MASTERING COMPLEXITY:

The path towards a cancer-free reality

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Introduction: cancer, a very complex enemy

This is the third and final paper in a series which began eight years ago, focusing on unravelling – and ultimately overcoming – the sheer complexity of cancer, one of humanity's oldest and most formidable foes. In the first two papers, we discussed how companion diagnostics have transformed cancer care, and how ongoing revolutions in gene sequencing technologies, as well as liquid biopsies, have led to further advances in personalised anti-cancer medicine. We concluded the second paper with a brief look at a possible future, in which novel technologies would help us truly conquer complexity.

How realistic is that objective, really? Can we really become masters of the complex biology that rules cancer, and slay that age-old enemy once and for all, ending a battle that has been raging since long before our species existed? And if so, what will this truly take? What types of technology are on the horizon that will keep us on the path towards mastering complexity?

Before we can hope to answer any of those questions, we must take a step back, and look at the complex enemy we are fighting through an unfiltered lens. Let's start with the easiest and hardest of questions: what is cancer? Cancer, most sources will tell you, is the uncontrolled cell division of abnormal, often poorly differentiated cells (versus healthy cell division for growth and repair). This is both highly informative and not informative at all. Yes, all cancers have this trait in common, but what does that really tell us about the nature of this group of diseases?

Firstly, and crucially, it should be clear from the incredible variety of different cancers – affecting different organs, in different cell types, with different mutations and different responses to a wide range of treatments – that this uncontrolled cell division can arise and manifest itself in an astounding number of different ways. Why is this? Given that there is a seemingly infinite way in which cells in our body can start replicating out of control, is cancer just a plain inevitable fact of life? Are multi-cellular creatures bound to be plagued by this unstoppable beast, as a direct result of having replicating cells in their bodies?

These questions are almost philosophical in nature (and hence maybe not fully answerable), but one thing is worth highlighting: cancer, in a way, is **a direct consequence of *our* incredible complexity.** It is, incidentally, no accident that the central theme of this series of papers is exactly that: for without complexity, there can be no cancer, and without harnessing, conquering and mastering that complexity, there can be no cure. Complexity is in itself a rather vague term, so let's leave the realm of the abstract behind and enter the fascinating world of facts and mind-boggling numbers.

Numbers, genes, mutations and permutations

There are trillions (around 30 trillion, to be more precise) of cells in our body[1]. Our brains are not equipped to deal with such figures, so it's hard to form a mental picture of this. Imagine for a moment we were made up of footballs (or soccer balls, if you prefer) instead of cells. 30 trillion footballs would fill up around 17 million Olympic-size swimming pools. That's a lot of footballs. That's a lot of cells. The point here is that, theoretically, cancer could arise in any of those cells, at any time during our lives.

More than 100 proto-oncogenes – genes that have the potential to turn cells into cancerous cells when mutated – are currently known[2]. Then there are tumour suppressor genes – mutations in which can prevent cells from holding back cancer – and sources vary quite widely in terms of how many have been identified (agreeing on a conclusive definition for these concepts is another layer of complexity in itself). Add to that the many genes involved in DNA repair and related mechanisms, and it is estimated that more than 1% of the 20,000 or so human genes are implicated in cancer. Let's call it 200 for simplicity. Not a staggering number in itself, but bear in mind that each (or almost each) of the 30 trillion or so cells in our body carry all of those genes. That's a LOT of strings of DNA that can get mutated and potentially lead to havoc in our bodies.

Each of those proto-oncogenes or tumour suppressor genes can undergo changes that lead to cancer in many different ways: there are well over a thousand mutations that are linked to cancer, and the list continues to grow. For example, if we consider the *EGFR* gene (which encodes the Epidermal Growth Factor Receptor, found on the surface of many different cell types), any of these can potentially lead to oncogenesis: exon 19 deletions, L858R point mutations, exon 20 insertions, T790M mutations, and many more. While not every conceivable mutation will have the potential to cause cancer, we're still talking about an enormous number of potential different mutations when we take into account the trillions of cells in our body.

Proto-oncogenes and tumour suppressor genes encode proteins that are part of incredibly complex signal transduction pathways, many of which are involved in the careful calibration of cell division throughout our body. The aforementioned EGFR receptor interacts with over 35 known protein targets. To take just one example, STAT3 is activated by EGFR, and the *STAT3* gene is in itself a proto-oncogene. The complexity of these signal-transduction pathways is a double-edged sword when it comes to cancer.

On the one hand, the existence of a number of redundancies and safety mechanisms means that usually one mutation in any given cell is not sufficient for cancer to arise. This is good news: statistically, the chances of e.g., 5 different oncogenic mutations arising over the course of the lifetime of a single cell are much, much smaller than just one such mutation. On the other hand, it also means that there are many different ways in which things can eventually go wrong, meaning that unfortunately no two cancers are truly the same at the molecular level.

The above is a lot to digest and, while the details aren't that important, the key message here is that **cancer and complexity are intrinsically linked**. It is no wonder, therefore, that cancer is so hard to beat. An often-coined statement is that cancer isn't a single disease but an umbrella term for many different diseases. In the past, this was generally interpreted as "breast cancer is different from lung cancer, which is different from lymphoma, and they each require different treatments". While this is certainly true, what it really means is "non-small cell lung cancer arising in non-squamous cells that have exon 20 insertion mutations in the *EGFR* gene and do not overexpress the PD-L1 protein is different from non-small cell lung cancer arising in non-squamous cells that do not have mutations in the *EGFR* gene, but are shown to overexpress the PD-L1 protein to a degree that over 50% of the tumour membrane's surface is covered in this protein, and they require different treatments".

