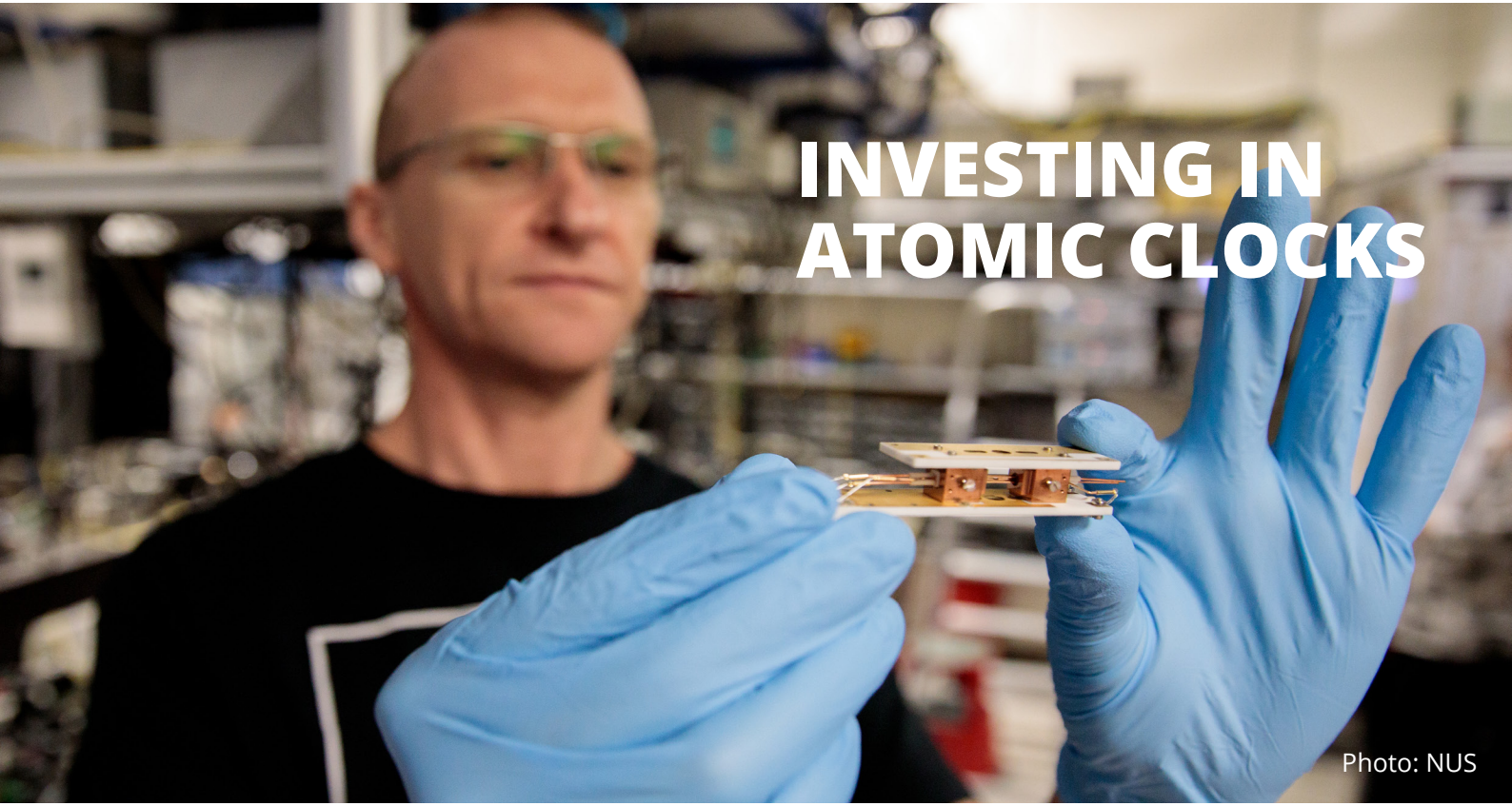
YOUR SG GUIDE TO
RESEARCH, INNOVATION AND ENTERPRISE

RIE NEWS

April 2019



INVESTING IN ATOMIC CLOCKS

Photo: NUS

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2 ELIMINATING BACTERIAL BIOFILM

Bacteria often exist in nature as biofilms – a sticky layer of densely packed communities of microbial cells that grow on living or inert surfaces – for better survival. They are found on almost all surfaces in non-sterile environments. In biofilms, individual bacterial species coordinate their behaviour with other to benefit the group.

A national consortium on biofilms has been set up to help companies gain better understanding of biofilm processes. Possible technologies that companies can adopt include engineered surfaces that can prevent unwanted microbial growth in food packaging, and sensors that can detect biofilm presence.

3 NEW TOOL FOR PLANT ENGINEERING

Scientists at the Singapore-MIT Alliance for Research and Technology have invented a nanotube carrier that is absorbed by the leaf of the plant to transform the genes of its chloroplast. Depending on the DNA inserted into the carrier, it can improve the plant's traits such as yield, height and disease resistance. The technique can be applied to spinach, watercress and garden rocket, pointing to new opportunities to improve the production and quality of vegetables that are eaten in Singapore.

Right: Researcher from the Singapore-MIT Alliance for Research and Technology (SMART) injects the nanotube carrier, which is absorbed by the leaf of the plant to transform the genes of its chloroplast. Photo: SMART

1 MUNCHING MUSHROOMS

A research team from the NUS Yong Loo Lin School of Medicine has found that seniors who consume more than two standard portions of mushrooms weekly may have 50 per cent reduced odds of having mild cognitive impairment. Two portions would be equivalent to approximately half a plate. The six types of mushrooms that are associated with reduced levels of mild cognitive impairment are golden, oyster, shiitake and white button mushrooms, as well as dried and canned mushrooms. We say gather some mushrooms for dinner tonight.

