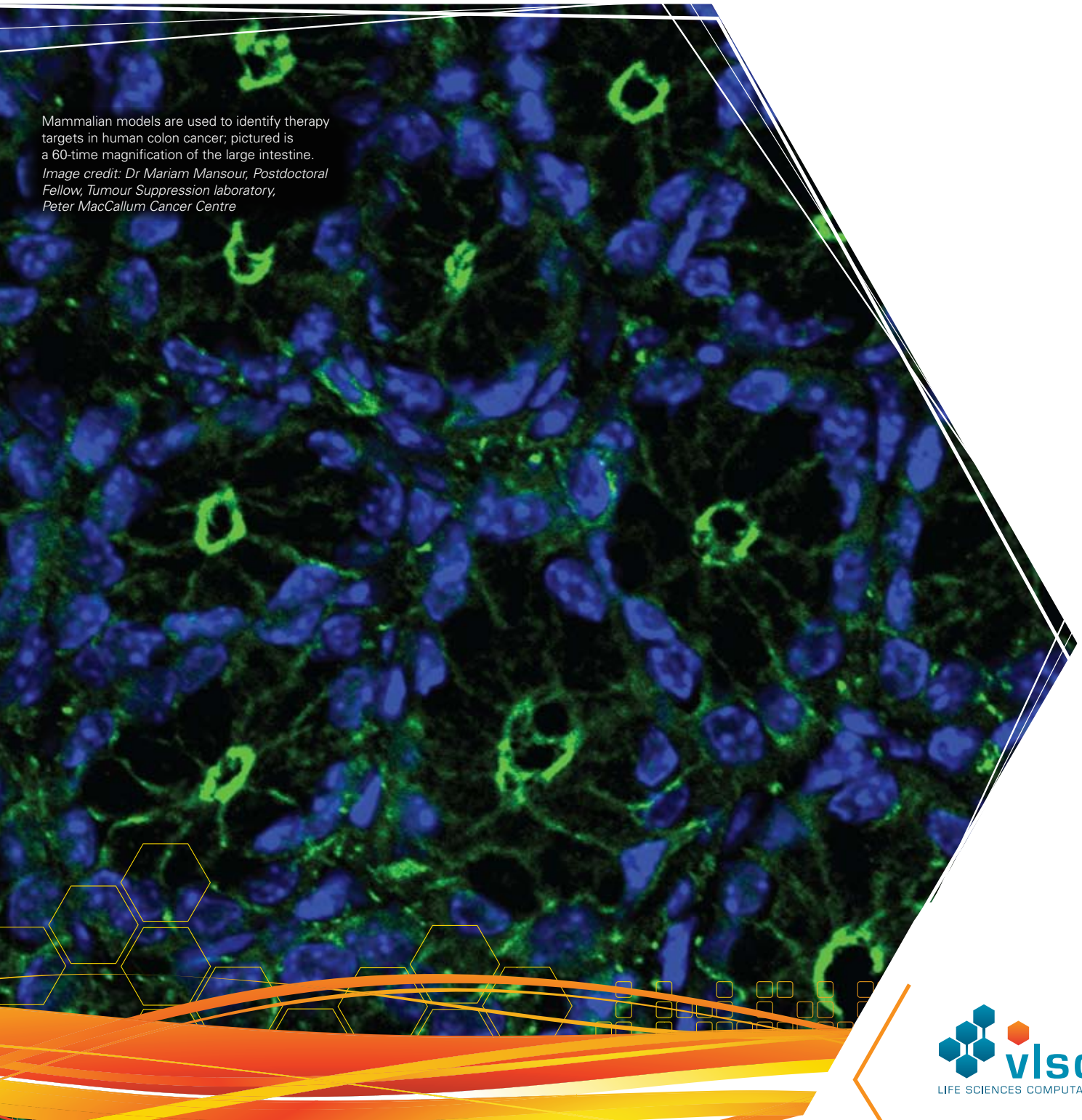
WHAT'S IN A NAME?
CANCER REDEFINED

Welcome to the brave new world of personalised cancer treatments — where your cancer will be rapidly typed and a personal treatment plan created with the help of supercomputer-inspired analysis.

Tim Thwaites, Science Writer



Mammalian models are used to identify therapy targets in human colon cancer; pictured is a 60-time magnification of the large intestine.
Image credit: Dr Mariam Mansour, Postdoctoral Fellow, Tumour Suppression laboratory, Peter MacCallum Cancer Centre

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LIFE SCIENCES COMPUTATION

"Cancer isn't simple. And the closer we look the more complex it gets."