There are well over a thousand mutations that are linked to cancer, and the list continues to grow

Layers of complexity

OK, that's a lot of technical jargon, but what does all of this actually mean? In a nutshell, attempting to treat cancer without knowing what is happening at the molecular level in the cancerous cells of that specific individual is bound to lead to failure in the majority of cases. For a long time, this was exactly our approach to cancer treatment: throw cytotoxic (cell-killing) chemotherapy at a cancer and hope that, in interfering with cell division, we end up killing enough cancer cells in a patient that can also hopefully deal with the various side-effects.

With the advent of targeted therapies and molecular diagnostics, things aren't quite as unguided anymore, but clearly they are still far from optimal. Having, for example, drugs that target *EGFR* mutations is a major step up from not having targeted therapies at all but, as explained above, the unfortunate truth is that there is a huge amount of variation between *EGFR*-mutated tumours. Apart from the points mentioned earlier, it is also important to highlight that even within a single tumour, there often is heterogeneity between different cancer cells: different cells within the same tumour may harbour different combinations of mutations or protein expression patterns. Therefore, when taking a tumour sample (whether solid or liquid) and sequencing its genetic make-up by determining the exact order of DNA base pairs through e.g. Next Generation Sequencing, or NGS (as discussed in Conquering Complexity), we may be missing information about cells not included in the sample, or cells that make up a minority of the sample.

If, for example, most cells in a tumour harbour a mutation that makes them sensitive to treatment with EGFR inhibitors, that would likely show up in an NGS test of a biopsy sample with that tumour. The oncologist would then proceed with recommending treatment with an EGFR inhibitor, and the tumour would initially show a good response. Unbeknown to anyone, however, was that a small number of the tumour cells harboured resistance mutations to EGFR inhibitors. After treatment with the EGFR inhibitor, the cells with the resistance mutations would become dominant, and the tumour would stop responding to the treatment, necessitating treatment with another type of EGFR inhibitor that is effective against those resistance mutations.

All of the above are just (rather simplified) examples of how multiple layers of complexity make conquering cancer an incredibly difficult task, and how in this era of precision medicine, companion diagnostics, NGS and liquid biopsies, we are unfortunately still quite far removed from mastering this complexity. So, what would this actually take?

Rise of the precision machines

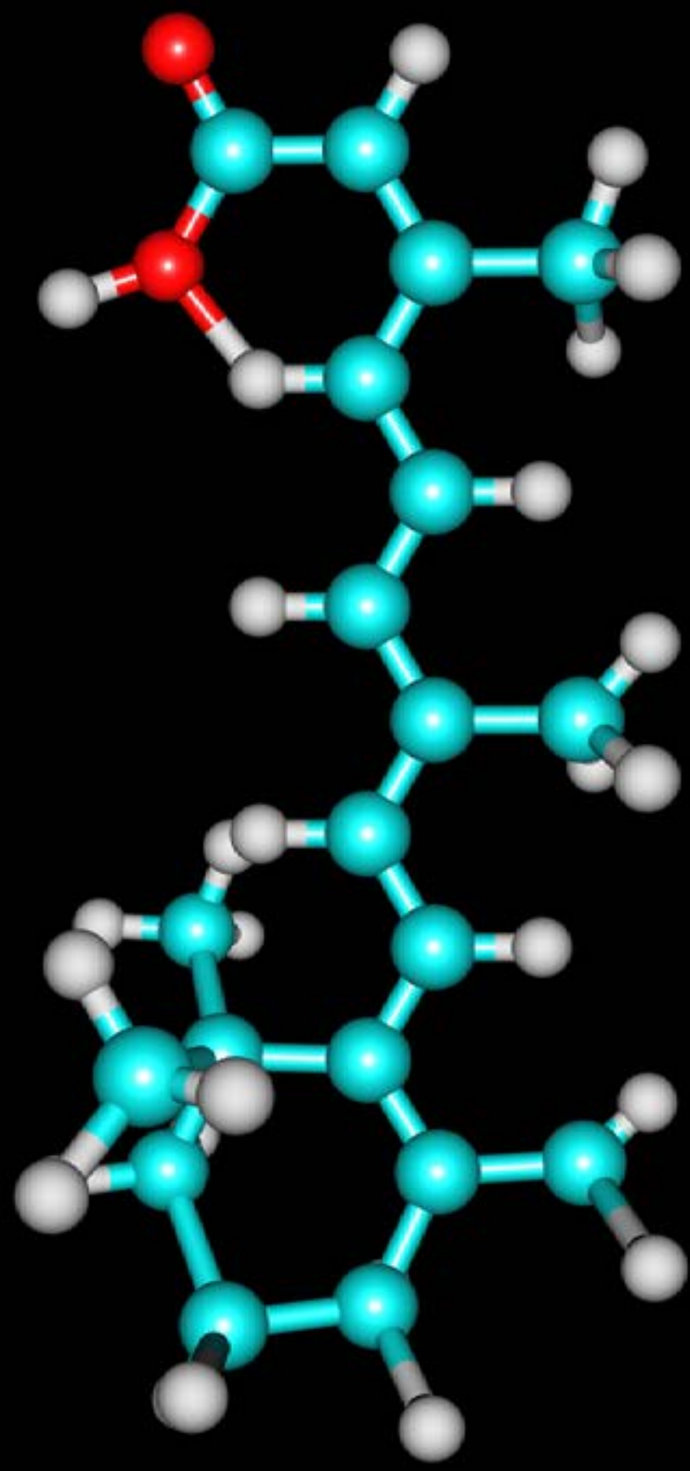
In the closing paragraphs of *Conquering Complexity*, we took a brief look at some of the future technologies that may help with further revolutionising targeted treatment of cancer. These included third-generation sequencing, labs on a chip, artificial intelligence and nanorobots. In this next section, we will spend some time exploring each of these in further detail.