Right: The six types of mushroom analysed in the study were all shown to be associated with reduced levels of mild cognitive impairment. Photo: NUS

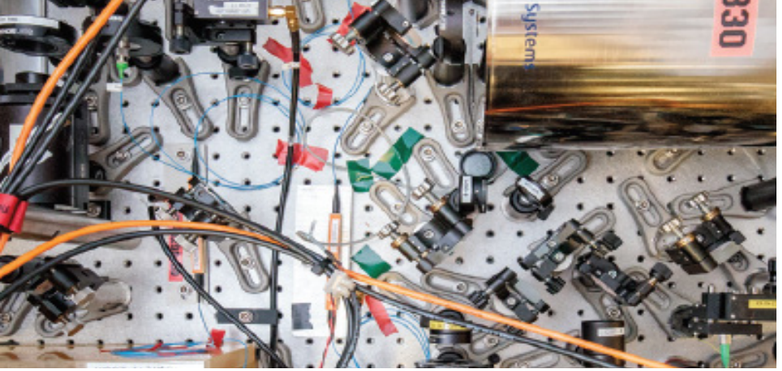
4 MEAT SCIENCE

Would you eat meat grown in our A*STAR laboratories? Cultured meat is the production of genuine meat using biotechnology instead of farming. Cells are retrieved from live animals and grown in bioreactors. Individual cells are harvested to make minced meat products or assembled and matured into tissues resembling whole meat cuts. A*STAR has existing capabilities in bio-production, which have attracted interest from cultured meat companies for collaborations.

Photo: A*STAR

5 SELF-HEALING MATERIAL TO REDUCE WASTE

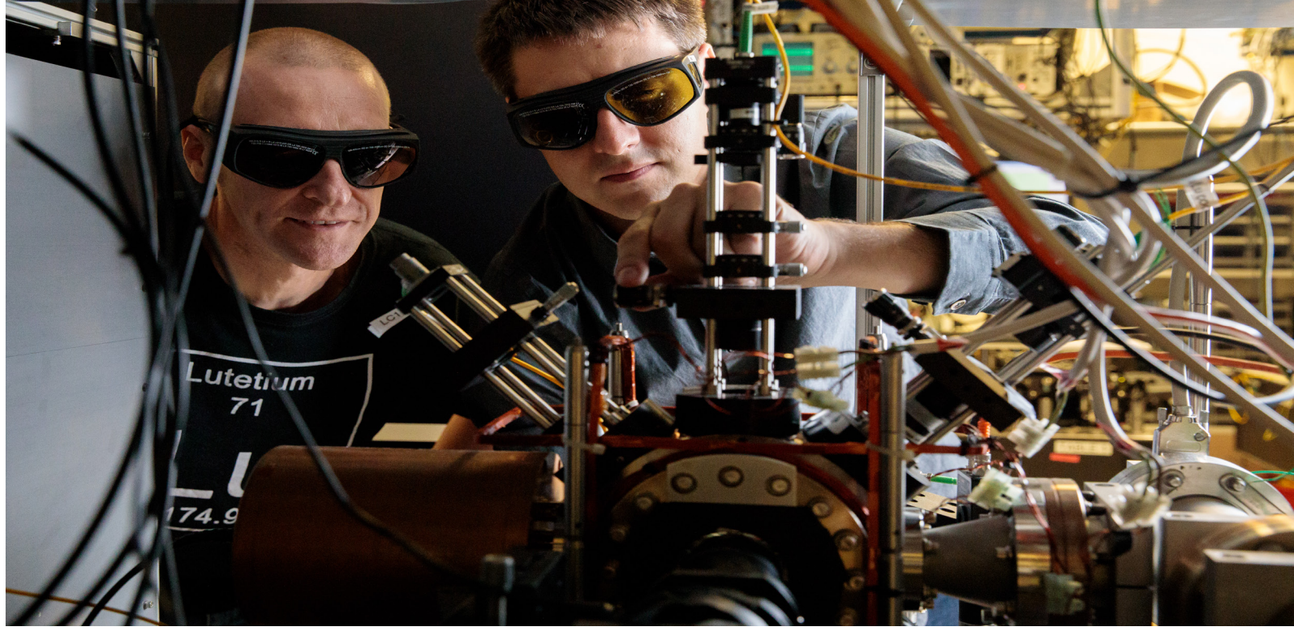
NUS scientists have created a material that repairs itself in both wet and dry conditions. Taking inspiration from underwater invertebrates like jellyfish, the material is transparent, stretchable, touch-sensitive, and self-healing. The invention could promote a greener environment when used to make electronics such as self-repairing and water-resistant touchscreens.



Operating the atomic clock takes dozens of lasers. This optical table holds the most important of them all. It's a clock laser - meaning that it locks to a very narrow energy transition of the atom. The tick of the clock is counted by measuring the oscillations of this light wave.

What is an atomic clock?

A clock is an oscillator. In an atomic clock, the oscillator is an electromagnetic field, such as a laser, and we "count" the oscillations of that field. The atom provides a reference telling us when the laser is tuned to the correct frequency so that each oscillation gives the same unit of time.

