FIVE YEARS OF PERSONALIZED ONCOGENOMICS (POG)

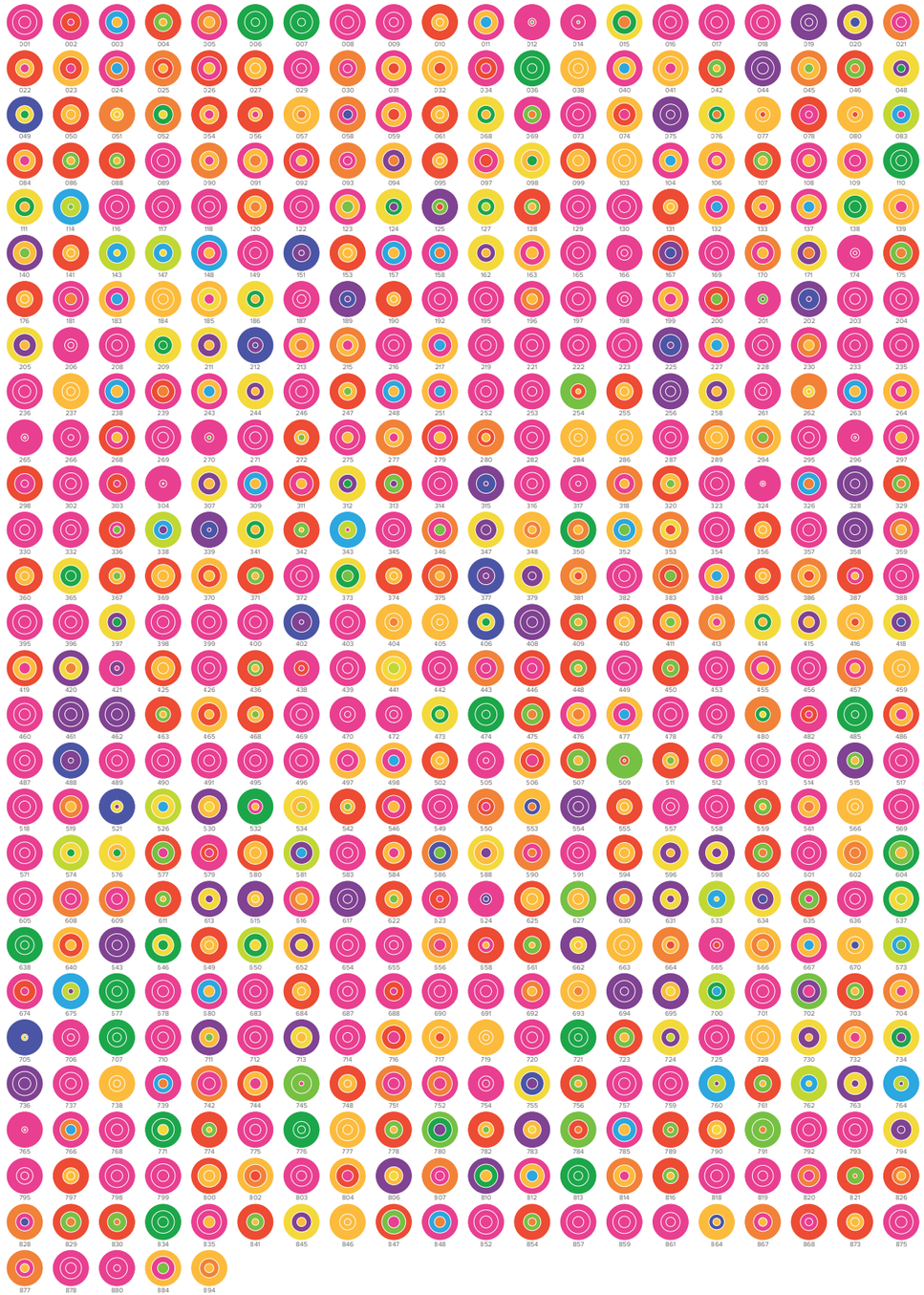
The **BC Cancer Personalized OncoGenomics (POG)** program is a clinical research initiative studying the impact of embedding whole genome sequencing into real-time treatment planning for British Columbian patients with metastatic cancers. It is a collaborative research study including many BC Cancer oncologists, pathologists, other clinical staff, researchers and technical personnel.

Since the launch of the program in 2012, POG has successfully recruited 1,000 patients with metastatic cancer and completed sequencing and analysis on more than 600. For those 600 patients and their clinicians, they had access to additional personalized information to inform their treatment decision options. BC Cancer is the only centre in the world conducting a study on the scope and scale of POG.

The majority of the funding for the direct cost of POG comes from the BC Cancer Foundation. That funding has been leveraged to obtain additional support for advanced research equipment, trainees, and related research programs such as the Terry Fox Research Institute's Canadian Comprehensive Cancer Centre Network and a new pan-Canadian clinical trial called CAPTUR, which will further align patients in POG with targeted treatments.

