

Written in blood

Maltese researchers are leading the way in developing new diagnostic tools for cancer. Dawn Gillies finds out more from Prof. Godfrey Grech and Dr Shawn Baldacchino.

Breast cancer survival rates have been improving steadily in recent years. In Malta, 86.9% of patients currently survive, up 7% over the last decade. Thanks to new targeted therapies, the outlook is increasingly bright. But precision therapies need precision testing.

Breast cancer diagnosis has reached new heights and with current tests using tissue biopsies, pathologists can classify patients for specific treatment. Precision medicine goes a step further. It provides more information, predicting the aggressiveness of the cancer and measuring the number of cells from the tumour that spread into the bloodstream.

This does not mean that all requirements in precision therapy have been met.

At the time of writing, there is no simple method to test patients' ongoing benefit from treatment or to measure different tumour areas from one sample. For this to be possible, we need super-sensitive tests. This is where Prof. Godfrey Grech and Dr Shawn Baldacchino at the University of Malta come in.

DETECTING THE UNDETECTABLE

During his PhD, Baldacchino studied a new class of breast cancer representing most cases of the triple negative type, which affects 12% of breast cancer patients in Malta.

In triple negative breast cancers, tests for estrogen receptors, progesterone receptors, and excess HER2 protein all result in negatives and are associated with aggressive tumours.

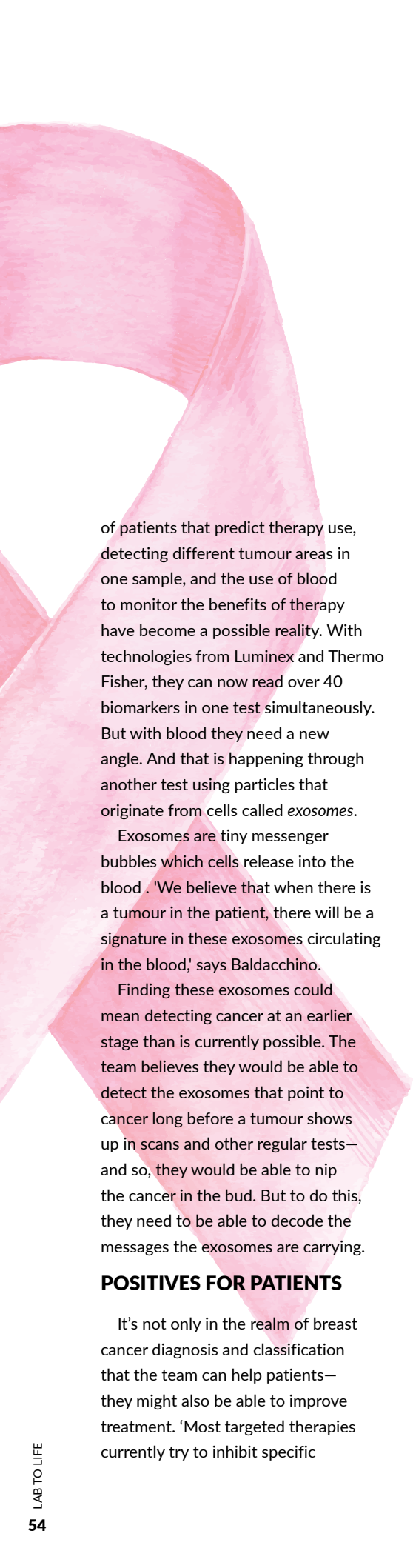
To detect this new class of breast cancer, Grech's team have created a new test that uses molecular substances we naturally produce in our body—biomarkers. By pinpointing the right combination of certain biomarkers, they can test for this new class within the triple negative breast cancer cases.

They initially used the test to look at biopsies from past patients. These exercises showed that they could accurately detect the cases—even in samples that were over a decade old! In fact, the test was so successful that the team is now working with biological testing industry giant Luminex to use it in hospitals worldwide. With a patent filed, research labs will get their hands on it later this year with the hope that by 2021 it will be used to directly help patients in hospitals.

However, there is more work ahead. Encouraged by the results so far, the team wants to take the test and other current biomarker tests a step further. They want to use a simple blood sample which is less invasive, allowing patients to be monitored during therapy.

PUSHING BOUNDARIES

With the method Grech and his team have optimised, obtaining information on new classes ▶



