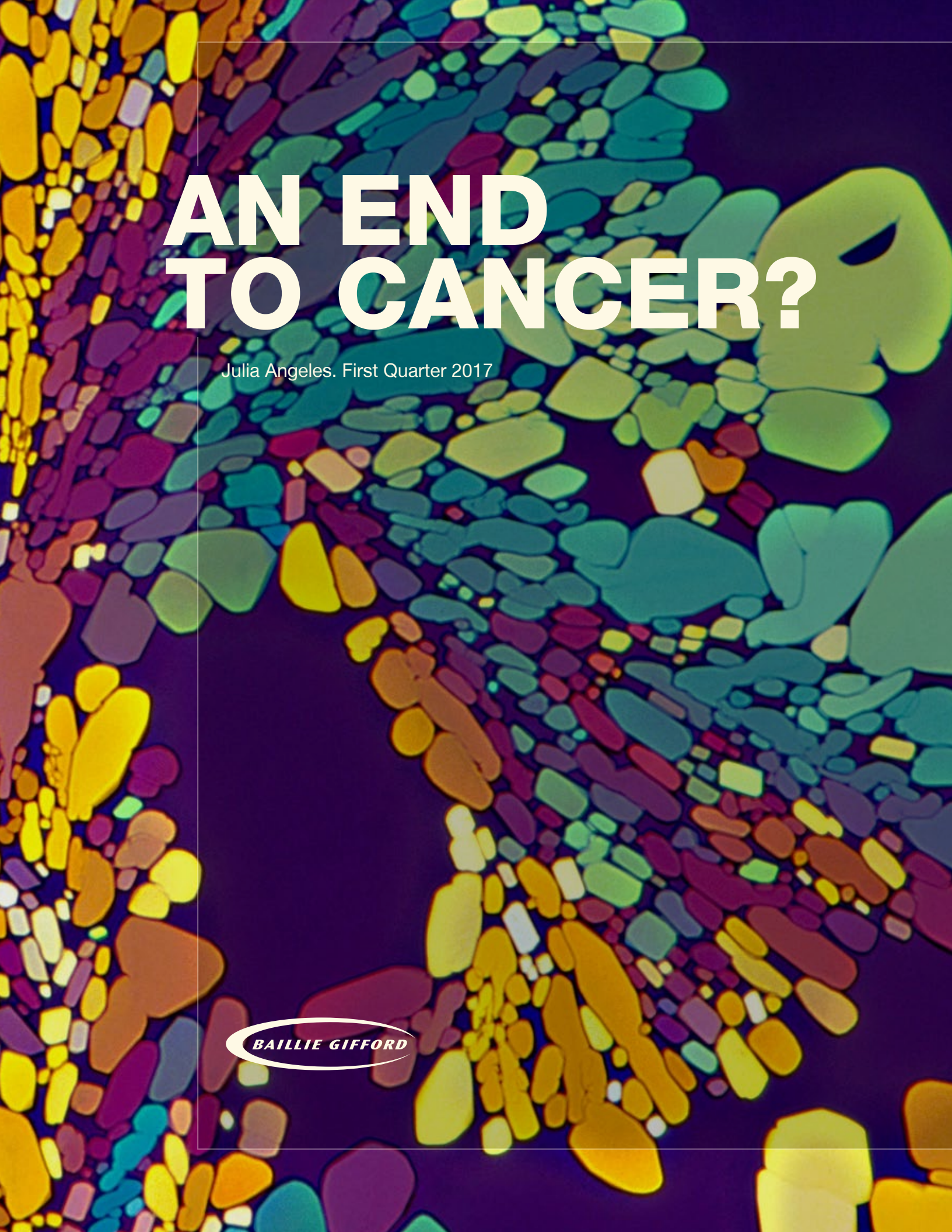

AN END TO CANCER?

Julia Angeles. First Quarter 2017

BAILLIE GIFFORD

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Julia holds a PhD in Economics from the University of Aarhus, Denmark and speaks fluent Russian and Danish. Before joining Baillie Gifford in April 2008, Julia worked as a Management Consultant at McKinsey & Company advising firms in Denmark, Russia and Hungary. Julia has been part of different global and regional teams within Baillie Gifford and is currently an Investment Manager in the EAFE Alpha Team.

Cover Image: Progesterone crystals.

An End to Cancer 40429 0117.indd
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Avastin, a biologic drug that is used for the treatment of different cancers.

AN END TO CANCER?

