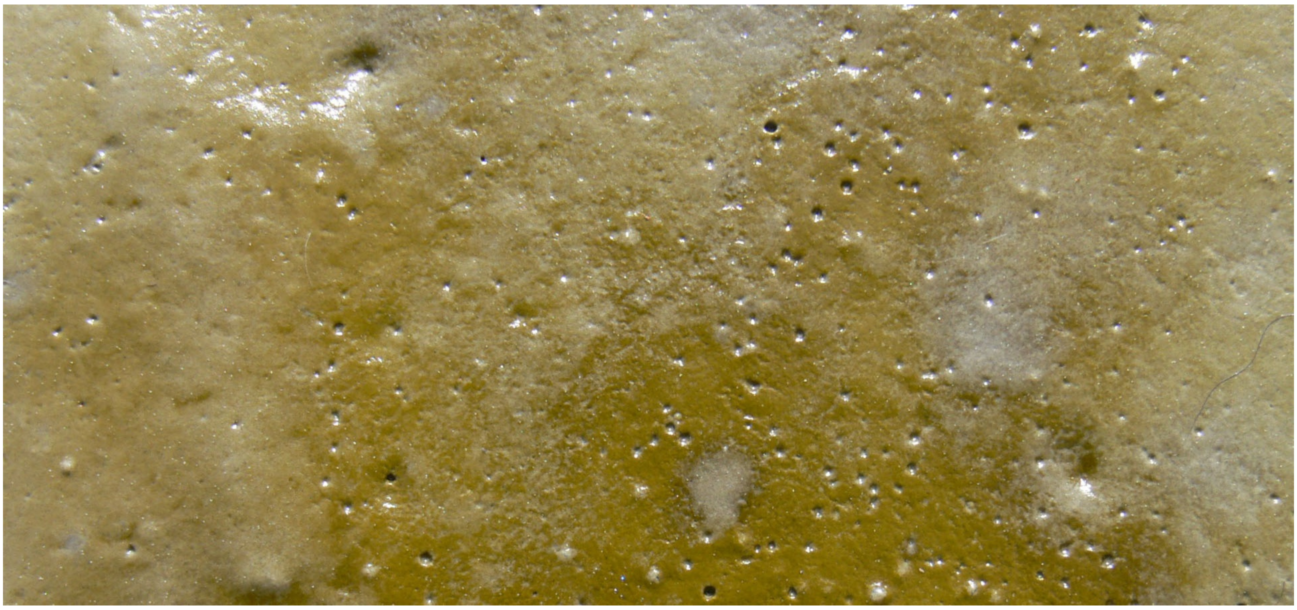

Biofilms are colonies of bacteria that can live on implants and cause infections, yet are resistant to antibiotics. Image credit: 'Biofilm sur vasePortAuray' by F.Lamiot is licensed under CC BY-SA 3.0

A mother and daughter team believe they can fight bioterrorism and antibiotic resistance using natural substances found in the ocean.

The substances are produced by marine bacteria and seem to be potent against biofilms - slimy sheets of bacteria that are a scourge of modern medicine.

It is only in the last few decades that scientists have realised how formidable a threat biofilms are.

Bacteria, it turns out, don't generally hang out on their own. When they sense the time is right – from signals they receive from other bacteria in their environment – they cooperate to build gated communities. They construct cityscapes, with edifices of carbohydrates, DNA and proteins, water channels, and even ghettoes for different types of microbe. There they live unassailable lives because, in their dormant state, antibiotics can't find them.

Such communities flourish on wounds, inside organs and on the surfaces of medical devices in the body, from Teflon catheters to titanium joints. This leads to infections, pain and even removal of the artificial joint.

Dr Cynthia Burzell hopes to disrupt those communities with substances she discovered while studying for her master's and PhD at St George's University, in Grenada, West Indies. She collected bacteria from the warm waters of the Caribbean and found that they produced compounds that could prevent biofilms from forming, wipe them out or slow their growth.

Dr Burzell has applied for patents on processes surrounding the substances and turned down the offer of a university job in the US which would have required her to relinquish them to her employer, she says.

Instead, she decided to set up her own company, Aequor, to exploit her findings. She joined forces with her mother, Dr Marilyn Bruno, a lawyer and entrepreneur, set up a laboratory in San Diego, California, US, and has spent the last seven years overcoming the many hurdles between marine organism and commercial product.