In 2017, POG research resulted in eight publications in peer-reviewed journals, from studies identifying genomic signatures that can predict responses to some treatments for breast cancer patients and the molecular characterization of metastatic pancreatic tumours to analyzing the cost-trajectory of using whole-genome analysis to guide treatment decisions. Ten presentations were delivered at high profile clinical or scientific events and several news stories were published about POG, including an award-winning documentary on CBC's *Nature of Things* called *Cracking Cancer*.

Over the past five years, the POG team has grown to include more than 200 people from across BC Cancer, including at all its regional centres. The impact and momentum of the resulting collaborations will continue to foster research studies and advances in clinical translation and outcomes for the foreseeable future.



MAKING ART WITH SCIENCE: INTERVIEW WITH MARTIN KRZYWINSKI

> *"We've been training to spot patterns ever since life began on Earth."*

Cancer is complicated. Decades of painstaking experiments, meticulous measurements and reams of computer code have resulted in a dizzying array of data about the disease that even the most mathematically inclined minds find boggling.

At BC Cancer's Genome Sciences Centre (GSC), scientists use this data to crack cancer's code, running DNA sequencing machines 24 hours a day, seven days a week, analyzing the three billion base pairs that make up approximately 30,000 genes within the 23 chromosomes of the human genome; errors in the code, known as mutations, result in the plethora of cancers we know too well. To date, the GSC has sequenced more than two petabases of DNA, or about the same as 66,000 whole human genomes.

How to make sense of all of these numbers? Enter Martin Krzywinski, staff scientist with the GSC. He makes art from it. From popularizing science to facilitating dialogue between disciplines and inspiring ideas for research, his data visualizations and illustrations aren't just pretty; they're helping to uncover clues about cancer.

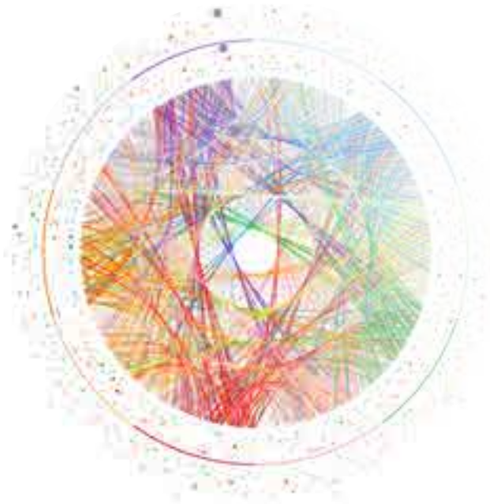
Popularizing science

In 2003, Martin did something simple, yet elegant, that made his colleagues, and the world, take notice.

"I looked at the way that people would traditionally represent chromosomes as horizontal lines, using diagonal lines to connect genes to represent relationships. I thought: turn the chromosomes into a circle. Put connecting lines on the inside."

Making a horizontal chart into a circle turned out to be really useful in showing similarity or dissimilarity between regions in a genome, for comparing genetic information between species or analyzing differences between cancer and normal DNA, for example. It's also a useful "stopgap measure," Martin says, a way to make-up for what's missing. "Visualization can indicate where to look when we don't really know yet."

He called the design Circos, and before he knew it, it was everywhere. After appearing in the *Catalogue of Somatic Mutations*, Martin began to see it in all sorts of peer-reviewed publications. But it wasn't just interesting to scientists. It appeared in the *New York Times* and on the back of a coffee table book by David Cronenberg. *Wired Magazine* asked him to make a version depicting the relationship between the characters on the popular television series, Lost. Circos wasn't just useful, it was beautiful.



"I think the reason why visualization of complex data works so well, is because we've been training to spot patterns ever since life began on Earth. We've had solid schooling in finding patterns, because we wanted to avoid predators. We aren't trained in mathematics in the same way. You can't fall back on natural faculties for it like you can for shapes."

Facilitating dialogue

Martin's work has been useful in BC Cancer's Personalized OncoGenomics (POG) program where whole genomes of cancer patients are sequenced and compared to DNA from their cancer. Visualizations can communicate this information quickly. It can also cut across specializations, which is important to POG's multidisciplinary teams.

To celebrate POG's fifth anniversary in July 2017, Martin made a graphic of all the individual POG patients that had been sequenced. He represented each patient as a circle with three concentric rings, shaded with 12 different colours representing different tumour types (see page 23). What you see in a circle is the three most similar tumour types, based on the genetic information of the patient's tumour sample, to their cancer. For example, despite a diagnosis of breast cancer, the mutations in a patient's cancer may be similar to a patient with colorectal cancer or quite different to another with breast cancer.

"Between the fundamental aspects to the overwhelming aspects of cancer, is where this art comes into play. Does it tell a story? Does it look like something you could understand even if you don't know what it is? In this example, the colours obviously mean something. The circles do too. So, now I can tell you a story about cancer."