BY JULIA ANGELES

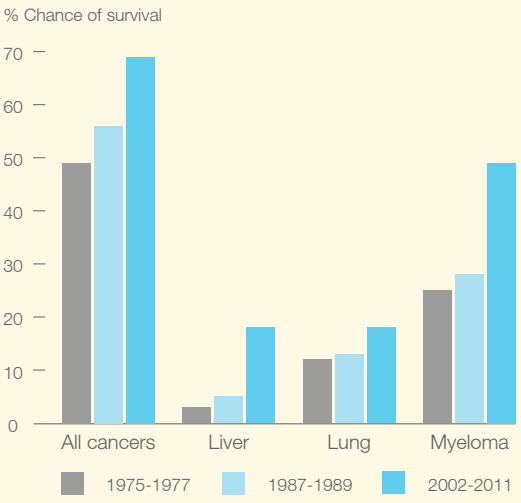
'To confront cancer is to encounter a parallel species, one perhaps more adapted to survival than even we are.' The Emperor of All Maladies by Siddhartha Mukherjee.

Cancer is one of the oldest diseases documented in medical research. The first description of cancer was found in an Egyptian papyrus dating back to 2,500 BC. Under therapy options, the ancient writer noted, 'There is none'. Since then, formidable progress has been made, both in our understanding of cancer as a disease and the therapies used to combat it. Now, we can offer cancer patients a wide range of treatments, e.g. radiotherapy, chemotherapy, surgery, and small and large molecule drugs. In the UK, the proportion of patients who survive cancer for ten or more years has doubled in the past 40 years. Yet notwithstanding the medical advances across the globe, around eight million people per year still die of cancer. It continues to be the second most common cause of death, exceeded only by heart diseases. What hope is there then of ever curing cancer?

I am optimistic. Recently, I spent a month in California learning about the advances being made in cancer treatments and meeting with a wide range of companies that are at the forefront of cancer research. This experience increased my enthusiasm for the view that as our knowledge of cancer is evolving, so we are reaching a tipping point. In the future, innovative treatment options will result in death rates from cancer shrinking to such an extent that we will be able to claim that we can cure cancer.

But before we begin to explore the scientific progress and the opportunities it brings, it is crucial to understand what cancer is and why we have failed to defeat it to date. Having done this, I will then share two promising technologies that I think have the greatest potential to bring us closer to a cure: the first is diagnostics, the other is cell therapy.

US Cancer Survival Rates - 5 year probability



Source: American Cancer Society

UNDERSTANDING CANCER

In 1971, President Nixon famously declared a war on cancer. Unfortunately, at that time, even the experts were going in blind: when the war on cancer was announced, no one understood the nature of cancer. And so, naively, the dream was to find a single silver bullet that would treat all cancers. Scientists and doctors tried every possible weapon they had at their disposal to fight cancer, including chemotherapy and radiotherapy. However, these treatments are like dropping bombs randomly from an aeroplane, hoping in doing so that they only hit enemy targets and not innocent civilians. Just as in real wars, this strategy works very poorly in fighting cancer. Chemotherapy, for example, kills both good and bad cells, makes patients suffer and in most cases does not cure the patient long term.

Luckily, we are not as naive as we once were, we recognise that cancer is a complex disease driven by many different genetic mutations. Every cell in our body contains genes that determine the behaviour of the cell. A well-behaved cell knows when to divide and when to stop dividing. A badly behaved cell doesn't know when to stop dividing. These badly behaved cells are cancerous cells. They keep dividing because something happens to the cells' genes that mean they give the cells the wrong instructions.

Cancerous cells appear in the human body every day. Frightening as this thought is, our bodies are not defenceless against cancer's onslaught. We have a powerful ally in this respect – our immune system. The immune system recognises and steps in to kill these badly behaved

cells. Unfortunately, with ageing, the cancerous cells become smarter, while the immune system becomes weaker. As a result, over time, the cancerous cells manage to escape the immune system and become a disease.

In order to eradicate cancer then, we need to develop treatments that will take out the cancerous cells before they can do widespread damage and we need to do so with as little collateral damage as possible. This is where our hope lies. The scatter gun approach to treatment that we have had to rely on to date, will, in time, become a thing of the past. The innovations in cancer treatments currently in development will mean that doctors will be able to target their treatments to individuals and their manifestation of the disease with greater accuracy and, therefore, with much greater likelihood of reaching a successful outcome.

It seems likely that we are at a turning point in the treatment and cure of cancer. This is because we are now much better-placed to accelerate the pace of learning about cancer's behaviour, helped by the decreasing costs of genome sequencing, collaborative data sharing projects in the cloud, smarter algorithms and increasing computing power. There has already been an important shift away from considering cancer in terms of the organ where a tumour forms, toward focusing on the genetic mutations that control cell division. Breast and lung cancer patients already receive treatments that reflect cancers' genetic mutations. However, it is still early days in making cancer treatment genuinely personalised, but this is the route that cancer medicine will ultimately take.

Scientists and doctors tried every possible weapon they had at their disposal to fight cancer... However, these treatments are like dropping bombs randomly from an aeroplane...

