THE NEXT 10 YEARS — VIEWPOINT

Cancer research: past, present and future

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Abstract | Research into cancer over the past 10 years has diverged enormously, partly based on the large number of new technologies that are now at our finger tips. With areas of cancer research so disparate, it is not always easy to identify where the next new findings and therapies might come from. With this in mind, we asked four leading cancer researchers from around the world what, in their opinion, we have learnt over the past 10 years and how we should progress in the next 10 years.

***Q** In your opinion, what have been the most important findings in cancer research in the past 10 years?*

Ya Cao. Cancer has been identified as a chronic disease[1]. In an attempt to battle this disease the World Health Organization have developed three principles on cancer prevention: they have estimated that current prevention strategies could prevent up to one-third of new cancers; they have suggested that improved early screening could result in the detection of one-third of cancers at an early stage; and they have proposed that a comprehensive treatment strategy could improve survival and quality of life for another one-third of patients with advanced cancer[2]. These strategies offer the most cost-effective, long-term control of cancer.

Cancer is a vastly complex disease exhibiting a plethora of changes in multiple genes. More and more attention is now being focused on the relationship between infection and cancer. For example, about 200,000 women die every year from cervical carcinoma, which is closely associated with human papillomavirus (HPV) infection. Importantly, a vaccine against HPV was the first cancer vaccine to be developed and should substantially reduce the incidence of cervical cancer. Besides HPV, *Helicobacter pylori* infection is linked with gastrohelcosis, which is the precancerous stage of gastric cancer[3]. Clearly, the relationship between *H. pylori* and gastric cancer is an important basis for developing an efficient therapeutic strategy for controlling *H. pylori* infection and, ultimately, gastric cancer.

In the post-Human Genome Project (HGP) era, researchers and scientists are again recognizing the importance of the molecular mechanisms of carcinogenesis from the genome-wide level[4]. On the basis of results obtained from the HGP regarding single-nucleotide polymorphisms (SNPs) and genome-wide associated studies (GWAS), numerous changes in SNPs and gene signatures have been identified[5]. Notably, these studies were carried out by combining large-scale population data and *in vitro* findings to address the molecular mechanisms of carcinogenesis.

The study of epigenetic changes that occur during carcinogenesis is rapidly developing into an important field of study. Epigenetic silencing that occurs through the CpG island methylator phenotype (CIMP), for example, embodies a novel viewpoint in cancer diagnosis and therapy[6]. The dynamic interplay between epigenetic signatures and post-translational modifications, including phosphorylation, acetylation and ubiquitylation, corresponds to the complicated regulation of carcinogenesis. In addition, non-coding RNAs, such as microRNAs, are also involved in the signalling networks that are associated with carcinogenesis.

Translational medicine is regarded as a switch from concept to practice. The change from 1-B (from bench to bed) to 2-B (from bed to bench) has allowed scientists and clinicians to focus more on patients in order to directly address the three most common issues in cancer prevention: diagnosis, therapy and healing[7]. Drugs that target specific molecules, such as the epidermal growth factor receptor (EGFR), are being used more and more to treat cancer patients[8]. Currently, clinicians are combining radiation therapies with pharmacological interventions, such as checkpoint inhibitors and molecules targeting signal transduction pathways and the cancer microenvironment, to treat cancer. Moreover, scientists are exploring the possibility of targeting pathogens, such as the Epstein–Barr virus-encoded oncoproteins, to improve radiation therapy in patients. Notably, with the rapid development of molecular imaging methods that target receptors, metabolic enzymes, apoptosis and blood vessels, imaging is becoming a powerful tool to understand the development and progression of cancer. Improved imaging techniques will also aid in the development of anticancer drugs and help to evaluate therapeutic effects in cancer patients.

Ronald A. DePinho. The past 10 years have brought many advances across a broad front. It is not specific advances that excite me but rather the collective whole. The cancer research community has reached a point of conceptual and technical maturity to mount a decisive assault on cancer. This optimism is fuelled by multiple important advances — a deeper understanding of the biological processes of cancer; comprehensive multi-dimensional cancer genome profiles; robust functional validation technologies; faithful genetically engineered mouse models; quantitative analysis of clinically annotated biospecimens; enabling nanotechnology; and other major discoveries. It is anticipated that cancer death rates will continue their steady decline through prevention, more effective early detection, genotype-informed drug application and the combined use of targeted therapies, including those harnessing the immune system. The increased use of target-engagement and response-prediction biomarkers in clinical trials holds promise for reducing the staggeringly high rate of failure in cancer drug development that has been seen in recent years, often occurring in late-stage clinical testing at an enormous cost to the pharmaceutical industry and to the patient. There is also a sense that the combination of existing and emerging therapeutic agents will elicit more prolonged responses that currently elude at least one-third of cancer patients.