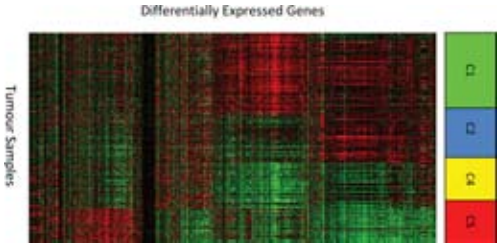
Professor David Bowtell (bottom right) with research team at the Peter MacCallum Cancer Centre.
Image credit: David Paul

The parts of the body from which traditional cancers derive their names—kidney, breast, bone, blood, ovary—are actually composed of blends of genetically distinct tissues. For this reason, tumours associated with particular organs can have more in common with counterparts in other organs, than with each other.

"As we delve deeper into the genetics of cancer, we are beginning to find is that ovarian cancer isn't just one cancer, and certain types of ovarian cancers have more in common with cancers of lining tissues in the breast or bowel" according to Professor David Bowtell, the head of the Cancer Genomics and Genetics Program at the Peter MacCallum Cancer Centre (Peter Mac), and Principal Investigator of the Australian Ovarian Cancer Study.

"We need to move away from terms like ovarian cancer—they're not helpful—and get to a stage where we talk about a cancer in terms of its molecular features and the way it should then be treated. The genomic analysis we've done already underscores the fact that 'ovarian' is a nonsense term. Most of these cancers don't come from the ovary - they just happen to be located anatomically in that space."

Working with clinicians, David's group has demonstrated that one type of ovarian cancer, notoriously resistant to conventional ovarian cancer therapy, is actually responsive to treatment with a drug normally prescribed for renal cancer. It is leading to a future where a person's cancer will be classified according to gene activity; where key compounds or "markers" related to specific biochemical pathways will indicate the underlying cause of the cancer and suggest the appropriate treament response.



Heat map: Gene expression microarray data is used to identify molecular subtypes of high grade serious ovarian tumours. Prof. Bowtell analyses genes that are up-regulated (red) or down-regulated (green) in each subtype, to gain insight into the molecular pathways important to each subtype.
Image Credit: Peter MacCallum *Cancer Centre*

Driving these new ideas are advances in technology—particularly the ability to sequence DNA rapidly using "next gen" techniques and to measure gene activity using microarrays. But all would be meaningless without the capacity of the latest supercomputers to sort out and manipulate the massive amounts of data generated. That is where the Victorian Life Sciences Computation Initiative (VLSCI) comes in.

"Supercomputing is going to be central," David says. "The data complexity driven by technology has grown super-exponentially, and with it the computational requirements. And it's not just hardware, but also the appropriate skill sets needed to manage it."

David's group, part of the International Cancer Genome Consortium, in collaboration with the Institute for Molecular Bioscience at the University of Queensland, is setting out to map the genomes of tumour cells from about 100 ovarian cancer patients and to match them to treatment responses.

The Peter Mac team is also involved in The Cancer Genome Atlas Project, which will assemble a comprehensive catalogue of all the genetic mutations in human cancers. This mammoth undertaking involves sequencing 500 samples of the most common cancers. David expects it will turn up cancer-related mutations in some hundreds of genes.

"But these mutations don't occur in isolation. What you would expect to see is that there will be combinations of mutations that go together. It is in plotting these interactions that the supercomputer will be especially useful, but it will be the role of bioinformaticians to find meaning within these diverse human cancer sequence datasets."

The bioinformatician's expertise is essential to this task, taking gigabytes of sequencing data, correcting for errors, aligning it into the three-billion base pair DNA sequence of the human genome, and then comparing that with the published reference sequence to pick up variations or mutations.

"Once you have your list of differences from the reference genome—typically about three million of them—you need to sort out the ones you think are connected with causing the disease. That's where you need people who really know about cancer," says Associate Professor Andrew Lonie, head of the Life Sciences Computation Centre (LSCC), based at VLSCI.

The LSCC is a central point for assistance for Victorian researchers, enabling access to the VLSCI's supercomputers and high performance computing. "If you've got a project which needs a bioinformatician, we can embed someone with the right skills to help out," Andrew says.

Melbourne's considerable expertise in cancer research is currently being drawn together into a joint venture known as the Victorian Comprehensive Cancer Centre. The collaboration between seven research organisations calls for some of them, including Peter Mac, to be housed in a new purpose-built edifice directly across the road from the Royal Melbourne and Royal Women's Hospitals.

"Having such equipment and skills locally makes a huge difference," Professor Bowtell says. "It means you have some control over processes which are critical to a whole lot of research programs—and do not become a hostage to the priorities of others."

"Also you become a magnet to draw good people to you. In Melbourne we can now say that we have all the pieces of the puzzle together and we are ready to go."

For further information about this research contact Prof. Bowtell at david.bowtell@petermac.org

To contact VLSCI, go to www.vlsci.org.au

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