EARLY DIAGNOSIS IS CRUCIAL

One of the important challenges in treating cancer is, unsurprisingly, the more time that passes before cancer is detected, the more difficult it is to treat the disease. Unfortunately, under current standards of care, at least half of all cancers in the US are diagnosed in the late stages (III and IV), leading to poor survival rates. This happens because early diagnosis screens are relatively inaccurate in the majority of cancers, while screening procedures can be very invasive, e.g. colonoscopy. Even when cancer eventually gets diagnosed, doctors struggle to identify cancer's genetic make-up accurately and to monitor the response of the disease to treatments. Early diagnosis could improve survival rates by five to ten times that of late-stage diagnoses.

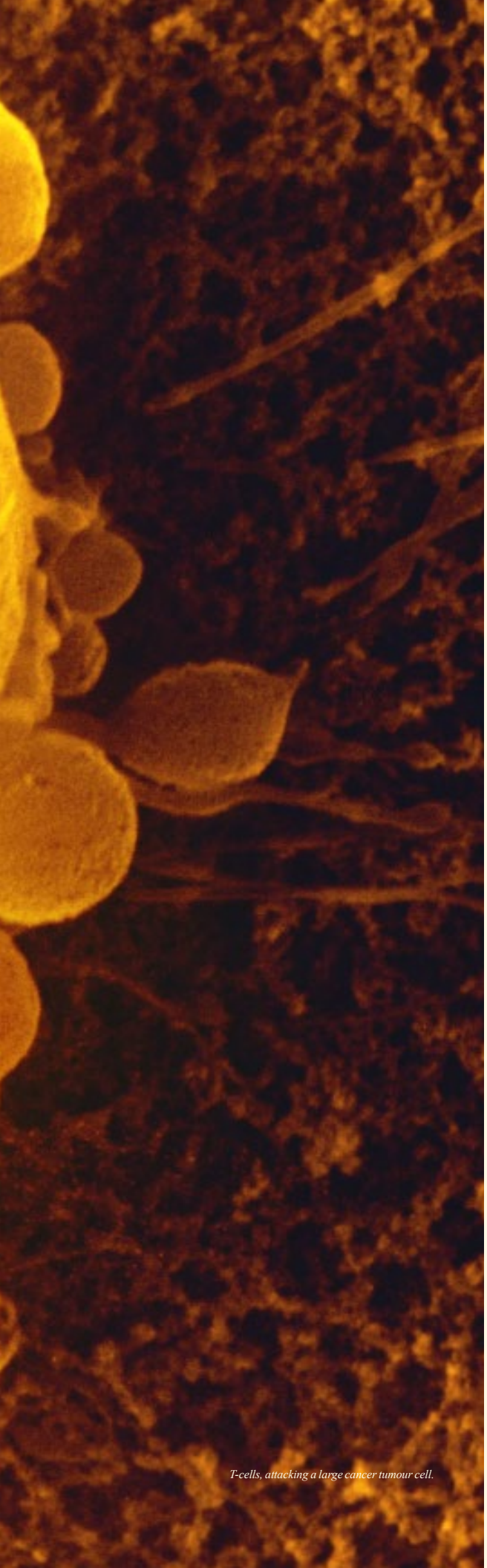
The company with the most ambitious plan to tackle the challenge of making a timely diagnosis and thus shaping a positive outcome for the patient is Grail, an unlisted start up, which is supported by visionary investors like Amazon's Jeff Bezos. Grail's aspiration is to introduce a single pan-cancer blood test that could be performed routinely on high-risk population groups and thereby detect cancerous cells in the body before they have the opportunity to gain the upper hand.

There are two reasons why a simple blood test could be particularly effective in diagnosing cancer. First, cancer leaves traces in the blood in the form of its genetic material. Second, thanks to decreasing genome sequencing costs, delivered by companies like Illumina, and increasing computing power, we are able to identify these traces. Grail's aim is to be able to identify cancer before patients even start experiencing symptoms and thus before it gets too complex to be treated.

To succeed in its aims, Grail's blood test will have to demonstrate a high degree of clinical accuracy and this is by no means a done deal yet. In the company's own words:

> *'Developing an effective early detection test that distinguishes between people with and without cancer is a 'needle in a haystack' problem and requires harnessing data from hundreds of thousands of people. Together, this creates an unprecedented data challenge.'*

Unprecedented, yes, but insurmountable, no. At its helm, is CEO Jeff Huber, who previously worked at Google at the intersection of life and computer sciences, but whose personal impetus for rising to the call to defeat cancer is the memory of his wife, Laura, who fought a losing battle with cancer having been diagnosed too late. Developing a high level of clinical accuracy will entail a lot of data, sequencing and computer power for storage and analytics, but Grail's perseverance, commitment and ability to attract talented people, mean it is well placed to overcome the challenges ahead.



T-cells, attacking a large cancer tumour cell.

