THE AUSTRALIAN

How a new 3D atlas of cancer cells may hasten a cure

A new era for genomics will supercharge precision medicine, starting with 'cell GPS maps' that will be open to the world's scientists.

By NATASHA ROBINSON HEALTH EDITOR

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Its potential has been described as almost limitless. It's known as spatial medicine and it is poised to accelerate the advances of the past two decades in genomics and gene screening.

With cutting-edge science able to reveal the private lives of cells and their interactions with the immune system, huge leaps in understanding of cancer, cardiovascular disease and chronic illnesses are moving faster and closer. Spatial medicine promises to accelerate the delivery of targeted, individualised treatments as cell atlases in mind-blowing detail are created and shared around the world.

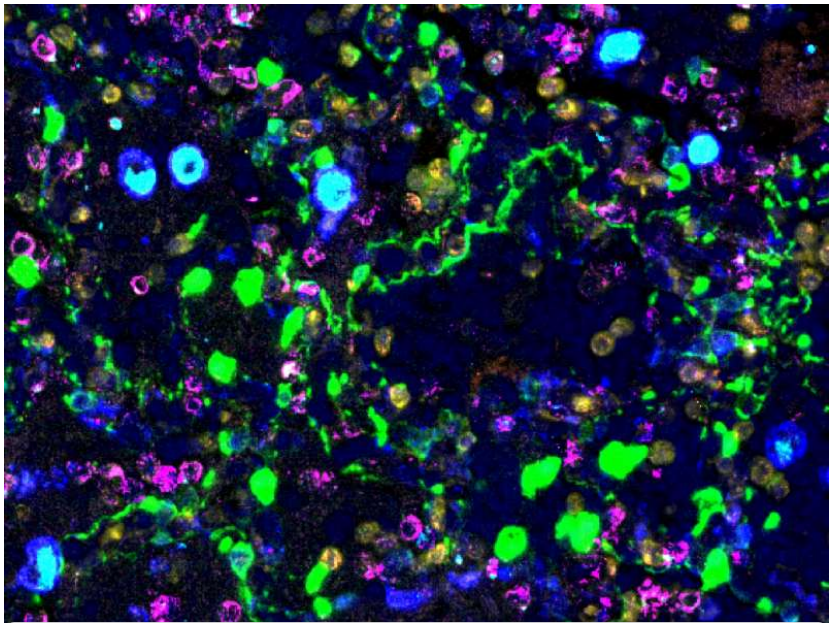
"I think what we are seeing is the real dawn of precision medicine," leading Australian spatial biologist Arutha Kulasinghe, the founding scientific director of the Queensland Spatial Biology Centre at the Wesley Research Institute, tells Inquirer. "Precision medicine is not how we described it five years ago. Spatial medicine is a new reality."

The new field is driven by seismic advances in what is known as spatial omics, a method of digital computational pathology that enables us to understand the body's cells and the way they interact with immune cells at the individual cellular level like never before. The images produced are akin to a cell GPS map.

In cancer, that's enormously important to making judgments about whether certain treatments will be effective. Cell neighbourhoods can be visualised in 3D and entire atlases of cancer types are being created.

Several leading Australian scientific institutes are carrying out intensive research in spatial biology. Now, Australian philanthropy has funded the world's first chair of spatial medicine research, a partnership of the Wesley Research Institute and the Frazer Institute at the University of Queensland. The inaugural chair, which Kulasinghe takes up this month, is being funded by the Wesley Research Institute and the Brazil family, a north Queensland farming family.

What is spatial medicine?



- Spatial medicine is a new field of medicine that is able to create digital cellular 'maps' of patient biology samples
- The field uses digital pathology methods to combine biology, data and computing to design highly targeted treatments
- Spatial medicine means the body's tissues can be digitally mapped in 3D so that tissues can be viewed in their native environment. Critically, how the immune cells interact with tumour cells in cancer can also be seen and understood via extraordinarily detailed digital images
- Spatial biology will transform how we diagnose, predict and treat disease.