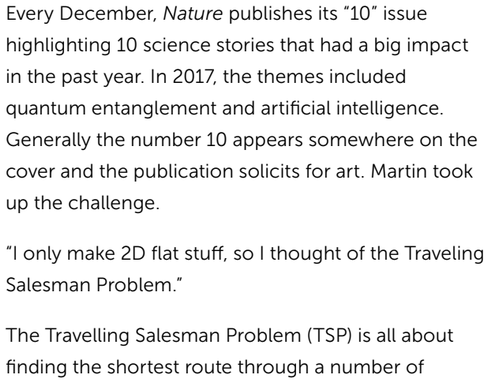
Insights and inspiration

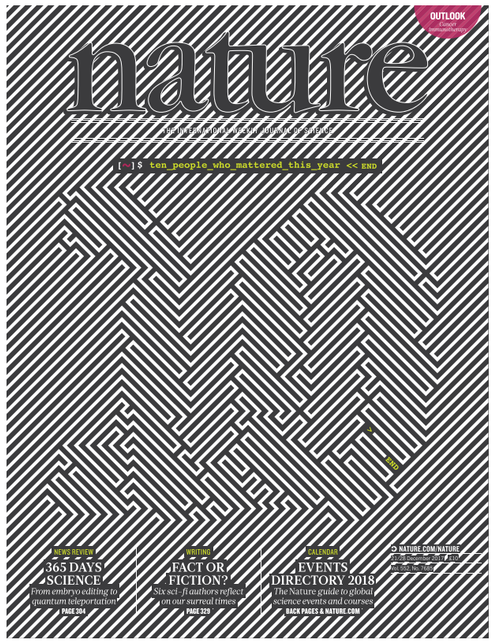
Every December, *Nature* publishes its "10" issue highlighting 10 science stories that had a big impact in the past year. In 2017, the themes included quantum entanglement and artificial intelligence. Generally the number 10 appears somewhere on the cover and the publication solicits for art. Martin took up the challenge.

"I only make 2D flat stuff, so I thought of the Traveling Salesman Problem."

The Travelling Salesman Problem (TSP) is all about finding the shortest route through a number of points without crossing the same point twice, and it's inspired a genre of art. TSP art are black and white images represented by dots that the artist tries to find the shortest path through without doubling back. The final product is zebra-like, full of dense lines where it is black, less dense where it is grey and no lines where it's white. Depending on the solution, the image could be compelling or just a bunch of lines. Martin did this with the number 10.

"You have to throw an algorithm at TSP art. There's the artificial intelligence angle. And it looks kind of tangled too, right? So I ran it and *Nature* ended up using it. It's striking. It's jarring. I like it. It fits my personality.





"A lot of the stuff that I make is not useful in the way that a hammer is useful. It's not a tool for getting something done. But hopefully it's inspiring. I think it gives people ideas. Or, perhaps, it helps to relieve the crushing burden of trying to understand science. I hope it puts people in a better mood; a mood that helps to maintain focus on science but provides relief in the form of a pleasant pattern. Maybe it even gives a scientist hope that their data has a pleasant pattern too. They just haven't found it yet."

PAIN & SYMPTOM MANAGEMENT

The role of nutrition and exercise during cancer treatment

Exercise and healthy eating programs have been shown in research studies to improve the health and well-being of women receiving chemotherapy for breast cancer. However, access to such programs is currently not a common part of cancer care. A project led by the BC Cancer Nutrition and Rehabilitation program, in collaboration with the Department of Physical Therapy at UBC, has examined how many physicians would refer patients to such a program, how many women would attend and what the benefits would be. As published in *The Oncologist* and *Medicine & Science in Sports & Exercise*, the researchers found that physicians liked having a pathway to refer women to a program they trusted. Women enjoyed the program and had improvements in fitness.

Now the team, co-led by **Drs. Ryna Levy-Milne,** Provincial Director for Therapeutic Oncology Services, and **Kristin Campbell,** Affiliate Scientist in Cancer Control Research, has received an **MSFHR Reach Award** to investigate the development of an exercise guidance program specific to cancer survivors in British Columbia. The Reach Program provides funding to support teams to co-develop activities that inform or improve further health research practice or policy-making. Previous research by Drs. Levy-Milne and Campbell has established that structured exercise after a cancer diagnosis is effective in managing symptoms, improving health and returning to normal life.

Post-operative pain control for breast surgeries using breast block technique

Pectoral nerve block (aka, breast block) is a relatively new technique for providing surgical anaesthesia and postoperative analgesia during breast surgery that relies upon the placement of local anaesthetic between the thoracic wall muscles. It allows local anesthesia for up to 36 hours postoperatively, and is even safe for patients who cannot receive general anesthesia. At the BC Cancer Surgical Retreat, **Drs. Sara Gough** and **Frances Chow** presented the results of retroactive analysis of 200 breast cancer surgeries using breast blocks. They found that providing breast blocks gave superior pain control and fewer post-anesthetic complications of drowsiness, nausea and vomiting. Breast blocks may also be correlated with reduced metastasis, which the researchers intend to explore through future research.