Third-generation sequencing, also known as long-read sequencing, is an umbrella term for a number of sequencing technologies currently under active development. Because of the potential for much longer reads (which means that the sequencers can "read" much longer fragments of DNA or RNA, instead of having to break them up into small pieces and then reconstruct the puzzle), third-generation sequencing comes with several theoretical advantages for genome science and precision medicine. It does, however, come at the cost of much higher error rates than we see from current NGS technologies, although these are expected to improve as the technologies reach maturity. One of the major advantages of these technologies is that they should be able to allow for monitoring DNA synthesis in real-time, which in turn could enable continuous data collection (this would, however, require massive computational resources to analyse; we will touch upon this point shortly). In addition, these technologies would reduce the need for sample preparation and would allow for analysis of DNA with limited starting material; data from Ipsos' Oncology Molecular Diagnostics Monitor tells us that lack of sufficient viable tissue is one of the major barriers to NGS testing that pathologists currently face, and these third-gen technologies would help circumvent this barrier.

Epi-omics and faulty switches

Earlier on in this paper, we discussed some of the ways in which cancer, and the genetic changes that lead to it, are complex. However, we glossed over one of the other major ways in which this complexity manifests itself: epigenetic changes. The more we understand about our biology, the more we come to realise that our genes are just one part of the story of life. Epigenetics is the study of how changes in the environment of our genes can impact how they work. While genetic changes are permanent and (outside of the realm of gene therapy) generally irreversible, epigenetic changes are much more dynamic. These patterns are in a constant state of flux, controlling when and to what extent specific genes are being expressed in individual cells. Sometimes, this process can go wrong, and abnormal epigenetic changes (such as changes in DNA methylation patterns that could force genes into an “on” or “off” state) could form a key component of oncogenesis. Unlike gene mutations, however, these types of changes cannot be detected through conventional sequencing technologies (such as NGS). Some third-generation sequencing technologies do allow for this detection.

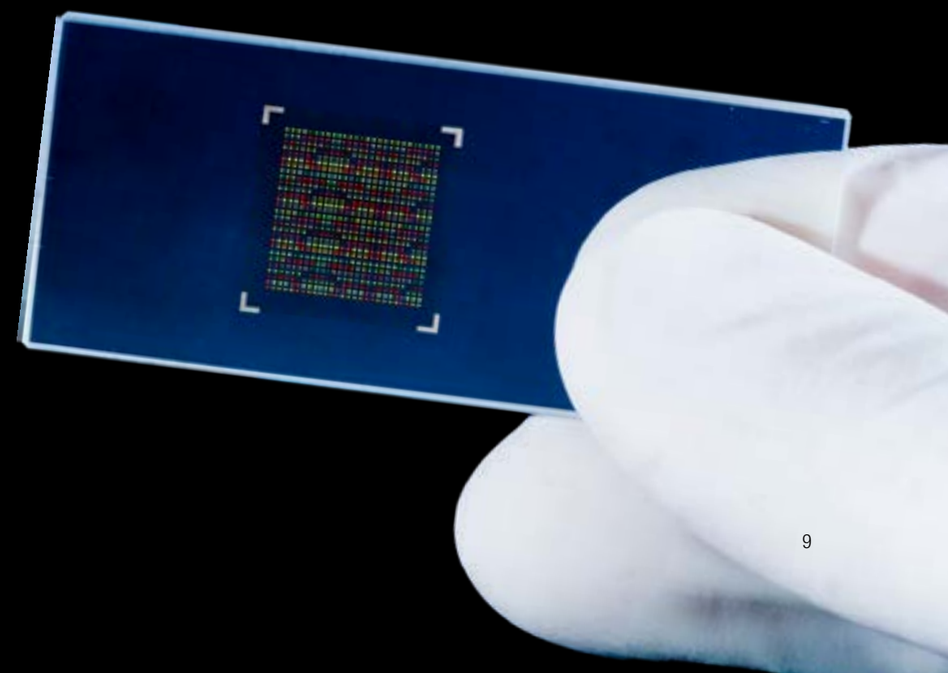
The above is an example of the expected transition from cancer “omics” to “epi-omics”, as discussed in a paper by Athanasopoulou et al.[3] Some of the other characteristics of third-generation sequencing feel truly futuristic, such as the promise of much greater portability (sequencers the size of a USB stick instead of the large devices currently used for NGS), and the ability to sequence individual DNA molecules (whereas NGS requirements mean that DNA must be present in sufficiently large concentrations in the sample).