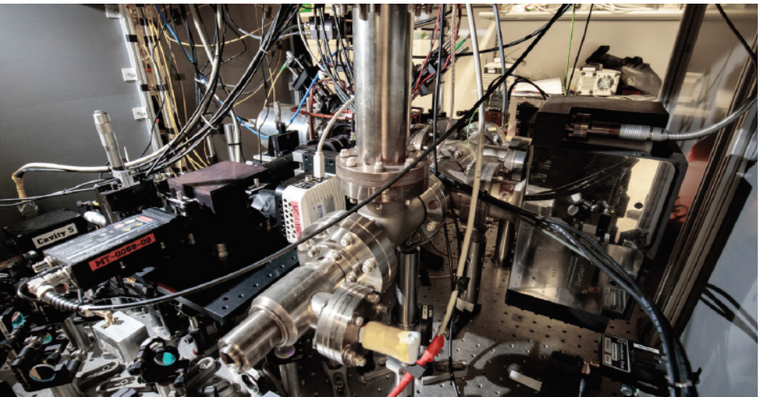


THE AMAZING ATOMIC CLOCK

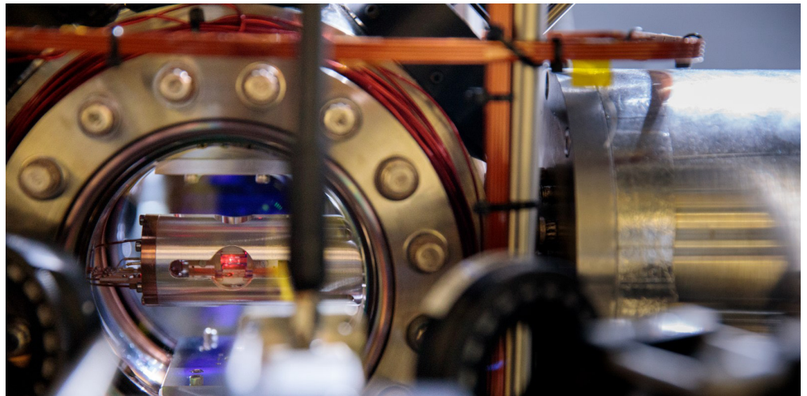
ASSOCIATE PROFESSOR MURRAY BARRETT IS ADVANCING STUDIES ON ATOMIC CLOCKS. A RECENT GRANT RECIPIENT OF THE NATIONAL QUANTUM ENGINEERING PROGRAMME, HE WANTS TO DEVELOP AN INTEGRATED CMOS CHIP FOR OPTICAL CLOCK APPLICATION. HERE ARE PICTURE OF HIS LABORATORY AT THE CENTRE FOR QUANTUM TECHNOLOGIES.

"Why are atomic clocks important? Clocks are an integral part of today's society as evidenced by the many applications dependent on the the global positioning system (GPS). Historically, improvement in clock performance has gone hand in hand with new or improved applications and there is no reason to think this won't continue."

— Associate Professor Murray Barrett (pictured above, left)



The portions of the experiments where atoms are fully enclosed and air-tight. A vacuum pump removes all the air so that a single ion can be kept for more than a day.



The ion trap is located within a cylindrical chamber - you can just see the ions glowing under the illumination of laser light in the middle of the window.

FEATURE

LEVERAGING NATURE'S POWER FOR SAFE, RESILIENT MATERIALS

NATURE SURROUNDS US AND OFFERS SEVERAL SOLUTIONS THAT CAN BE TAPPED, IF WE LOOK CLOSER

Professor Oded Shoseyov is an inventor who studies some of the most amazing materials that nature took billions of years to perfect.

"In nature, everything is self-assembled. The common feature about nature's materials is that they need no one," he said.

One of the fascinating research that Professor Shoseyov has undertaken with the aid of nature is making Type 1 collagen using a transgenic tobacco plant.

He thinks that collagen is probably the most important biomaterial for humans.

"Collagen accounts for about 25 percent of our dry weight. We have nothing more than collagen, other than water, in our body," he said.

Collagen is needed in a wide range of procedures from aesthetical ones, like dermal fillers to reduce wrinkles, to more sophisticated medical implants, like heart valves. However, the sources of these collagens are not safe, as they are mostly from animal and human cadaveric tissues, which can contain viruses.

This situation prompted Professor Shoseyov to search for a safer way to produce collagen.

"When looking for a better and safer solution, I immediately think of plants as they do not harbor human pathogens, and are extremely cost-effective protein producers," he said.

He went on to clone all the five human genes responsible for making Type 1 collagen in humans and introduced them into a transgenic tobacco plant. The plant now acquires the ability to make brand new human collagen.

Top: Professor Oded Shoseyov's collagen-producing tobacco greenhouse.
Bottom: Finished collagen products that are sold to clinics.
Photos: Professor Oded Shoseyov

Professor Oded Shoseyov sharing his inventions at TED talk. Photo: Professor Oded Shoseyov

Today, Professor Shoseyov grows 25,000 square metres of the tobacco plant in greenhouses in Israel. The leaves of the plants are transported to factories, where the process of extracting the collagen starts. The end result is a collagen identical to what we have in our body.

"This is not science fiction. It is happening now. We are using plants to make medical implants," he said.

In another project, Professor Shoseyov and his team pioneered the combination of the strongest material produced by the plant kingdom 'nanocellulose' with the most elastic material produced by the insect kingdom 'resilin'. This resulted in a tough, elastic and transparent material.

The material, also known as Resilin-CNC, can be used by itself or with other materials to enhance their mechanical properties. These materials include epoxy resins, polyurethane, and Plexiglas.

The technology was licensed to a start-up company in Israel, Smart Resilin Ltd, which scaled up production of the resilin and developed applications with industrial partners. These applications include high performance sport shoes, hair-straightening products, touch screens, textiles, structural foams for mattresses, car seats, and additive manufacturing "inks".

Having achieved successful commercialisation of many of his ideas, Professor Shoseyov is currently looking at 3D printed hybrid skin implants. The implant is made of biomaterials that support cell proliferation and differentiation, artificial corneum that enables gas exchange, and physical barrier that prevents infection.

