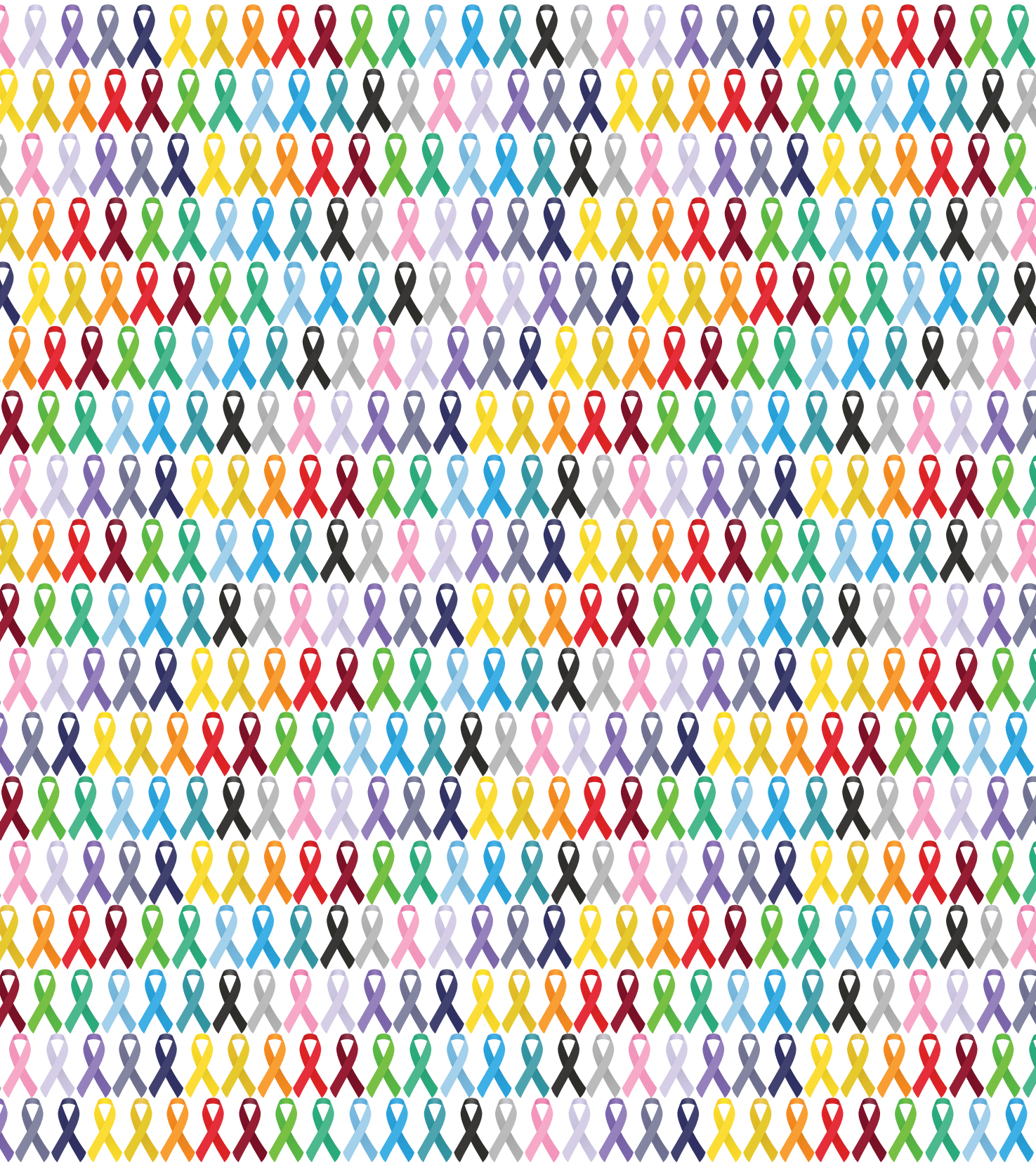

CUSTOM CANCER VACCINES

Could personalised vaccines hold the key to revolutionising the treatment of cancer?

When Bill Gates was asked to be the first guest curator of *MIT Technology Review*'s annual list of 10 breakthrough technologies, the world of science and technology sat up and took note. Not only would his choices have the potential to profoundly affect our lives, but they would be focussed on healthcare and the reduction of extreme poverty – the two primary goals of the Bill & Melinda Gates Foundation.

Amongst Gates' curated list was research into the relatively unknown field of personalised cancer vaccines, which use a person's own immune system to attack tumours. One of the most exciting breakthroughs in oncology in decades, such vaccines hold out the possibility of providing the right treatment to the right patient at the right time, instead of applying a one-size-fits-all treatment to all patients.