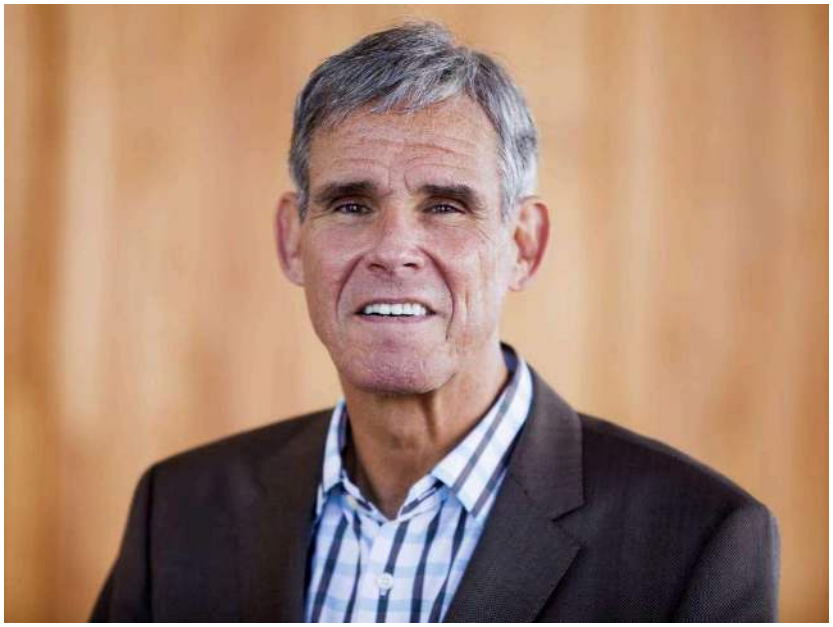
Eric Topol: ‘We’re seeing the dawn of a new era in medicine’

Renowned American cardiologist, scientist and author Eric Topol called the coming healthcare revolution 18 months ago when he named spatial medicine as a new branch of medicine. The professor of molecular medicine and founder and director of the Scripps Research Translational Institute in San Diego proclaimed then that it was a field no longer in the realms of science.

“We’re not just talking now about spatial omics or spatial biology. We actually have a new field of medicine,” Topol told Inquirer this week from the US. “I think this field is going to lead to cures for cancer and not just remissions.

“Spatial biology or spatial omics is one of the hottest areas of life science because we never before have had the ability to track biology in both space and time. So it’s a whole other dimension.

“Australia is absolutely at the centre of the worldwide collaboration that is occurring in spatial omics. I’m thrilled to see Australia establish the first chair position in spatial medicine in the world.”



US cardiologist Eric Topol, a global leader in genomics, has coined the term spatial medicine to describe the next frontier of precision medicine. Picture: Reuters

Why spatial biology is so important

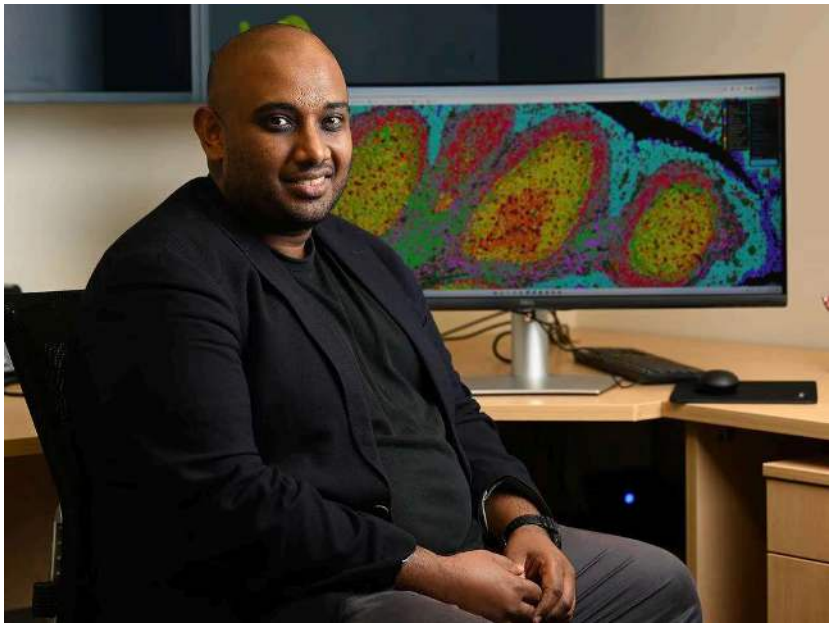
Kulasinghe has been at the forefront of spatial omics in Australia for more than a decade.

This week Inquirer spoke to him as he prepared to launch into the world an extraordinary three-dimensional digital atlas of lung cancer. Here is what he has to say, in his own words, about the scope and potential of spatial medicine.

“For every solid tumour type out there – such as breast cancer, head and neck and lung cancers – pathologists look at a stain in two dimensions with a method that was developed 150 years ago. It’s really informative in terms of the shape of where the cancer is, but it tells us no more information.