'We're not chemists,' said Dr Burzell. 'I think that's one of the reasons it was difficult for us in the beginning. We couldn't tell people what the chemical was – we just knew that it worked.'

So hiring a chemist was an early step, as was getting some third party testing done from a well-known chemicals company, which concluded, according to Dr Burzell, that 'there is nothing else known that can remove these biofilms at non-toxic doses'.

'We thought we could work with them but they said: "Come back to us when you have a kilo (of the substances),"' said Dr Bruno.

They've now managed to achieve that goal, and have gone back to the chemicals company, as well as some companies in Europe as they decide what steps to take next.

Aequor is now using an Indian firm to synthesise more of the 30 chemicals in the portfolio and scientific interest is growing. However, commercial interest is slow to manifest as drug companies often prefer to focus on cancer and diabetes blockbusters, rather than dedicate resources to lower-margin antibiotics.

Biological attack

The US National Institutes of Health and Department of Defense are looking for substances that could quickly combat superbugs and decontaminate surfaces after a biological attack, explains Dr Bruno, and are now exploring some of Aequor's chemicals.

> 'Bacteria are very smart. When they know they have something blocking them they find another way.'
>
> *Prof. Sara Soto, Barcelona Institute for Global Health, Spain*

To build commercial interest, Aequor has turned to the EU and is using an SME instrument grant for their ABD project to synthesise the chemicals and undertake testing for EU regulatory approvals as new biocides and antibiotics.

Other scientists are also turning to the sea for biocides but are casting their nets wider, screening thousands of microalgae for molecules capable of breaching a biofilm's defences as part of the EU-funded NoMorFilm project.

Professor Sara Soto from the Barcelona Institute for Global Health, Spain, who coordinates the project, says attacking biofilms is tricky. You have to try to stop them sticking to the surface but also to disrupt the system that the bacteria use to communicate.

'Bacteria are very smart. When they know they have something blocking them they find another way – they mutate. They can attach to all surfaces – tables, titanium, prosthetic material, skin – it's very difficult to prevent.'

The microalgae come from three collections – two in Portugal and one in France – and are screened by Prof. Soto's group, after which promising molecules can move to other institutes for chemical analysis, testing on animal models and, eventually, commercialisation.

Of 200 species examined so far, more than 10 look promising, says Prof. Soto.

Protecting ourselves

Meanwhile, an extraordinary discovery about our most familiar chemical – water – may lead to a completely different way of protecting ourselves from biofilms.

A few years ago, Professor Jacob Klein, now at the Weizmann Institute of Science in Israel, announced that water molecules, under the right conditions, can assemble themselves into tiny clusters that behave like ball bearings – and that's what they do inside our joints, keeping them lubricated even under the intense pressures to which we subject them.

The ramifications of his discovery, known as hydration lubrication, are still unfolding, but it looks like one application could be a new way of coating artificial objects in the body such as catheters or stents, which are prone to contamination, so that, from a microbe's point of view, they are a less congenial home.

Water molecules will cluster around positively charged salt ions. Water contains oxygen atoms which, being slightly negatively charged, will turn inwards towards the ion while the hydrogen atoms of water will stick out, thus forming a shell of water molecules around the charge.

These so-called hydration shells have an intriguing pair of properties – they are both strong and fluid, which makes them the perfect lubricant. Now Prof. Klein, along with Dr Ronit Goldberg and Dr Weifeng Lin, is trying to harness hydration shells to make surfaces inhospitable to bacteria.

'If you could somehow arrange for the surface of your material to be covered by a layer of very highly hydrated species (group of similar molecules), anything approaching the surface just sees a layer of hydration shells – and they don't want to stick.'

In his current project, called BiofoulRepel, he is no longer working with simple sodium ions but with phospholipids – the building blocks of cell membranes. These have heads that stick out from whatever they are attached to and – it turns out – pull water molecules towards them to form large hydration shells.

They form layers that love to cling to negatively charged surfaces, including most biosurfaces in the body, such as cartilage, and also to plastic surfaces from which implants and other biomedical devices are made. So could they provide the coating that's needed to protect surfaces from biofouling?

In tests, funded with a grant from the EU's European Research Council, Prof Klein's team has shown that there's a drop of 80 % in the amount of biofoulant that will stick to a plastic surface covered with certain of these lipids, compared with plastic alone.

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