"Scientists are on the cusp of commercialising the first personalised cancer vaccine," wrote Gates. "If it works as hoped, the vaccine, which triggers a person's immune system to identify a tumour by its unique mutations, could effectively shut down many types of cancers."

Cancer vaccines are unknown territory but the prospect of their success is rapidly altering the landscape of cancer treatment. If a person's own immune system can be utilised to defeat many types of cancers, one of the world's greatest killers could be subdued by matching treatments to individual patients. That treatment would be precisely tailored to stimulate the immune system to react to specific tumours.

"By using the body's natural defences to selectively destroy only tumour cells, the vaccine, unlike conventional chemotherapies, limits damage to healthy cells," wrote Gates. "The attacking immune

Rightc : Moderna's research centres on strands of genetic instructions called messenger RNA, or mRNA, which it proposes to use to instruct the body to treat the disease on its own

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LÉLIA DELAMARRE, A SENIOR SCIENTIST IN CANCER IMMUNOLOGY AT GENENTECH

cells could also be vigilant in spotting any stray cancer cells after the initial treatment."

For Lélia Delamarre, a Senior Scientist in Cancer Immunology at Genentech, a biotechnology company based in San Francisco, it all makes perfect sense. "For all the blood, sweat and tears that go into designing new medicines, one of the most powerful weapons against disease resides in our own bodies," she wrote in *Scientific American*. "We just need the right tools to unleash it."

Alongside her colleague, Ira Mellman, Delamarre first proposed personalised cancer vaccines to the company's senior management back in 2012. Her case was simple: utilise the incredible disease-fighting system that evolution has bequeathed us to fight cancer on its own terms.

"Over millions of years of evolution, our body's immune system has become exquisitely refined to protect us from foreign invaders such as bacteria and viruses, or from harmful changes arising in our own cells, like cancer," wrote Delamarre. "The immune system is the ultimate partner in combatting disease

because it has multiple lines of defences, is adaptable, and has memory. Vaccines – perhaps the most transformative breakthrough in the history of medicine – are effective precisely because they harness this unique power. By using vaccines to train the immune system to recognise and attack foreign proteins (called antigens) found in pathogens, we've brought infectious diseases like smallpox, polio and measles to their knees. We may now be in position to effectively use this approach in our fight against cancer."

How has this become possible? Through rapid improvements in genomic sequencing and computer science. Both have enabled researchers to identify and characterise cancer mutations (called neoantigens) in individual tumour samples and at much-reduced cost.

"Scientists are seizing this opportunity to develop new cancer vaccines tailor-made for each patient," wrote Delamarre. "The process starts with sequencing the genome of a person's cancer to identify tumour-specific mutations and predict the neoantigens. That information is used to create a new and unique vaccine. As a result of vaccination, the patient's immune system learns to recognise and attack the cancer cells expressing those specific neoantigens. It's the ultimate form of personalised medicine."

A number of companies are pushing into this new territory, including Genentech, which has teamed up with the German company BioNTech as part of a $310 million deal, and Moderna Therapeutics, a Massachusetts-based biotechnology company. The latter has partnered with pharmaceutical giant Merck and has already begun human trials.

Moderna's research centres on strands of genetic instructions called messenger RNA, or mRNA, which it proposes to use to instruct the body to treat the disease on its own.

The first person to be enrolled in Moderna's study was Glenda Cleaver in the US, with Moderna's software producing a list of 20 protein targets specific to her cancer. Its scientists then assembled DNA building blocks to create the recipe for her treatment, with Moderna's vaccine teaching the body how to recognise protein targets that appear only on the cancer cells.

Melissa Moore, who heads up RNA research at Moderna Therapeutics, told *Wired*: "Once you understand how to get these medicines where they need to be you can just change the sequence and make a new medicine very quickly. It's a complete sea change in our abilities."

Above: Melissa Moore, who heads up RNA research at Moderna Therapeutics

Yet despite the potential there are numerous challenges, not least the fact that the technology is unproven. The cost of making a separate treatment for every single patient is also high, with the challenge of making tailor-made treatments an economically viable product a steep one. For example, it took around 100 people to make the treatment for Cleaver. As such, personalised cancer vaccines face a familiar challenge: how to produce a product cheaply and get it to where it needs to be quickly.

Nevertheless, if these issues are addressed and personalised cancer vaccines are proven effective, they will revolutionise the treatment of cancer.

"Unlike any other type of medicine in history, all patients diagnosed with cancer may benefit from these individually tailored treatments," says Delamarre. "Combined with checkpoint inhibitors or targeted therapies, they could have a dramatic impact on cancer treatment in the near future and may ultimately become the backbone of all cancer therapy.

"Evolution has given us an incredible disease-fighting tool in the form of our immune systems," she added. "By putting that tool to work, we have great potential to realize a new era of cancer treatment."