Matthias Ernst. Much of the cancer research carried out in the past decade has been preoccupied with assigning the vast genomic information generated through The Cancer Genome Atlas (TCGA)[9] and similar projects, and to the cancer hallmark concepts introduced by Hanahan and Weinberg[1]. We can now better distinguish the few driver mutations from the many passenger mutations in individual cancer genomes, and evidence indicates that tailoring treatment to molecular signatures rather

than to the histological grade of tumours increases response rate[10]. However, we now also appreciate a mutational landscape with few 'mountains' that represent common genes mutated in many cancers, and a large number of 'hills' that represent the majority of infrequently mutated genes that are found in a small number of cancers[11]. In light of the vast discordance between these hills, even among cancers of the same tissue origin, we now understand the incremental advantages they individually confer to tumour progression. As a corollary, we now face the more daunting prospect of having to therapeutically target many hills rather than, as originally anticipated, focusing solely on the few mountains.

High-throughput sequencing of cancer genomes has revealed that somatic mutations are clustered in a small number of signalling circuits and that such mutations often circumvent the need for physiological engagement by ligand-occupied growth factor receptors. Although the discovery of non-coding RNAs has added a new layer of complexity to the molecular drivers of cancer development, they frequently affect the same recurring pathways. We predicted that the ever-increasing number of mutations in these pathways would follow the oncogene addiction paradigm and would equate to increased proliferation and tumour growth. Instead, and in particular for pathways including RAS or MYC, we have realized that this concept is undermined by an endogenous safeguard response: the induction of apoptosis[12,13] and oncogene-induced senescence[14]. The reliance of these intracellular stress mechanisms on intact p53 has highlighted the therapeutic potential of the large proportion of tumours that have not yet lost wild-type p53 and that therefore remain susceptible to therapeutic activation of p53 pro-apoptotic pathways. Meanwhile, our molecular understanding of the balance between anti-apoptotic BCL-2 proteins and their pro-apoptotic BH3-only counterparts heralded the first clinical trials with BH3-mimetics to curb the excessive survival signals received by cancer cells. Autophagy is another example of a physiological response hijacked by cancer cells that enables them to survive conditions of prolonged cellular stress[15]. The induction of autophagy in cancer cells can also contribute to the paradoxical cytoprotective effect that occurs in response to radiotherapy and some chemotherapy, and this explains why drugs that inhibit autophagy are now being investigated in the clinic.

Inflammation has long been linked to cancer, but only in the past decade have we understood how inflammatory cells, and other components of the tumour stroma, fuel tumour progression by creating a microenvironment that is enriched for the same cytokines that are the protagonists of the chronic inflammation associated with liver, stomach and colon cancers. Indeed, inflammation is a tumour-enabling characteristic that affects and converges on almost all types of solid cancers to enable many of the hallmarks of cancer and to foster the progression of incipient neoplasias into full-blown malignant tumours.

Sophisticated knockout studies in mice and zebrafish have provided us with a dazzling view of the plasticity of many systems and their inbuilt redundancies. This is now recognized as a major reason why even the most efficacious targeted drugs fail to act as long-lasting 'magic bullets' — and why even the best personalized approaches mostly delay disease progression but rarely eradicate it. We could not anticipate how short-lived the therapeutic responses would be owing to drug resistance, which seems to emerge with the predictability of a 'whac-a-mole'. The recent discovery that cancer cells express different protein isoforms that limit the use of the initially promising BRAF inhibitors serves as a prominent example[16–18].

Karen Vousden. The past 10 years have seen substantial advances in both our understanding of cancer and the technologies that

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are available to study it. There have also been many exciting breakthroughs in the development of rationally designed therapies that offer us new ways of treating or preventing cancer. I've highlighted a sample of these findings here — but there are many others of equal impact and importance.