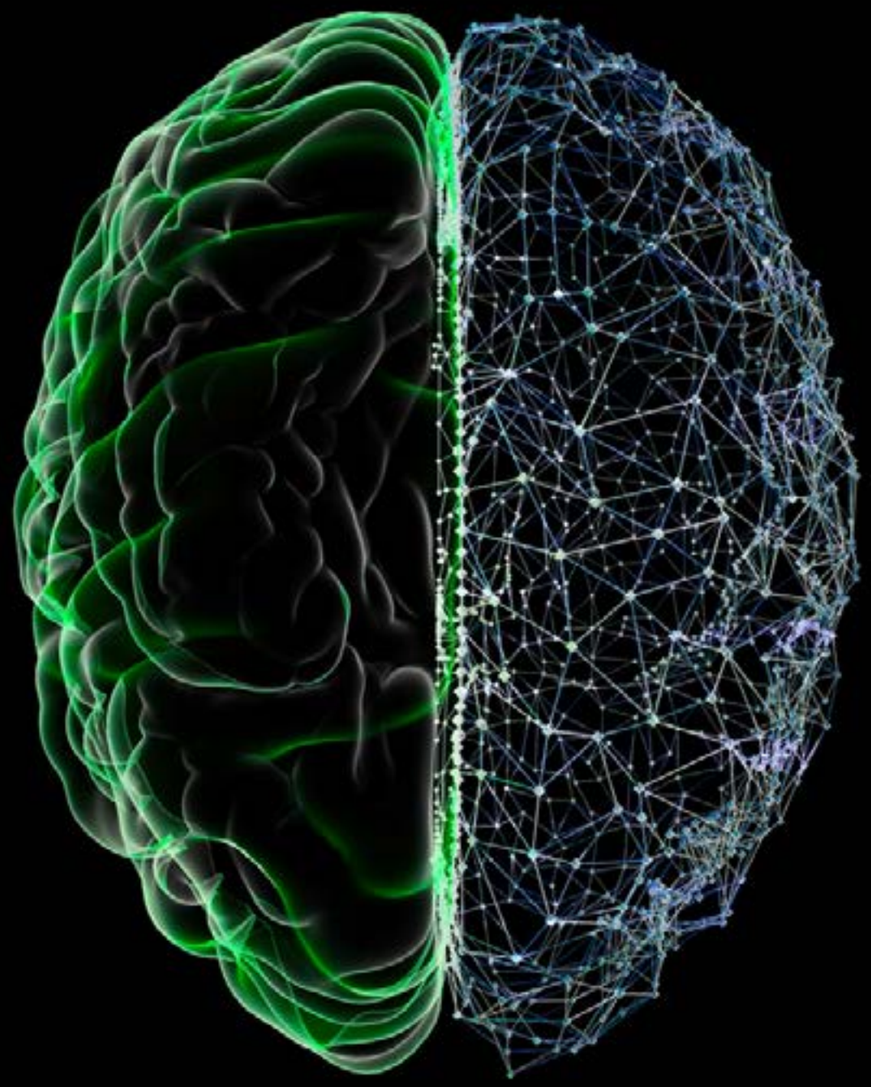


From the workbench to the bloodstream: labs on a chip

Labs on a chip take the portability element a few steps further: rather than conducting tests in vitro, these theoretical devices would enable real-time in vivo tracking, i.e., continuously monitoring cells or even pieces of genetic material that pass through these devices inside a human body (for example, in the bloodstream) and updating a connected device (such as a smartwatch or other external monitor) whenever abnormalities (such as oncogenic mutations) are detected. Patterns in aberrant protein expression or epigenetic changes could also be monitored and reported. No longer would invasive tissue samples or (less invasive) blood samples need to be taken for separate testing on a sequencing device: testing would essentially be a passive, continuous state, analogous to smartwatches that track heart rate continuously (but many times more sophisticated).

Apart from the necessary advances in material science, miniaturisation, implantation, battery power, the capturing and sequencing techniques required to make this a viable and reliable reality, the other major challenge is the enormous amount of data that would be generated on a continuous basis by such connected health devices. It is already a considerable challenge for oncologists to decide on optimal sequencing strategies (sequencing as in deciding on which drug to give first, not the kind of sequencing we explored above… even language can get very complex!) for patients whose tumour could potentially respond to multiple classes of targeted therapies. Now imagine that those oncologists are given a continuously updated stream of data on which combinations of mutations, protein expression patterns and epigenetic changes are present in different parts of a single tumour, as well as in circulating tumour cells and tumour DNA fragments that are making their way through the patient’s body. Deciding on a course of action when faced with such data would require a superhuman effort, and this is where artificial intelligence has a crucial role to play.





While humans are equipped with brains that can understand complexity in ways that no other mammal can, truly mastering complexity will require the assistance of artificial brains.

Artificially intelligent nanorobots

Artificial intelligence is everywhere in both medical and general literature nowadays, and the healthcare setting is no exception (see, for example, this excellent paper recently written by Roberto Cortese, on the doctor-patient relationship in the generative AI era). It is also one of the most controversial areas when it comes to potential applications for AI, as the consequences of e.g., a false treatment recommendation by AI tools could have devastating consequences. Nevertheless, it is becoming increasingly clear that the amounts of data generated by multiple diagnostic toolkits are getting harder and harder for human doctors to analyse and base informed decisions on. Substantial computing power is required, and this must go beyond simple calculations or basic algorithms: AI programmes must be able to mine vast amounts of data – potentially updated on a continuous basis as discussed above – and arrive at evidence-backed recommendations. While we're still quite far removed from the futuristic scenario described in the above section, AI tools are already being employed to help with areas such as interpreting digitised slides (see the Owkin MSIntuit CRC[4] test as one such example) to free up pathologist time and standardise scoring. Given the speed at which AI advances are taking place in general, it is all but certain that AI will continue to play a larger and larger role in fighting cancer. While humans are equipped with brains that can understand complexity in ways that no other mammal can, truly mastering complexity will require the assistance of artificial brains.