"Our vision is to use the printer in the operation room and use the patient's own stem cells," he said.

The project will start with animal studies followed by clinical trials when funding is secured.

Of all his many innovations, one experiment that remains the most memorable to him is his work to inhibit the growth of citrus pollen tube to prevent seed formation in citrus. Hoping to achieve this through the use of recombinant "cellulose binding protein", he found that the protein did the opposite – the pollen tube grew more and faster.

"On hand, we now had a method to make citrus fruits with lots of seeds that nobody wants," he mused.

But something did come out of this incident. Professor Shoseyov realised that he now had a tool that accelerated plant growth. This discovery led to a technology developed by a company to grow and commercialise the first fast-growing Eucalyptus trees for the pulp and paper industry in Brazil.

Professor Shoseyov continues to seek inspiration for new ways of producing useful materials through nature's processes. He believes that one day spent observing the environment is equivalent to many years spent in the lab.

"Nature had billions of years to perfect the most amazing materials and structures. And we better learn from nature and not spend our time on reinventing the wheel," he said.

Professor Oded Shoseyov serves as an expert member on the Scientific Advisory Board (SAB) for the Singapore-MIT Alliance for Research and Technology (SMART)'s Disruptive & Sustainable Technologies for Agricultural Precision (DiSTAP) programme. The programme looks to revolutionise how food is produced to meet the demands of a growing population in an increasingly resource constrained world. DiSTAP is a highly collaborative effort between SMART and the Temasek Life Sciences Laboratory (TLL), and is supported by the National Research Foundation under CREATE.

COMMENTARY

THE BUSINESS OF BIOFILMS

PROFESSOR STAFFAN KJELLEBERG, CENTRE DIRECTOR OF THE SINGAPORE CENTRE FOR ENVIRONMENTAL LIFE SCIENCES ENGINEERING, TELLS US WHY IT IS IMPORTANT FOR INDUSTRY TO UNDERSTAND BIOFILMS

Professor Staffan Kjelleberg. Photo: Singapore Centre for Environmental Life Sciences Engineering

The launch of the Singapore National Biofilm Consortium (SNBC) marks the beginning of a new phase of biofilm and microbiome research and translation for Singapore, founded on the world-leading science generated by the Singapore Centre for Environmental Life Sciences Engineering (SCELSE).

For Singapore, the timing is perfect. SCELSE has established a significant profile for biofilm and microbiome research in local and international landscapes. NRF has recognised the potential of biofilm and microbiome research by supporting the SNBC as an appropriate expansion of this research into the translational arena.

Biofilms are estimated to be worth US$5,000 billion internationally every year across a range of applications. Biofilms and microbiomes are fundamental to every ecosystem and hence influence all aspects of life – both natural and man-made. In an urban ecosystem like Singapore, this involves the built environment, resource management, water and food safety and security, public health and medical applications.

In fact, both locally and abroad, the industry is realising the potential of incorporating biofilm and microbiome understanding and research into addressing the many challenges facing our society.

From cosmetics to oil and gas, numerous industries worldwide invest heavily in dealing with microbial biofilm challenges or harnessing their potential. Further to this, biofilms and microbiomes are being employed to restore and promote the natural processes that maintain health and wellbeing across all aspects of urban life.

While biofilms have been recognised as problematic or advantageous in several industries, many are not equipped to understand and address the specific problems or opportunities. This may involve controlling unwanted biofilms, but as is often the case, it can also involve employing biofilm communities to perform particular functions in a cost-effective, efficient and sustainable manner.

SCELSE's ability to provide guidance and solutions for these diverse systems is based on the centre's expertise in understanding core biofilm commonalities across systems. We have used universal biofilm traits to control and direct microbial community behaviour in broad-ranging systems, for sustainable environmental, industrial, engineering, public health and medical applications.

Microbial biofilms are the oldest form of life. As such, they have evolved an amazing metabolic capacity and present great potential for efficiently and sustainably accomplishing many sophisticated and complex tasks.

The SNBC provides a much-needed link between Singapore's research institutes, institutes of higher learning, government agencies and industry, to help unravel these complexities for biofilm and microbiome technology translation. It provides members with access to knowledge and know-how for solutions tailored to the conditions relevant to members.

The SNBC also enables access to international research and industry expertise through a partnership with the UK's National Biofilms Innovation Centre and its extensive network of 30 university members and more than 70 industry partners.

In addition to utilising the consortium's know-how and international connections, SNBC members can also participate in training and technology workshops to facilitate industry-academia interactions, and apply for seed funding for technology development and applications. This will enable members to work with biofilm and microbiome researchers to create a tailored approach, and establish its viability before engaging in an expanded commitment.

SNBC focuses on four areas of research commercialisation: clean surface technology for regulating biofilm development; environmental monitoring of biofilms; microbiome engineering for functional applications; and framework and methodology tools and technologies for high-resolution assessment of microbiomes; all of which are relevant to wide-ranging applications.

Several of our industry partners are already SNBC members, having realised the translational potential of biofilm and microbiome research. These members traverse very different industries with varying needs, such as household surfaces (Procter & Gamble Singapore Innovation Centre), integrated water treatment (Flotech Controls), food nutrition/technology (Danone Nutricia Research; Ferrero), and imaging (Carl Zeiss), as well as skin health (L'Oréal), oil/gas (Exxon Mobil), and cleaning/hygiene (Chrisal).

In line with Singapore's strategic R&D planning, the evolution from SCELSE to SNBC demonstrates how investment in an RCE drives not only research excellence but also provides the means to address very fundamental challenges for an urban ecosystem.