The development and implementation of the vaccine against genital HPV infection is an incredible success story[19]. The potential advantages of cancer prevention as opposed to cancer therapy are obvious, but many prevention strategies are difficult to put into practice — especially those that involve long-term lifestyle changes. The International Association for Research on Cancer (IARC) monograph that concluded "HPV types 16 and 18 are carcinogenic to humans" was published in 1995 (REF. 20), and the progress since then has been remarkable. The HPV vaccine has yet to be proven to prevent cervical cancer, as this will take decades to ascertain, but the implementation of a wide-scale vaccination programme in so many countries — despite significant objections — is a major step forwards. This is a shining example of what can be achieved when epidemiologists, molecular biologists, immunologists and public health clinicians collaborate.

Unprecedented advances in our ability to sequence genomes, measure the expression of genes and non-coding RNAs (the involvement of which in cancer has been another massively exciting development[21]) across the entire genome, and analyse epigenetic, proteomic and metabolomic profiles on a similarly large scale are already having a big impact on the direction of cancer research and the vision of how cancer patients should be treated[22]. It seems that these technologies are putting the personalized analysis of tumours tantalizingly within our grasp, and are helping to define and identify biomarkers that should allow us to direct cancer therapy based on an understanding of the pathways that operate in an individual tumour, rather than crudely treating all malignancies from a particular organ site as one disease. This concept of personalized medicine is not a new idea, of course. For example, George Beatson of Glasgow, UK, first suggested the concept of hormonal control of cancers in a *Lancet* paper in 1896 (REF. 23), and differentiating hormone-sensitive from hormone-resistant breast cancers is now standard care for patients with this disease. However, the progress over the past decade in our ability to characterize the inner workings of each tumour is raising the hope that this rational approach can be applied to a much greater depth and to all cancer types.

Massive-scale sequencing has also allowed us to identify the likely common driver mutations that underpin malignant development[4]. There have been some astounding successes using this approach. The identification of *BRAF* mutations in melanoma and the speed of development and use of *BRAF* inhibitors in clinical trials is one example[24]. Neomorphic mutations in the metabolic enzymes isocitrate dehydrogenase 1 (IDH1) and IDH2 are another[25], but there are many more. These and other large-scale information-gathering exercises are delineating the underlying networks and pathways that are commonly and recurrently mutated in different cancer types, information that will be used to develop and improve targeted therapies. A pleasing extension to this is the concept of synthetic lethal approaches[26], as demonstrated so elegantly by the use of poly(ADP ribose) polymerase (PARP) inhibitors in BRCA-deficient breast cancers. Although each of these therapies may hit subsequent problems with resistance and other unanticipated issues[27], the proof of principal that they provide is hugely satisfying.

Q ***Where do you expect progress to be made in the next 10 years?***

Y.C. In the future, chemoprevention needs to be an important part of cancer research and will need to be promoted as a lifestyle choice. Strategies to popularize knowledge of cancer prevention through health education and tobacco control should help to ensure that cancer prevention is promoted as a key public health task to governments in many different countries. Currently, at least one-half of all cancers are diagnosed in developing countries, and ways of targeting and treating cancer in these countries are desperately needed. Vaccination is one possible route, and the Chinese government has recently planned widespread immunization using the hepatitis B vaccine. This should help to reduce the incidence of liver cancer. Moreover, as much of this programme is focused on controlling infection, the incidence of infection-associated cancers should greatly decrease over the next 10 years.

Meanwhile, based on the success of screening for specific tumour protein markers, such as α-fetoprotein (AFP) and prostate-specific antigen (PSA), several new cancer biomarkers will be included in routine medical examinations. Moreover, screening of specific molecular targets will guide and enhance the effective development of personalized or individualized medicine[28]. Clearly, a change from an emphasis on treatment to an emphasis on the prevention of cancer and on combining both treatment and prevention will be instrumental for an effective strategy for eliminating this chronic disease.

Answering basic scientific questions in cancer will continue to be a key point of emphasis in life science research. Molecular profiles from all types of tumours will be developed, and conventional oncological pathology will be integrated into the discipline of molecular pathology. The interplay between pathological and morphological changes and molecular signatures will guide diagnosis and therapy in cancer[1]. Metabolic reprogramming is proving to be widespread in cancer cells and is regarded as an emerging hallmark of cancers. Studying and elucidating the relationship of metabolic disorders and cancer should provide new ideas for molecular intervention mechanisms and may also help to promote a new field that will provide metabolism-based targets for cancer patients. In addition, 'omics' in cancer together with systems biology will effectively answer numerous key scientific questions in carcinogenesis[4].