Another area of incredible future potential is that of nanobots, which we briefly touched upon in the second paper of this series. As we wrote back in January 2022:

"The next – and perhaps ultimate - step in the more distant future would be pairing this ability with nanobots that permanently inhabit individuals' bodies, dispensing targeted doses of highly specific drug cocktails, or physically destroying wayward cells, in an extremely localised matter in response to the information passed to them through the chips and AI agents."

Since then, a plethora of new articles have been published in the media on the subject. General interest in this space appears to be picking up at a rapid pace, and while the picture painted in the above quote is still far away in the future, these miniature robots are expected to start making a real impact in the not-too-distant future. This recent paper[5] in the *Journal of Hematology & Oncology* provides an in-depth analysis of the advances of such bots for the future treatment of cancer. As its authors note "*the development and application of nanorobots in cancer treatment are becoming a vigorous research area*", but also "*the translation of experimental nanorobots […] into the clinical arena* ***is limited by the complexity and heterogeneity of tumor biology****, the lack of comprehensive understanding of nanomaterials-biology interactions, and the absence of scalable synthesis and mass production technologies*". They also noted "*to realize the full potential of nanorobots in the field of cancer treatment, material and* ***AI scientists should work closely together with medical researchers***." One of the most important realisations in recent years is that very few of the expected future technological advances in the companion diagnostics and cancer treatment space will be possible without artificial intelligence.

Being less human

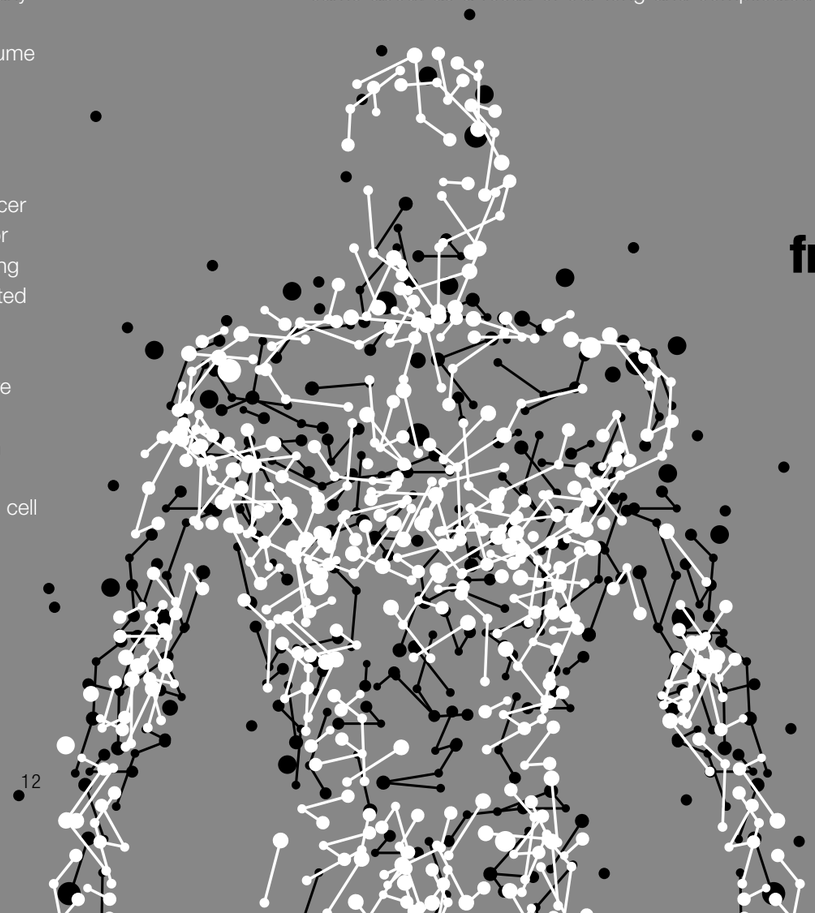
Fundamentally, all of these developments – even the most technologically advanced interventions – still feel like trying to patch up a system that is flawed at its very core: the cells that make up our bodies, the complex biological machines that are the result of billions of years of evolution, without forethought. If someone were to design a human body from scratch, they would not include thousands of different ways in which the components that make up that body can go rogue and start destroying it from the inside out.

Do we therefore need to think of this problem in a completely different way? What if, rather than detecting them early and getting rid of wayward cells, we could stop cancer-causing mutations, full-stop? What if we could turn our cells into permanently benign building blocks that never turn against us? Are oncogenic mutations truly inevitable? Is preventing all somatic mutations in our cells an impossible mission? In the introduction to this paper, we talked about how complexity and multicellularity are inextricably linked, and cancer is a direct consequence of this multicellular complexity. But perhaps this is oversimplifying things.