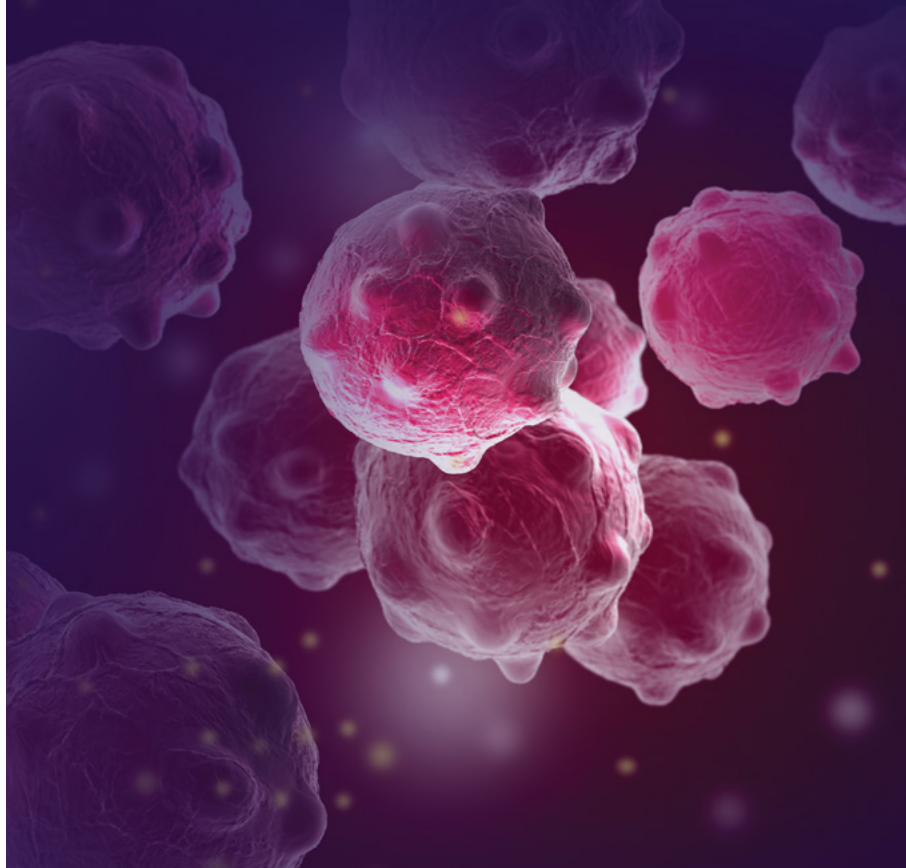
of patients that predict therapy use, detecting different tumour areas in one sample, and the use of blood to monitor the benefits of therapy have become a possible reality. With technologies from Luminex and Thermo Fisher, they can now read over 40 biomarkers in one test simultaneously. But with blood they need a new angle. And that is happening through another test using particles that originate from cells called *exosomes*.

Exosomes are tiny messenger bubbles which cells release into the blood. 'We believe that when there is a tumour in the patient, there will be a signature in these exosomes circulating in the blood,' says Baldacchino.

Finding these exosomes could mean detecting cancer at an earlier stage than is currently possible. The team believes they would be able to detect the exosomes that point to cancer long before a tumour shows up in scans and other regular tests—and so, they would be able to nip the cancer in the bud. But to do this, they need to be able to decode the messages the exosomes are carrying.

POSITIVES FOR PATIENTS

It's not only in the realm of breast cancer diagnosis and classification that the team can help patients—they might also be able to improve treatment. 'Most targeted therapies currently try to inhibit specific





Prof. Godfrey Grech, Dr Shawn Baldacchino and the team
Photo by James Moffett

receptors and proteins to stop the uncontrolled growth of cancer cells,' Grech says. But through their research, the team has found that targeting the low activity of specific complexes of proteins in tumour cells is key. Their research models show that increasing the activity of these protein complexes is possible using specific drugs.

This is true for triple negative breast cancer, where the amount of PP2A protein is extremely low. The PP2A protein enables the body to fight the cancer, so increasing its activity would create a chain reaction in the body which could limit the growth and spread of that category of cancer cells.

This approach to treatment has applications beyond triple negative breast cancer. Grech is hopeful that PP2A production could be amped up for different types of cancer too, and lead to positive results.

MANAGING THE UNMANAGEABLE

When organising a project like this, it's expected that things won't go to plan. One of the biggest challenges for Grech's team has been establishing collaborations with other groups across the globe. They need these connections to provide the samples required to test their systems. With other groups working on similar projects, time is a limited resource. Thankfully, the team found collaborators in Leeds (UK), and Barcelona (Spain), allowing the group access to the samples they need.

What is certain is that support for this work has come in many shapes and forms.

The project received funding both from public donations and the Malta Council for Science and Technology. Baldacchino also found an ally in the charity foundation Alive with the help of the Research Trust of the University of Malta (RIDT). He is the first recipient of funding from them, and their first graduate.

PREDICTING THE FUTURE

Thanks to projects like these, cancer research has a bright future in Malta. The team has their product launch to look forward to later this year, which will see a drastic reduction to the time and effort it takes researchers and doctors to determine the type of breast tumour.

But a lot of challenges lie ahead. The biggest challenge will come in the move to early stage cancers. These cancers have low levels of substances to detect, which means that any test they develop will have to be extremely sensitive in order to be effective. Successfully identifying these cancers would signal a massive breakthrough for the global medical community—and, more importantly, for patients. Early detection through basic blood tests would open the door to early stage treatment and a higher rate of survival. Nothing could matter more. **T**

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