The increasing global migration patterns are challenging in epidemiology. Clearly, epidemiological studies in populated areas that exhibit a high incidence of cancer may need to be revisited and perhaps reinvestigated. Samples acquired from susceptible populations and cases need to be stored for future study. Moreover, the development of molecular epidemiology will provide some new evidence in aetiology, diagnosis and therapy of cancer from the whole-population level.

Developing anticancer drugs that are based on proven molecular targets will still be an important topic. Cancer drug development will move from validation and testing in the traditional cancer clinical trial to biomarker-driven and hypothesis-testing trials[29]. These types of trials will specifically address and focus on proof of mechanism, proof of concept and individualized medicine with pharmacogenomics (that is, the '3Ps'). Biological hypothesis-testing trials will provide new opportunities in personalized therapy for tumour patients. The trials will be based on new biomarkers selected from laboratory studies and moved into translational trials, which should lead to the development of a unique model of molecular biomarker-based patient selection.

Translational medicine in cancer must be based on a close relationship between basic science research and clinical trials. Strategies in cancer prevention and therapy, as well as basic research, will provide the evidence needed for implementing personalized, predictive, preventive (or pre-emptive) and participatory medicine (that is, the '4Ps'). Furthermore, cooperation between multiple disciplines and maintaining a tight link between basic and clinical medicine will establish a new mechanism for collaborative actions against cancer, the theme of this years Annual World Congress on Cancer, which took place in China. In addition, the continued input of substantial finances from non-governmental organizations, such as the Bill & Melinda Gates Foundation, should help to further support research focused on major health problems, such as cancer and HIV.

R.A.D. The TCGA project[30–32] and functional genomic screens[33] are revealing many new cancer genes, providing new potential therapeutic points of attack. Although encouraging, it is worth emphasizing that these genomic discoveries are just a beginning. The conversion of validated targets into highly effective drugs with durable clinical responses requires a clear clinical path hypothesis for drugs entering the pipeline. Realization of such a programme necessitates an in-depth preclinical effort to fully define the biology and mechanism of a target, as well as a clear understanding of the genotypic and cell biological context in which the new target serves a rate-limiting function in tumour maintenance. So, in the coming decade, as the TCGA and functional genomics deliver a comprehensive compendium of the genetic events driving the major cancers, it is fair to ask whether the cancer drug development ecosystem, spanning discovery to clinical proof-of-concept, is optimally structured to harness the full clinical potential of these breathtaking scientific advances. I think not. Serious operational deficiencies prevent systematic and reliable execution along the multitude of preclinical activities that are needed to illuminate an optimal path forwards. Traditionally, academic institutions celebrate the individual and serve as the major engine for the discovery of novel targets. In a rather random process, a handful of such early stage discoveries might then fuel venture-backed biotechnology companies, which would in turn drive these programmes to a level of preclinical or clinical validation that is sufficient to attract substantial financial investments from pharmaceutical companies that are needed for late-stage clinical testing and commercialization. This model, which has yielded marginal clinical and economic success, has experienced major changes that have moved us farther away from a solution. Over the past few years, many large pharmaceutical companies have downsized their internal research programmes with the goal of preserving capital to license drugs at clinical proof-of-concept from biotechnology firms. Coincident with this trend, the recent economic crisis severely limited the availability of venture capital, resulting in historic lows in the creation of new companies, particularly companies with early stage 'lead' drugs or drug targets that require a longer period of investment before generating any financial return: a route that has traditionally delivered the lion's share of our novel innovative drugs. On the academic front, although translational efforts have increased, the preeminence of hypothesis-driven research and the emphasis on trainee development has not been conducive to the creation of multidisciplinary teams that are driven by the mandate to perform all of the critical preclinical studies needed to fully understand the importance of a novel target and to test new drugs against such targets in the best model systems available. The types of 'applied' experiments needed to make timely go or no-go decisions in cancer drug development are often not aligned with the generation of high-profile manuscripts that support the aspirations of graduate and postdoctoral trainees for top careers in academia and industry.

> "It is vital that we are not tempted to divert funding away from basic research in the erroneous belief that we somehow know enough."