Humans, of course, are not the only multicellular creatures on this planet. We share the Earth with many other animals, who are fundamentally made up of the same building blocks: trillions of cells that are constantly required to balance cell replication with cell death. It would therefore be reasonable to assume that they are all subject to roughly the same risk of cancer. This is, however, absolutely not the case. Some mammal species are extremely cancer-resistant, such as mole rats, elephants and whales. Elephants and whales have something in common: they are big. Generally, large and longer-lived mammals are more resistant to cancer than small and short-lived ones (such as mice). Therefore, the argument near the beginning of this paper, that one of the reasons for the complexity that drives cancer is simply the sheer number of cells in our bodies, suddenly seems a lot more shaky. A blue whale, for reference, has roughly 100 quadrillion cells[6]. That's 100,000 trillion. Hence, their likelihood of developing cancer in any cell should be a lot higher than it is in humans; it appears that evolution has counteracted this by equipping them with better anti-cancer mechanisms.

These species still get mutations (though some at a lower rate), but it appears that more mutations are needed for cancer to arise, i.e., they generally have more effective processes in place to stop those mutations from leading to cancer. Elephants, for example, have multiple copies of the *TP53* gene[7], an important tumour suppressing gene that encodes a protein (p53) which binds to DNA when it gets damaged, either facilitating its repair, or instructing the cell to enter a state of apoptosis (programmed cell death). Naked mole rats typically arrest cell proliferation earlier[8]; interestingly, when some of their key tumour suppressor genes are inhibited (with drugs), this tends to lead to apoptosis instead of proliferation (as it does in humans or mice). Hence, they seem to have extra fail-safe mechanisms that force cells into self-destruction when something appears to be wrong with normal control mechanisms. They also seem to have a more stable epigenome, which means fewer cases of epigenetic alterations that could potentially lead to cancer.

We cannot swap bodies with these creatures. Maybe this will be a reality in the distant future, but in the meantime, perhaps we will be able to develop drugs based on their cell biochemistry, applying some of their anti-cancer tricks to our own cells. Artificial intelligence will likely have a key role to play here, trawling through a large volume of data related to other species, and seeing which strategies would be compatible with human biochemistry (without any negative effects). This could take the form of targeted therapies to intervene with cellular pathways, but what if we could permanently amend our genetic make-up so it is more similar to those of cancer-resistant species? For example, what if we introduced extra copies of *TP53* (as in elephants), or cell proliferation suppressors as in naked mole rats, into our genome? This brings us to the subjects of gene therapies and genetic engineering. Doing this safely will not be easy (and comes with ethical concerns), but what if – in the distant future – we could engineer our genomes so we are naturally cancer-resistant without any drawbacks? Again, a question fraught with ethical conundrums, but putting those aside for a minute: we'd be eliminating the lethal genetic traps that came about as a result of our long and complicated evolution. We'd truly be mastering complexity.



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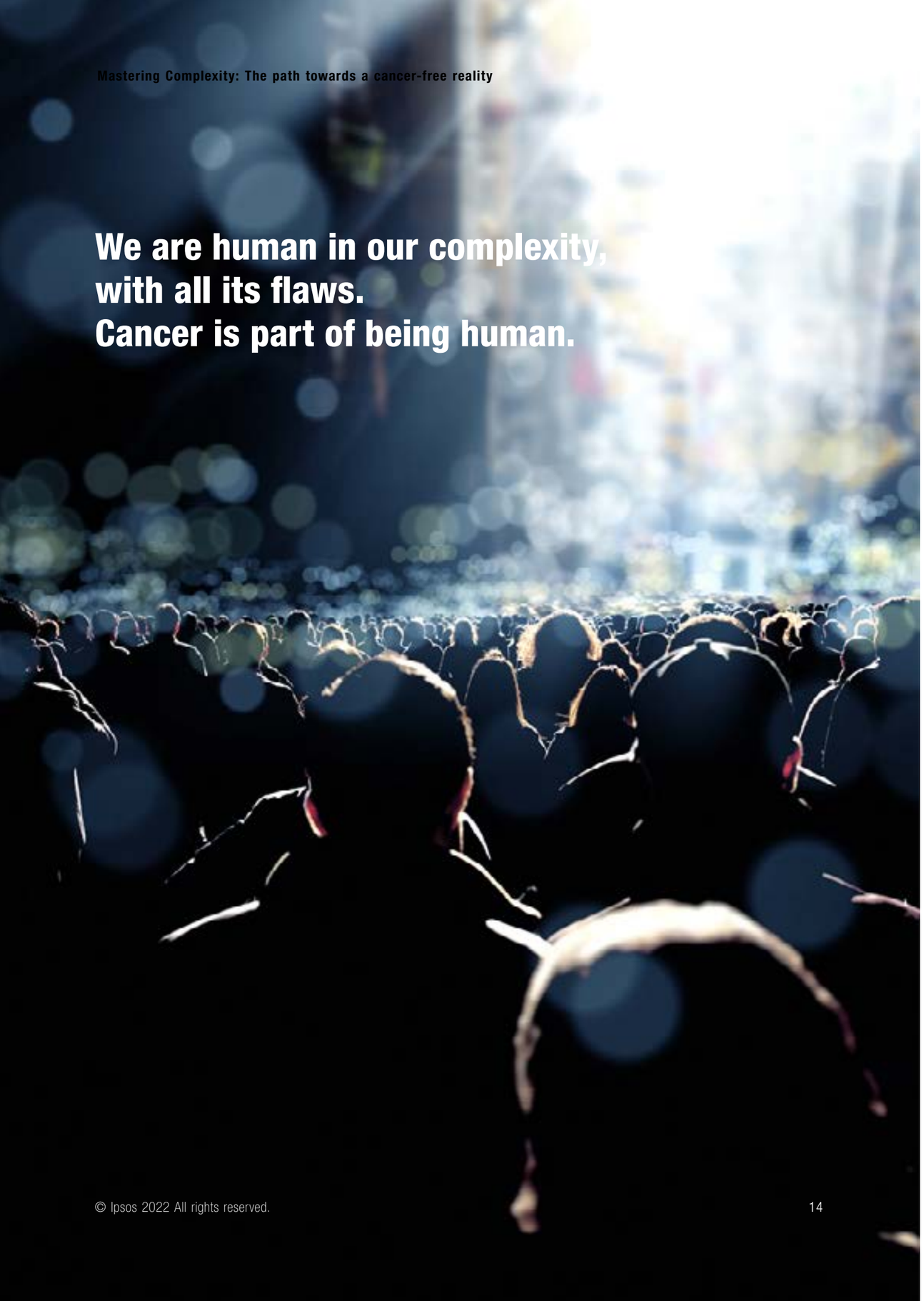