The Singapore National Biofilm Consortium was set up by the National Research Foundation in February to provide a platform to connect researchers and companies for the translation of biofilm and microbiome research into industry-ready solutions.

INTERVIEW

WHY MICROPLASTICS ARE SO HARMFUL

MICROPLASTICS CAN ENTER THE OCEAN FOOD CHAIN AFTER BEING CONSUMED BY MARINE CREATURES. **PHD STUDENT EMILY CURREN** TELLS US HOW MICROPLASTICS CAN ALSO HOST TOXIC BACTERIA ON ITS SURFACE, AND HOW WE CAN PLAY A PART IN REDUCING PLASTIC MARINE WASTE

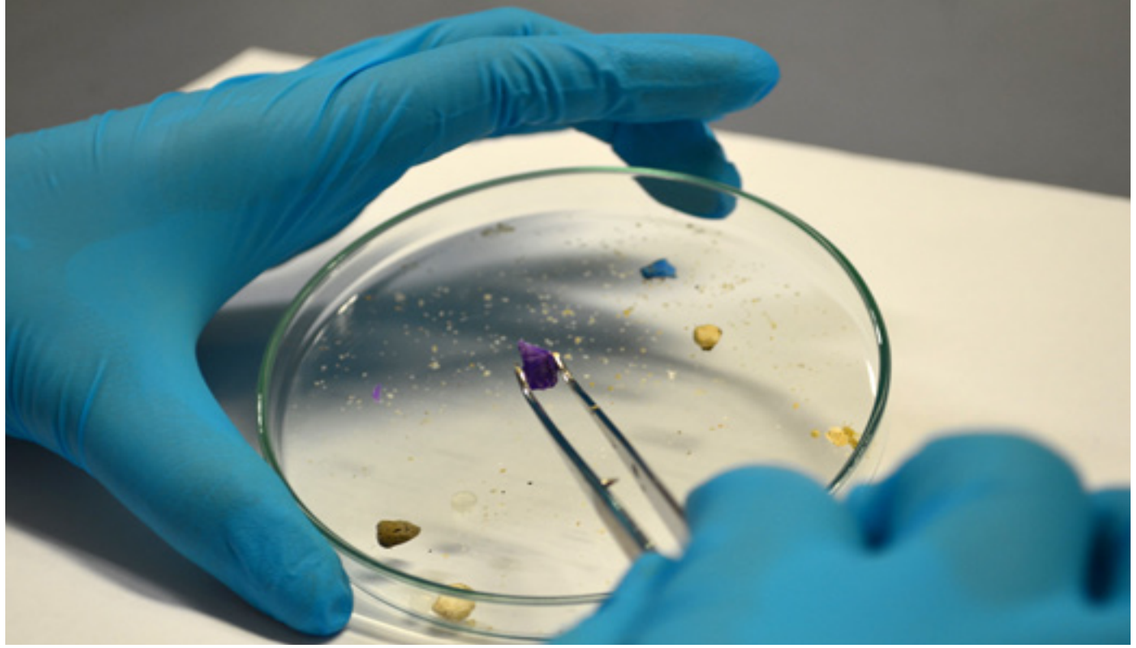
Why did your team decide to identify toxic bacteria on the surface of microplastics?

Microplastics are known to form a large proportion of plastic pollution in marine environments. However, the role of these plastics as habitat or transporter of microorganisms is not well understood. Microplastics could serve as a habitat for marine microorganisms including toxic bacteria and algae. In recent years, research has reported that harmful algal blooms have been increasing more frequently globally. Some bloom species are known to produce marine biotoxins that could be harmful to other marine organisms, mammals and even humans. Therefore, identifying those microorganisms attached on microplastics and examining the role of microplastics associated with these microorganisms are critical in protecting our coastal ecosystem which we depend on greatly for resources and food.

Our team works on harmful algal blooms, especially on marine toxins and toxic species which increasingly cause harm to our coastal ecosystem. We started with bacteria because it is the simplest single-celled organisms on our planet and also the most abundant type of organism. Since microplastics impact the food chain, we would like to know the types of bacteria present on microplastics, especially toxic types that can impact human health. Our goals are to identify all harmful and toxic microorganisms which are attached to the surfaces of microplastics, and not just bacteria.

Can you tell us more about the types of bacteria found on the microplastics?

In our study, we found more than 400 different types of bacteria on microplastics. Some of the bacteria found were beneficial to the environment and human, while some were toxic. The beneficial bacteria include those that are hydrocarbon degrading, for instance