“What spatial biology can do is take a tissue sample and make an almost technicolour image, which is like a movie. It enables us to understand tumours at the cellular level.

“And so instead of looking at two markers, as we’ve been doing for the past century, we’re able to now look at millions of individual cells. This technique is known as spatial omics and reveals to us the private lives of cancer cells. We’re able to now look at the millions of cancer cells and learn how they’re communicating with each other, how they’re communicating with immune cells, and so on.”



Arutha Kulasinghe of the Queensland Spatial Biology Centre, who has created the first digital atlas of lung cancer, is taking up the world's first chair of spatial biology at the University of Queensland, funded by the Wesley Research Institute. Picture: Lyndon Mechielsen

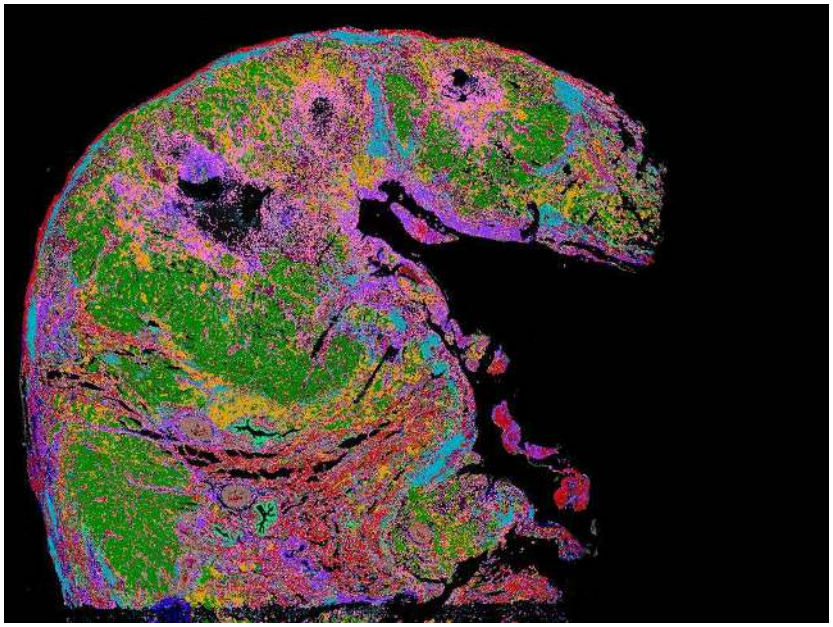
The immune link

"Immunotherapies, which have revolutionised the treatment of many types of solid tumour cancers, rely on immune cells engaging and recognising the tumour. Tumour cells have a cloaking mechanism that protects them from immune cells.

"What immunotherapies do is de-cloak the tumour cells so that the body's immune cells can go in and kill those tumour cells. So what this field of spatial medicine has been developing is ways and methods of how we can understand how these cells communicate and how the tumour cell communicates with the immune cells.

"We profile tissue specimens for the entire immune landscape. We create these really pretty pictures that become digitised images. Every cell has an x, y and z coordinate. And all of a sudden it's not a biological or clinical challenge, now it's a computational challenge. So when we digitise one of these images, it's about five to 10 terabytes of data. We're looking at a million individual cells from each patient biopsy.

"And now we can see all the different flavours of the tumour cells. We assume tumours are homogeneous or they're all the same, but the way they metabolise glucose is very different, the way they behave in certain locations is very different, and so what spatial medicine allows us to do is build these complex digital maps of tumours that enable us to identify patterns associated with therapeutic benefit and non-benefit. It also allows us to identify patterns of resistance to therapy, and so that becomes useful for the oncologists because they know at the time of diagnosis whether a particular drug is likely to work.



A cellular digitised atlas of the lungs compiled by the Queensland Spatial Biology Centre, where every cell is now assigned a cell type, location in a coordinate system – equivalent to a cell GPS map. These images are by digital pathology methods and used in spatial omics and spatial medicine.

“We’ve learnt a lot from the mapping of the human genome and the development of genomics. It’s fundamental to everything we do. But this is a new frontier in precision oncology that is really about figuring out predictive biomarkers, which are characteristics of the tumour that can be targeted with therapies at the time of diagnosis.

“This is critical because the two most expensive drugs on the PBS today are immunotherapies. Immunotherapies cost the Australian government $1bn a year but they work in only about 20 per cent of patients.