An afterthought: shedding our mortal coils

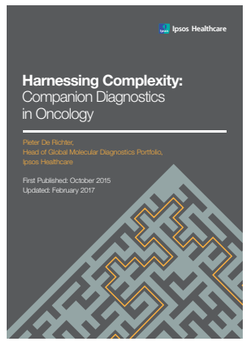
We touched upon the distant future in the paragraph above. Let's take this one step further: do we really need cells? Do we really need DNA, that bringer of life that has given us so much, whose beautifully flawed nature has brought about all the diversity that surrounds us, but has also caused untold misery and sorrow, by unwillingly and unwittingly forcing cells to spiral out of control, consuming and devouring our health in the process, robbing us of everything we were granted in the most painfully ironic twist of fate? Can we part ways with those mortal coils, and eliminate not just cancer as a disease, but the very concept of it? Imagine, for a minute, that we were to create robots, not made of cells, but of cogs and steel, and we were to upload our minds into them.

There would be no more cancer.

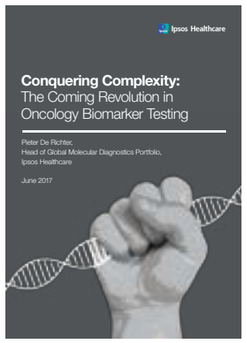
The above might seem like an exercise in futility, a flight of fancy that leads us nowhere, a useless fantasy that discards all that makes us human. This, however, is exactly the point: we are human. We are human in our complexity, with all its flaws. Cancer is part of being human.

What is also part of being human is an incredible drive for innovation and a knack for overcoming adversity, no matter how complex. In my opinion, conquering cancer by harnessing those qualities is perhaps the greatest challenge that we as a species have ever faced. I remain convinced that, one day, we will get there. That day, we will truly be masters of our own complexity.

A journey through complexity



Harnessing Complexity
2017 (updated from 2015)



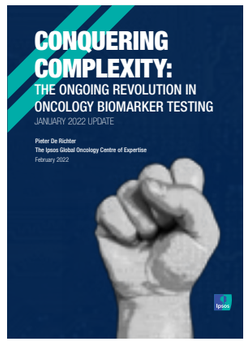
Conquering Complexity
2017

As this is the final paper in a series of three, let us wrap up with a look back at the journey of discovery that started with Harnessing Complexity, way back in 2015 (with a later update in 2017). We began by highlighting that the treatment of cancer has become significantly more complex since the arrival of companion diagnostics, and that the relationship between those diagnostics and their clinical utility is not always a straightforward one.

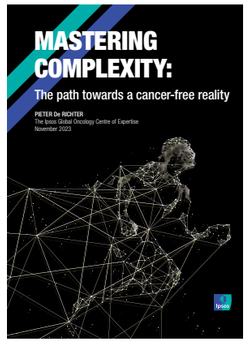
We reviewed perceptual data taken from the Ipsos Molecular Diagnostics (MDx) Monitor, which showed that a majority of HCPs agreed with the clinical utility of testing for key biomarkers, despite a lack of universal consensus. We discussed the relative benefits and drawbacks of drugs being approved for all patients versus a specific patient subject whose tumours harbour specific mutations or overexpression profiles. We delved deeper into different methodologies for testing, and the use of different test kits, and looked at real-world behaviour data from the Ipsos MDx Monitor to showcase that there is a high degree of fragmentation when it comes to the uptake of those methodologies and kits.

Towards the end of the first paper, we briefly cast our minds to the (then) future, bringing up the concepts of Next Generation Sequencing and liquid biopsies as having the potential to revolutionise the companion diagnostics landscape. We concluded by stating that cancer is complex, and that an understanding of its complexity leads to opportunities that can be harnessed by doctors, and by drug and diagnostics manufacturers, ultimately benefiting the patient.

In Conquering Complexity, first written in 2017 and then updated in 2022, we dove much deeper into the ongoing revolution, analysing both the NGS market and the liquid biopsy market in greater detail. Again, we drew upon data from the Ipsos MDx Monitor to highlight the perceptions and actual behaviour of healthcare professionals to illustrate the profound impact those twin revolutions were – and still are – having on the oncology treatment landscape. We then looked at the intersection of those two trends, bringing up the concept of liquid-biopsy based NGS panels.