Microplastic samples in a petri dish. Photo: NUS

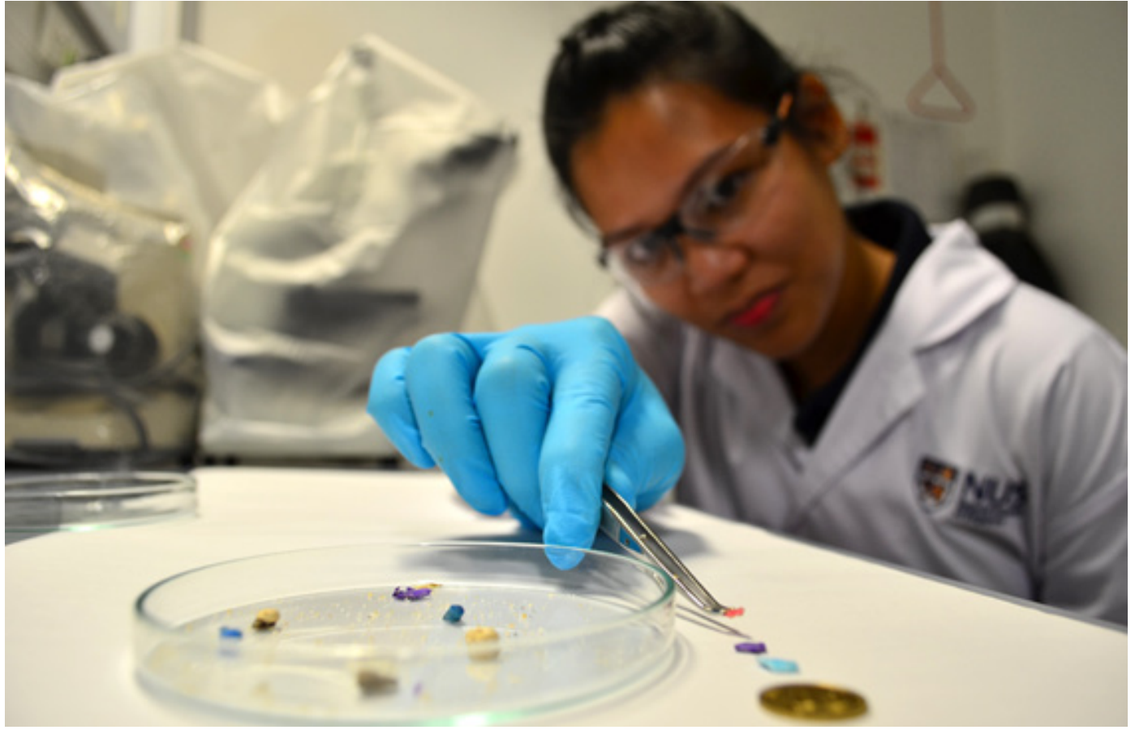
from the genus Erythrobacter, which has been used to clean up oil spills. We also discovered nitrogen-fixing bacteria, which is another good example of beneficial bacteria. These bacteria are usually present in soil and are able to fix atmospheric nitrogen into usable forms for plants. Potentially pathogenic bacteria from the genus Vibrio and Pseudomonas were also detected, and these are pathogens that can threaten human health. Other interesting bacteria, which we have discovered, are those usually found in deep-sea hydrothermal vents, and in thermophilic environments such as hot springs.

It is interesting that your team also found the presence of beneficial bacteria. How can we harness the benefits of such bacteria?

The presence of these oil-degrading bacteria provides nature-friendly alternatives for the mitigation of toxic hydrocarbon pollutants in the marine environment. Oil-degrading bacteria have already been used to clean up oil spill in some countries. There are several types of oil-degrading bacteria present on these microplastics, the way forward is to test on these different species. In the near future, we might be able to deal with plastic pollution.

What is the biggest problem of toxic bacteria surviving on the surface of microplastics?

From several recent studies, microplastics are known to transfer to humans through the food chain. However, apart from the human health impacts,



PhD student Emily Curren examining microplastic samples. Photo: NUS

the biggest problem about these harmful or toxic microorganisms including bacteria surviving on microplastics, is the spread and transport of these harmful organisms to new coastal regions. Some of these microorganisms could be invasive and could strive in the new environment, reproduce, dominate and destroy the local ecosystem and threaten food resources such as fisheries.

How can we play a part in tackling this issue?

A large proportion of marine litter in the environment is caused by anthropogenic land waste, and this includes microbeads and single-use plastics. One way we can contribute to the reduction of plastic marine waste is to avoid the use of cosmetic or facial products containing microbeads. Countries such as New Zealand and France have already banned the use of microbeads in cosmetic products. This is because microbeads in facial cleansers or toothpastes are small enough to escape wastewater filtration systems and will enter the marine environment. We should also avoid the usage of single-use plastics like straws and disposable cutlery. The issue of microplastic pollution is a global one, which requires the effort of every individual to tackle it. The only way to do this is through education and public awareness programmes.

After finding more than 400 different types of bacteria on microplastics, what is the next step for you and your team?

Our group is currently doing preliminary work investigating the ability of microplastics being a vector for the dispersal of non-native microorganisms and developing a rapid method for identifying such species in the field. Non-native microorganisms are those that are not currently present in our local waters but have been introduced by anthropogenic means such as shipping or by rafting on marine debris like microplastics. These non-native species can be a threat to our coastal ecosystem as they could wipe out local species which are beneficial and destroy our local ecosystem. Moreover, some of these microorganisms are capable of forming blooms, which could be detrimental to our aquaculture industry, as it would lead to massive economic losses. In recent years, harmful algal blooms are increasing in both frequency and distributions, and some species are capable of causing large scale blooms that result in the mortalities of fish, whale, marine birds and mammals.

Why did you decide to focus your career on research in marine biology?

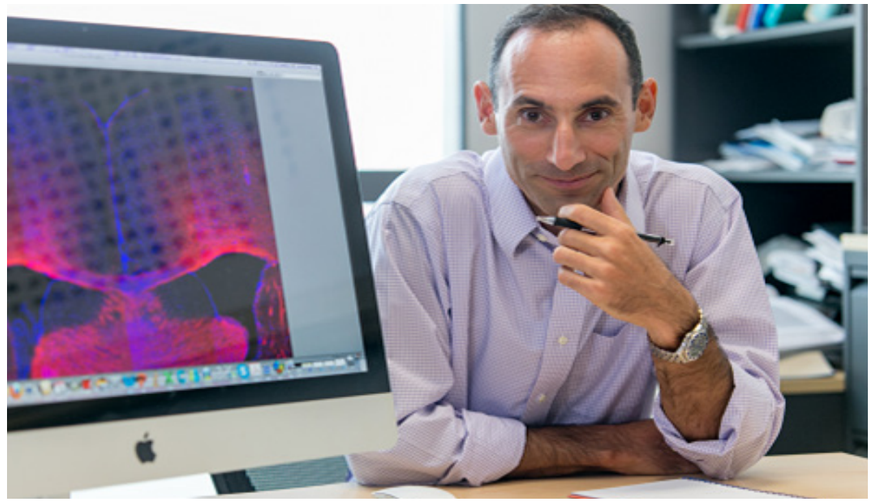
I majored in biomedical sciences for my undergraduate degree. After graduating, I came across the Tropical Marine Science Institute, which opened the door to the field of marine research. The ocean is a very interesting place with many secrets. There are many species in the marine environment that are yet to be discovered. The interactions between marine organisms and their abiotic environment are very complex and there is so much that is unknown. When I came across marine algae, I found the cyanobacteria a very special organism to study because of its hardiness and its ability to survive in a wide range of environments. The presence of toxic species among this group of organisms also makes its study very relevant, as Singapore is an island nation that is surrounded by a rich biodiversity of marine life, and toxic blooms of cyanobacteria will have many implications on our coastal ecosystem.

