

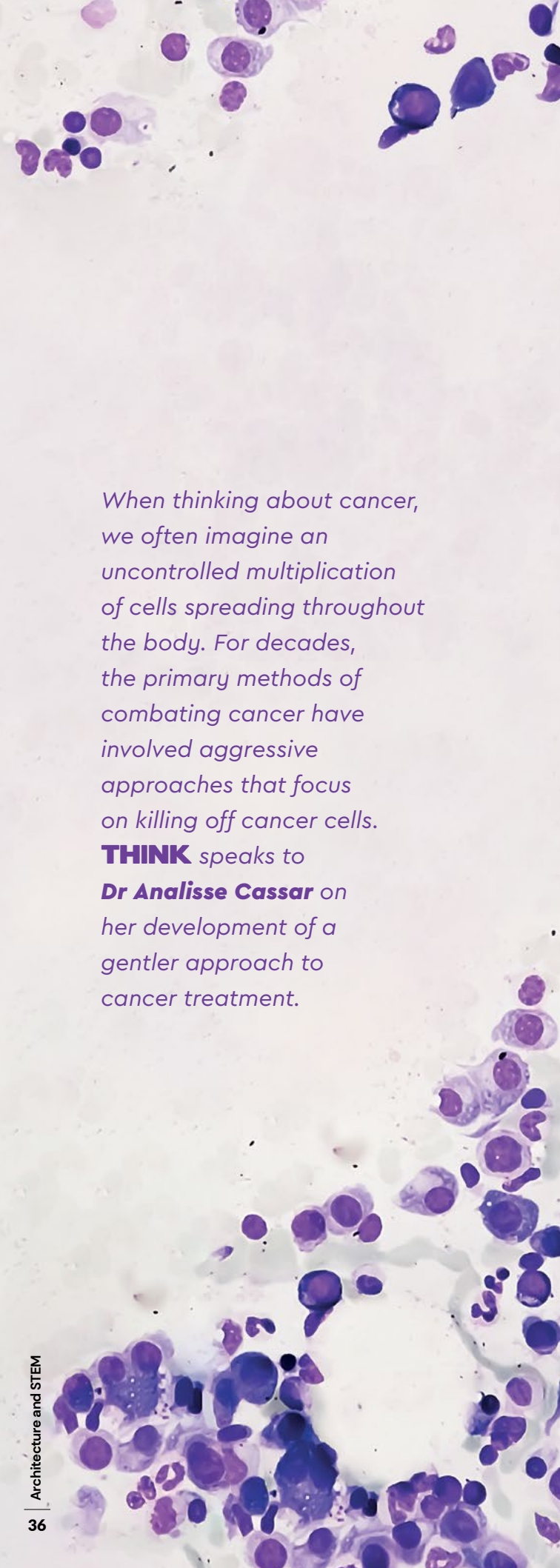


Harnessing Nature to Accelerate

CANCER CELL AGEING

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When thinking about cancer, we often imagine an uncontrolled multiplication of cells spreading throughout the body. For decades, the primary methods of combating cancer have involved aggressive approaches that focus on killing off cancer cells.

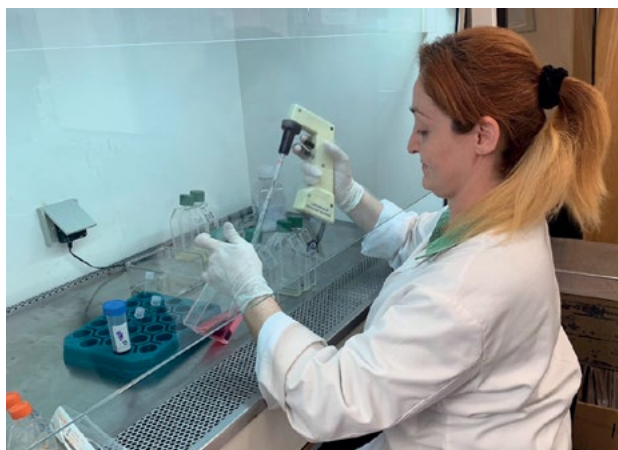
THINK speaks to **Dr Analisse Cassar** on her development of a gentler approach to cancer treatment.

Cancer treatments like chemotherapy and radiation can be harsh on patients, as they inadvertently kill healthy cells vital for our body's daily functioning. Taking lessons from treatments for acute promyelocytic leukaemia, a new approach to cancer treatment is gaining traction by encouraging cancer cells to mature more quickly, rather than aggressively killing them. Led by Dr Analisse Cassar, a UM-based research team is developing a gentler approach that forces cancer cells to mature or 'age' with the help of compounds derived from natural sources. With further research, this innovative method offers a gentler alternative to traditional therapies, reshaping the way we think about cancer treatment.

A NEW WAY OF THINKING ABOUT CANCER CELLS

Cassar, a cancer researcher with the Cancer Therapeutics group within UM's Faculty of Medicine and Surgery, is leading her team in discovering novel approaches which can be used to combat cancer. She explains that cancer cells, like stem cells, behave as if they are 'stuck' in time. 'The truth about many cancers is that the cells are immature,' says Cassar. 'They multiply quickly

Dr Analisse Cassar
Photo by Dr Oriana Mazzitelli



without ever maturing fully into functioning cells, which is why they're so harmful.'