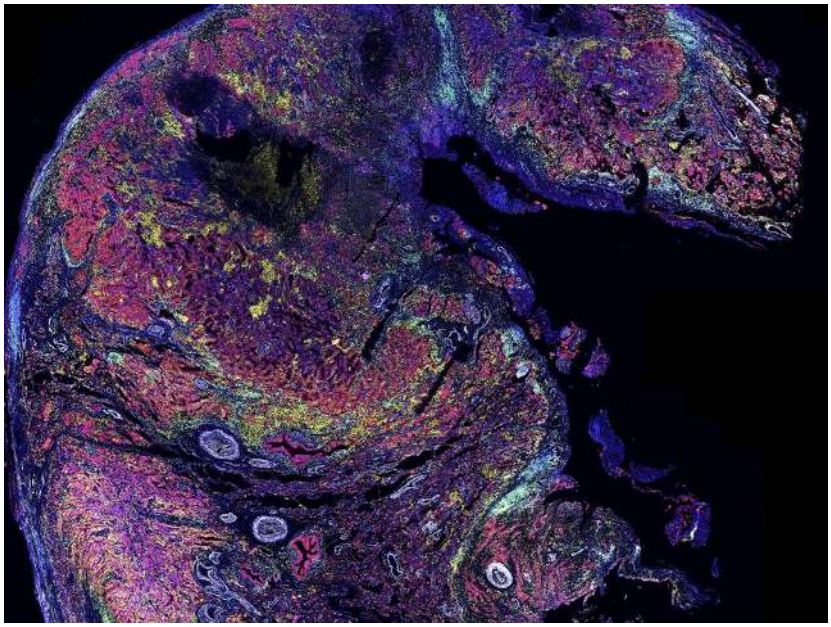
“The challenge for the field is how do you identify that 20 per cent and how do you identify the 80 per cent so you can tailor the therapies and give those patients that are likely to respond the drug and then find an alternative or a more effective way to treat that 80 per cent.”

The lung cancer atlas

“Ten years ago, the whole world was given what’s called the cancer genome atlas, which is the genetic information of multiple cancers. It was incredibly powerful at the time and it has enabled scientists to create individual atlases of cancer types. The cancer genome lung atlases came out in 2014 and it took hundreds of researchers to put that together.

“Our lab of 25 people has now built a working model of a lung cancer atlas, working really closely with Yale Medical School and with clinical teams from Greece.

“Our lung cancer spatial clinical atlas will map where every single cell is in a lung cancer tumour. We’ve almost completed this work, and once it is submitted and published we’ll make the atlas open to scientists across the world. It’s incredibly detailed and will become a fully searchable atlas and an incredible resource for the world. The global lung cancer community – whether you’re in Kenya or in New York – will be able to go in and mine the dataset that we’ve built.



The cellular architectural landscape of lung cancer revealed by digital pathology methods and used in spatial omics and spatial medicine, showing cancer tumour regions (red) and immune cells (yellow and blue).

“Scientists and clinicians will be able to search the atlas against particular genes, proteins and particular cells. It will reveal how these genes, proteins and cells appear in the lungs, and specialists will be able to understand spatially where these genes, proteins and cells are in responders and non-responders to standards of care such as immunotherapy and chemotherapy.

“The atlas will also reveal variation in immune cells from early to late stage and how therapies work differently in males and female. This has never been done before. And so it’s really, really powerful for the field.

“Our next aim will be to build a breast cancer atlas and then a head and neck atlas.”

The global effort to combat cancer

“Every major science institution in the world, including Australia’s scientific institutes and bodies, which are at the forefront of this science, has realised that spatial medicine is the future of precision medicine. To understand diseases better, institutes need a lens of spatial biology and need to build expertise around that. The challenge is no one lab has really built teams that span patient cohort studies, the data science, and then the signature development of cancers all together.

“A single lab cannot execute on this end to end. In the spatial community, we’ve got about 17 to 30 labs worldwide, including several in Australia, at any one time collaborating with each other.

“I think what we seeing is the real dawn of precision medicine. We now have the tools to be able to mine images for really deep patient therapeutic insights. We go from the lab through profiling large patient cohorts, examining tissue samples of people with lung, breast, head and neck, skin, ovarian, colorectal cancer, multi-institutional studies. We have 10 computational data scientists who mine this data, because the challenge is that with these new types of images with millions of cells it becomes a data puzzle.

“What bringing this all together will do is enable us to accelerate the past 10 years of effort we’ve invested in this space, to get these discoveries that are being made around the world into the clinic for the benefit of patients.”

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