Your team collected microplastics from all around Singapore, including Lazarus Island, Sembawang Beach and Changi Beach. What is a typical day at work like for you?

Most of my work is actually done in the lab. We occasionally go out for field trips and cruises. A typical day of fieldwork includes us collecting samples from beaches and also going on research or survey cruises along the Johor or Singapor Straits. During such cruises, we usually begin in the morning by measuring seawater-associated environmental parameters such as salinity, temperature as well as the biomass of microorganisms on sites. We also collect seawater samples for further analyses in the lab. In the afternoon, back at the lab, we will process the samples we have collected, for instance filtering seawater samples and counting the species abundance present in each sample.

FEATURE

DHA DISCOVERY PAVES WAY TO BETTER NUTRITION FOR PRETERM BABIES



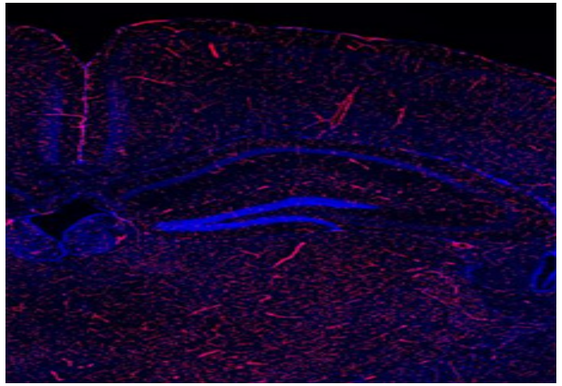
A Duke-NUS team, led by NRF Investigator Professor David Silver, recently found that LPC-DHA is critical for normal foetal and infant brain development. Photo: Duke-NUS Medical School

It has long been understood that docosahexaenoic acid, or DHA, plays an important role in the development of the brain. Apart from its role in brain development in infants, DHA is also essential for the maintenance of normal brain functions in adults.

However, due to the presence of the blood-brain barrier (BBB) in the brain, substances - including DHA - are prevented from entering it freely, says Dr Bernice Wong, a research fellow at Duke-NUS Medical School's Cardiovascular and Metabolic Diseases Program.

Dr Wong, together with a team led by NRF Investigator Professor David Silver, recently discovered that a natural form of DHA made by the liver, called Lyso-Phosphatidyl-Choline (LPC-DHA) or known simply as activated-DHA, is not just important, but critical for normal foetal and infant brain development. They also found that primarily, this modified form of DHA can only reach the brain through a specific 'transporter'.

It is only in this modified activated-DHA form, and via the lysolipid 'transporter' protein known as Major Facilitator Superfamily Domain containing 2a (Mfsd2a) that DHA is able to enter the brain.



A coronal section of the brain, where Mfsd2a (shown in red) is highly enriched in the microcapillaries of the blood-brain-barrier. Photo: Duke-NUS Medical School

In human prenatal brain development, this DHA is rapidly acquired at the end of the second trimester. This coincides with the development of the BBB, and continues after birth, till two years of age, said Dr Wong, who is the lead author of the study.

Earlier, together with his collaborators, Professor Silver, the study's PI, had already identified four families with inactivating mutations in the Mfsd2a receptor that presented with severe microcephaly, highlighting the importance of the uptake of activated-DHA for human brain growth and function.

In this study, the team made use of Mfsd2a-deficient mouse models to show that Mfsd2a is uniquely required postnatally at the BBB for normal brain growth and DHA uptake. This correlation between animal and human genetic studies prove that Mfsd2a and active-DHA are required for proper brain development.

This project, funded by the National Research Foundation, could potentially pave the way for the development of nutritional products for preterm infants, who are predicted to have lower levels of DHA in the brain. The team also hopes that the discovery could help ageing adults, as well as patients with multiple sclerosis, in which both ageing and multiple sclerosis results in the loss of white matter, a brain structure that is rich in lipids.

"Our research is beginning to reveal the fundamental importance of LPCs in brain health and other critical organ systems. Thanks to the outstanding scientific infrastructure at Duke-NUS and generous support from the NRF Investigatorship, we have established a pipeline to translate our findings into clinical therapeutics through our commercial partners," says Professor Silver.

The NRF Investigatorship is designed to support excellent Principal Investigators who have a track record of research achievements that identify them as leaders in their respective fields of research.

Dr Bernice Wong, Research Fellow Cardiovascular and Metabolic Disorders Program, Duke-NUS Medical School

Photo: Duke-NUS Medical School

Dr Bernice Wong is a Research Fellow at Professor David Silver's lab, and is the lead author for the research project on Mfsd2a and active-DHA. She tells us more about herself and the research.