Conquering Complexity
(updated) 2022



Mastering Complexity
2023

Wrapping up the second paper, we once again looked towards the future, introducing many of the concepts that this third and final paper focuses on in greater detail. We noted in the 2022 update that we were only in the early stages of an accelerating revolution in molecular diagnostics; even one year later, this feels like an understatement.

That brings us to this third and final paper, in which the distant future takes centre-stage, and in which we explore highly theoretical concepts that may one day allow us to achieve the goal stated in the title. If the world of AI-powered nanobots and mind uploading seems very far removed from the opening paragraphs of the first paper, this is by design. The concept of testing a tumour sample for common DNA mutations and then choosing a targeted therapy based on this information, as straightforward and entrenched as it may now seem, is in itself an incredible achievement that was simply inconceivable in the era of non-targeted chemotherapies. Human ingenuity and perseverance in the face of this truly insidious enemy has given us a number of remarkable tools to hit cancer at the most fundamental level. While the battle is far from over, who really knows what the future holds?

In closing, this third and final paper is dedicated to hope: to the hope for a future in which we no longer have to deal with resistance mutations, no longer have to regularly subject patients to frequent biopsies, no longer have to painstakingly try to come up with a drug sequencing plan for patients with rare combinations of mutations, no longer have to tell patients that unfortunately there are no more viable options to treat their cancer. To the hope that this future will come fast enough for the many cancer patients who are out there whose oncologists are desperately trying to find a path through the layers of complexity.

To the hope that, one day, life without cancer will be a simple reality.

About the Research

The Ipsos Global Molecular Diagnostics Solid Tumours Monitor is a multi-stakeholder, physician-reported syndicated patient and laboratory record database, capturing perceptions towards and usage of molecular diagnostics tests in solid cancer types. Participating drug-treating physicians are screened for specialty, level of seniority and number of drug-treated cancer patients seen per study wave and must be the primary decision-maker for their patients. In addition, participating pathologists must be involved with preparing samples, ordering cancer-related molecular diagnostics tests and/or performing/interpreting cancer-related molecular diagnostics testing in solid cancers, and must be aware of the methodology and/or brand used for cancer-related molecular diagnostics tests. Each wave, participants complete a perceptual usage and attitudes questionnaire, before providing de-identified information on a predefined quota of oncology patients seen in consultation / laboratory samples handled in practice, retrospectively (across a pre-defined list of solid tumour types). Data used in this article were collected online in US, France, Germany, Italy, Spain and the UK, and collected both online and via pen & paper in South Korea. Sample sizes are provided alongside the relevant charts.

Contact OncologyCoE@ipsos.com for more information.

www.ipsos.com

References

1. Revised Estimates for the Number of Human and Bacteria Cells in the Body | PLOS Biology. 2023. Revised Estimates for the Number of Human and Bacteria Cells in the Body | PLOS Biology. [ONLINE] Available at: https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1002533. [Accessed 24 October 2023].
2. Pappou EP, Ahuja N. The role of oncogenes in gastrointestinal cancer. Gastrointest Cancer Res. 2010 Nov;(Suppl 1): S2-S15. PMID: 21472044; PMCID: PMC3047044.
3. Athanasopoulou K, Daneva GN, Boti MA, Dimitroulis G, Adamopoulos PG, Scorilas A. The Transition from Cancer "omics" to "epi-omics" through Next- and Third-Generation Sequencing. Life (Basel). 2022 Dec 2;12(12):2010. doi: 10.3390/life12122010. PMID: 36556377; PMCID: PMC9785810.
4. www.owkin.com. (n.d.). MSIntuit CRC | AI Cancer Testing | Owkin. [online] Available at: https://www.owkin.com/msintuit-crc [Accessed 8 Nov. 2023].
5. Kong, X., Gao, P., Wang, J. et al. Advances of medical nanorobots for future cancer treatments. J Hematol Oncol 16, 74 (2023). https://doi.org/10.1186/s13045-023-01463-z
6. Jian Zhang, Rolando Del Aguila, Colette Schneider, Brandt L. Schneider, The Importance of Being Big, Journal of Investigative Dermatology Symposium Proceedings, Volume 10, Issue 2, 2005, Pages 131-141, ISSN 1087-0024, https://doi.org/10.1111/j.1087-0024.2005.200414.x.
7. Michael Sulak, Lindsey Fong, Katelyn Mika, Sravanthi Chigurupati, Lisa Yon, Nigel P Mongan, Richard D Emes, Vincent J Lynch (2016) TP53 copy number expansion is associated with the evolution of increased body size and an enhanced DNA damage response in elephants eLife 5:e11994. https://doi.org/10.7554/eLife.11994
8. Zhao Y, Tyshkovskiy A, Muñoz-Espín D, Tian X, Serrano M, de Magalhaes JP, Nevo E, Gladyshev VN, Seluanov A, Gorbunova V. Naked mole rats can undergo developmental, oncogene-induced and DNA damage-induced cellular senescence. Proc Natl Acad Sci U S A. 2018 Feb 20;115(8):1801-1806. doi: 10.1073/pnas.1721160115. Epub 2018 Feb 5. PMID: 29432174; PMCID: PMC5828632.

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