NEW WEAPONS TO FIGHT THE DISEASE

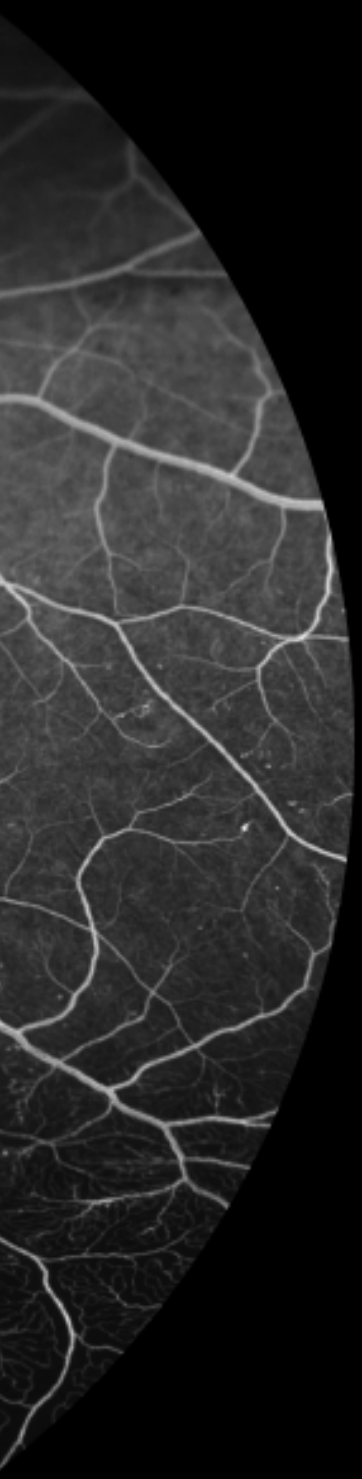
What is even more encouraging is that we now have new tools to fix one of the underlying causes of cancer, which is, as we have said, the failure of the immune system to identify and kill cancerous cells. Perhaps the most promising new tool in this respect is cell therapy. The premise of cell therapy is to provide the immune system with new weapons to fight the disease.

In this regard, the T-cell is the main protagonist. T-cells are a type of white blood cell that can identify and kill other cells. It is fascinating how cell therapy works: first, we take a blood sample from a cancer patient. Then, we isolate the T-cells from the blood and modify them so that they can easily identify and kill cancerous cells. Finally, we introduce these modified T-cells back into the patient. The T-cells then become serial killers, chasing cancerous cells and eliminating them.

Although early days, this treatment is already having a large impact on patients' lives. Some of the patients in the clinical trials who did not have any other treatment options available and were getting ready to die went into complete remission after cell therapy.

There are a few companies that are making good progress bringing cell therapy to the market. For example, Kite Pharma and Juno Therapeutics might get first approvals for some blood cancers during 2017. Kite Pharma feels very optimistic. The company thinks that over the next five years, cell therapies will be approved for all types of blood cancers and we will have proof of concept for solid tumours too.

One of the important challenges associated with cell therapy is that its complexity necessitates a lengthy production time. It could take up to a month to produce the therapy and some patients might die before the treatment is ready. However, a California-based company, Berkeley Lights, might have a solution. It has developed very clever hardware and software systems that substantially simplify the process of working with cells. For example, the company is able to perform a range of complex cell manipulations, like genetic engineering, growth and quality control, in the same piece of equipment. Berkeley Lights' vision is to bring cell therapy to the patient's bedside, to make the treatment simple and affordable. If it, and others, can achieve this, cell therapy would become a revolutionary treatment in cancer.



AN END IN SIGHT?

Finally, I would like to share an idea of how a cancer treatment might look in the future by connecting together the scientific advances I described earlier.

Imagine a patient of 70 years old, who goes through an annual routine health-check. The patient's blood is sent to Grail and the test returns positive for cancer. The patient pays another visit to the doctor, where his blood is taken again. This time, the cancer traces and T-cells, the two main characters of the battle, will be isolated from the blood. The cancer traces are then analysed to find out why the cells started misbehaving. Then, the T-cells will be modified so they are an exact match for the misbehaving nature of the cancerous cell. The fact that the cancer was caught early means that it will not have enough intelligence to know to avoid the strengthened T-cells. Patients could be cured with two simple blood samples!

This is just one of the ideas for future cancer treatment. There are many other interesting technologies that could help defeat cancer. While it is hard to predict the future, I think it matters more to try to understand the large trends rather than trying to be too precise about the future. I genuinely believe that as we move away from traditional systems, dominated by large pharma companies treating chronic diseases, to a world where prevention and cure becomes an integral part of healthcare, many exciting opportunities will arise, not just in the field of cancer, but across healthcare as a whole.

Fluorescein angiogram showing an untreated malignant choroidal melanoma tumour

CURIOUS ABOUT THE WORLD

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