In healthy bodies, cells grow, mature, and eventually die, making room for new, fully functional cells. However, cancer cells are different. They don't follow the usual life cycle. Instead, they multiply without maturing, leading to an overgrowth of useless, immature cells that accumulate in the body's systems. In the case of leukaemia, for instance, the problem isn't just that cancer cells multiply quickly; it's that these immature cells take up space that should be filled by mature, fully functioning blood cells.

FORCING CANCER CELLS TO MATURE

This is where differentiation therapy comes in – a technique that forces cancer cells to mature. Think of it as pushing these cells to 'grow up' and stop multiplying. Differentiation therapy has already seen significant success in the treatment of a specific type of blood cancer known as Acute Promyelocytic Leukaemia (APML). Once considered 90% fatal, APML is now approximately 75% curable thanks to the use of ATRA-differentiation therapy, which pushes immature cancer cells toward maturity.

Cassar's work builds on this success but expands it further, using natural compounds to achieve the same results in other types of cancers.

'The cancer we tackle often has a block in maturation, and forcing it to age removes its ability to proliferate rapidly. Once a cancer cell matures, its lifespan is short,' explains Cassar.

THE ROLE OF NATURAL COMPOUNDS IN CANCER TREATMENT

What makes Cassar's approach even more unique is her team's use of natural compounds to drive this process of inducing cancer cells to mature. 'We've been studying a wide range of natural chemicals', says Cassar, 'including extracts from plants and even sea cucumbers and axolotls, which are known for their regenerative properties.'

Unlike synthetic drugs used in conventional treatments, these natural compounds offer a gentler approach. They are less toxic, making them ideal for patients who cannot tolerate aggressive chemotherapy or radiation treatments. 'Our aim is to provide an effective treatment that doesn't harm patients,' Cassar emphasises. 'Natural compounds are promising because they can target cancer cells with potentially fewer severe side effects than those often seen in traditional cancer treatments.'

EPIGENETICS: TWEAKING THE CELL'S GENETIC MATERIAL

In addition to using natural compounds, Cassar and her team also employ epigenetic modifiers to tweak the genetic material of cancer cells. Epigenetics refers to changes in how genes are expressed without altering the actual DNA sequence. This is crucial because cancer cells can often resist treatment by shutting down the genes that would otherwise make them susceptible to drugs.

'Epigenetic modifiers allow us to "unzip" or "open up" parts of the cancer cells' genetic material that were previously closed off to treatment,' explains Cassar. 'By doing this, we make the cells more vulnerable to the natural compounds we're using, increasing the effectiveness of the treatment.'

This two-pronged approach – using natural compounds to push cancer cells toward maturity and employing epigenetic modifiers to enhance the effect – has already shown promising results in various cancers, including leukaemia, osteosarcoma, and neuroblastoma.

A GENTLER APPROACH FOR VULNERABLE PATIENTS

One of the most significant advantages of Cassar's approach ➤

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is that it does not work by directly killing cancer cells and thus doesn't kill healthy cells, either. Conventional treatments like chemotherapy can be extremely hard on the body, causing severe side effects such as immune suppression, hair loss, and nausea. In some cases, these treatments are so toxic that they pose serious risks for vulnerable patients.

'Our treatment avenues offer a potentially less harmful alternative,' says Cassar. 'This makes it ideal for patients who are too frail to undergo aggressive treatments. It's also a much better option for children and young adults, whose bodies are still developing. These groups are particularly vulnerable to the long-term effects of harsh cancer treatments, such as infertility or developmental issues.'

By offering a treatment that focuses on ageing cancer cells rather than killing them outright, this strategy promotes a future where cancer therapies are not only more effective but also kinder to patients.

THE ROAD AHEAD

While this new approach is promising, there's still much work to be done. Cassar's team has made remarkable progress, but they are now applying for funding to test their novel therapeutic approaches in animal models to ensure that the treatment is safe and effective. 'It's a long road to clinical trials, but the results so far give us hope,' she says.

Cassar is optimistic about where this research is headed. 'We're not

there yet, but the potential for this treatment to be used alongside conventional therapies is promising,' she explains. 'The idea is not to find one miracle drug that cures all cancers, but to combine different approaches. The more angles we can attack cancer from, the better our chances of success.'

A MORE COMPASSIONATE FUTURE FOR CANCER TREATMENT

In the end, Cassar's work represents a shift toward more compassionate, patient-centred care. By focusing on natural compounds and less toxic therapies, her team hopes to offer patients an alternative to the harsh treatments of the past.

'Cancer treatment doesn't have to be as brutal as it's been in the past,' she says. 'By harnessing nature to age cancer cells, we're offering a gentler, but equally effective, path forward.'

As this innovative research moves toward clinical trials, it offers new hope for cancer patients everywhere – especially those who have suffered most from the side effects of conventional treatments. With a combination of natural compounds and epigenetic tweaking, this approach could pave the way for more effective and much kinder cancer therapies in the future. **T**

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