In a nutshell, what is your research about?

DHA is important for brain and eye development. However, due to the blood-brain barrier in the brain, DHA taken from food does not reach the brain, unless it is in an altered form made by our livers, which we term 'active-DHA'. Our research focuses on looking at the role of this active-DHA in the brain.

What was the turning point that led you to become a scientist in this field?

I was given the opportunity to study the role of Mfsd2a in the eye as part of my PhD project. At the time, Professor David Silver had recently discovered that Mfsd2a is important for DHA accumulation in brain, but I had the opportunity to determine its function in the eye. Working with this delicate organ was particularly challenging for me, as I met with several roadblocks in the first year of my PhD.

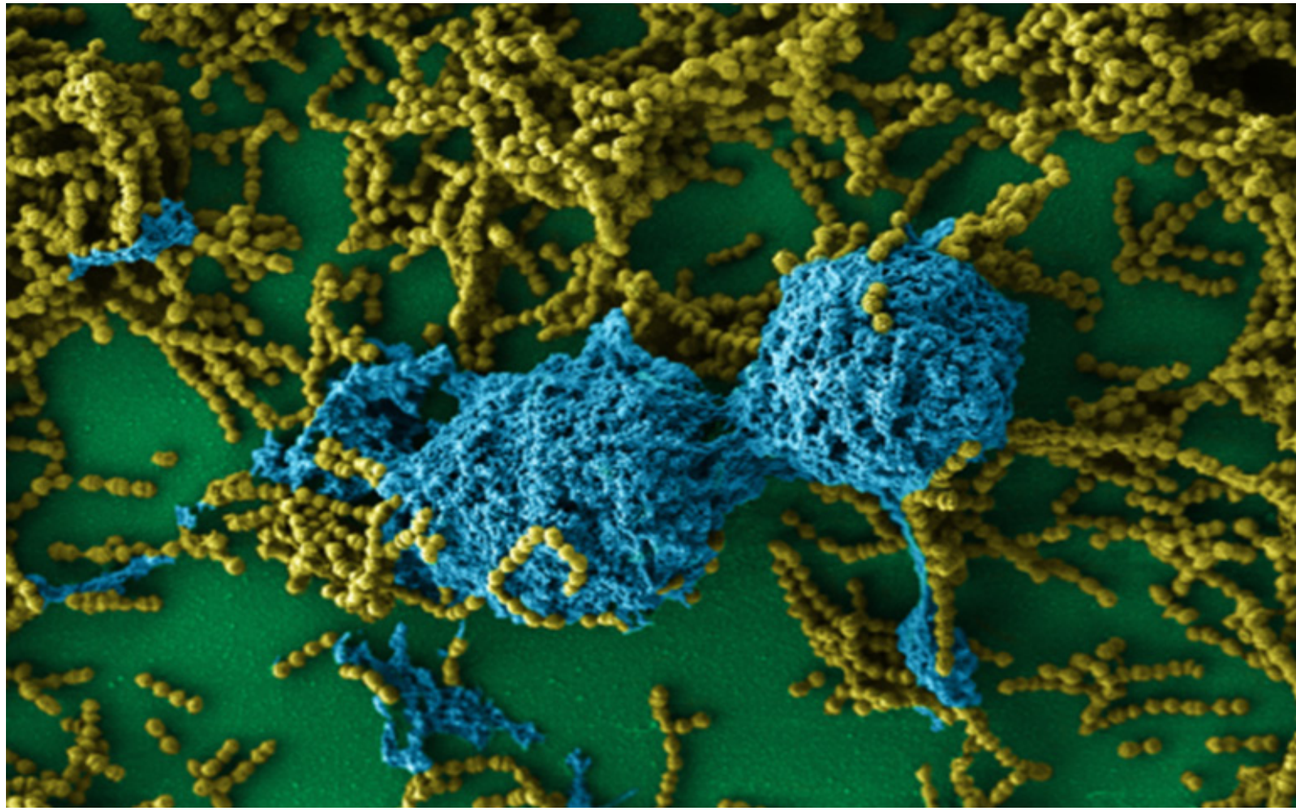
With Prof Silver's guidance, I found Mfsd2a to be highly expressed at the retinal pigment epithelium, a major blood-eye barrier located at the back of the eye, and showed for the first time that it plays an important role for DHA accumulation in eye. This suggested that Mfsd2a transport could be exploited for the delivery of small molecules into the eye for the treatment of eye diseases. Knowing that our discoveries may lead to new therapies for patients keep me motivated.

What are your ambitions for the future?

I have a long way to go for my scientific training, but I hope to become an independent researcher one day. Prof Silver and I are co-inventors on a patent application (PCT) for the treatment of eye diseases with a focus on Age-related Macular Degeneration (AMD), a leading cause of blindness in developed countries.

The treatment options for wet AMD, which is characterised by the formation of leaky blood vessels, are limited to anti-angiogenic therapeutics delivered by ocular injections that are inconvenient and invasive. There are no treatment options for dry AMD to date. I hope to be able to contribute to the development of a potential therapy for AMD. Moreover, I would like to understand the mechanism by which LPC-DHA contribute to eye and brain function.

SCIENCE IN PICTURE



Biofilms are complex microbial communities that are associated with surfaces and are the oldest and most widespread mode of life. They are found on almost all surfaces in non-sterile environments.

Applications of biofilm research are broad – ranging from developing antimicrobial coatings on medical implants to prevent infections inside the human body, to sensors that can stop waterborne pathogens from travelling to household taps, and to food packaging that prevents bacterial growth.

This photo shows bacterial biofilm invading and killing host cells (in blue). Photo: Singapore Centre for Environmental Life Sciences Engineering

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