So, in the decade ahead, what is needed is a new organizational construct. This construct should be embedded with the rich, innovative culture of academic science but should also be populated by goal-oriented, milestone-driven staff scientists, whose primary mission is to systematically enlist the entire compendium of emerging cancer targets into a full array of quality-controlled *in vitro* and *in vivo* validation assays that are designed to achieve full verification of the cancer relevance of a target and identification of those targets with the highest importance (not just any validated target) for drug discovery. In addition, securing the knowledge needed for the major advances in cancer drug development will require a creative but directed culture, it will take patience, comprehensiveness and resources, and it will require full unencumbered access to extant models and technology. It is my view that academia is the only environment that is in a position to take on the challenge of building this construct of applied cancer science. Such an applied cancer science programme would be responsible for the timely and systematic large-scale genetic and functional analyses that are needed to define cooperative relationships among all known and unprecedented cancer targets that govern the diverse biological hallmarks of cancer[1]. It is worth emphasizing that the issue is not whether a gene is important in cancer but in what genotypic or cell biological context its extinction would lead to tumour regression. The ultimate goal of such efforts would be to generate rational co-extinction strategies for specific cancers: targeting single elements is generally not sufficient to elicit durable clinical responses[34] — the only goal that patients care about.

As drugs are developed for these cooperative targets, this organization would be responsible for testing these drugs, alone and in combination, in a diverse array of model systems in order to pressure-test the clinical hypothesis to the maximum extent possible at the preclinical stage. There is a growing appreciation that if a drug does not work in today's refined *in vivo* models, then the chance for clinical success is low. It is also my view that model system testing should encompass the full range of hundreds of genome-annotated cell lines in two-dimensional (2D) and 3D cultures, primary human cancer tumour cells maintained *in vivo* and genetically engineered mouse models of cancer, as each possesses strengths and weaknesses and each provides vital information on drug action alone and in combination in specific genotypic and tumour-type contexts. Beyond these preclinical efforts, target validation must continue in early stage clinical testing for which pre-imaging, post-imaging and biopsies are essential to leverage our emerging capabilities in tumour genotyping, assessment of target engagement and on-mechanism responses to therapy to guide genomics-based medicine. Collectively, these investments are modest relative to the cost of a failed Phase III clinical trial.

The implementation of an applied cancer science paradigm will require a cultural shift in academia to one that rewards team work, applied science and the achievement of specific goals and milestones. The realization of maximal progress in this coming decade will come with the confluence of knowledge, technology and the organizational constructs capable of driving discovery science to clinical end points. Such an effort would deliver higher quality programmes for our patients in clinical trials, attract private sector investments to produce marketed products and ultimately mark this decade as the one that dethroned this emperor of maladies.

M.E. With existing large international cancer consortia, the next decade will see unprecedented opportunities arising from an explosion of DNA-sequencing capabilities for ever decreasing costs, and to enable personalized genome and expression data to become a reality. Supplemented with information on epigenetic modification, the cancer proteome, metabolome and all the other 'omes' that are yet to come, this compendium will allow us to reconstruct a timeline of progression for individual tumours and provide novel opportunities for personalized treatment. Equally important, this information will define and validate stage-specific surrogate markers for diagnosing disease and for monitoring treatment response or relapse. Integrating all these data is the key to developing more effective personalized and, most likely, multipronged treatments that help to eradicate the entire tumour, rather than merely interfering with its growth. The ultimate success, however, will depend on how well we can understand and predict resistance, by combining the insight gained from therapeutic investigations using complimentary *in vivo*, *in vitro* and *in silico* cancer models.

Much effort will need to go into deciphering metastatic signatures, as metastases are what ultimately threaten the patient's life, and examples from pancreatic cancer make a clear case that metastasis-initiating cells require driver mutations beyond those required within primary tumours[35,36]. Epigenetic mechanisms, including DNA methylation and histone modifications, will need to be factored in more vigorously, as they not only confer heritable phenotypes (such as the silencing of tumour suppressor genes), but are also constant companions for the incremental steps of the neoplastic cell's journey to metastatic disease. We also need to better understand whether and how to therapeutically target cancer stem cells. This might be more straightforward in tumours in which cancer stem cells function in a hierarchical fashion and possess phenotypes that are stable traits. Tumours in which cells with stem cell-like properties arise in a stochastic manner and retain phenotypic plasticity, however, could prove more challenging[37]. Understanding the nature of tumour cell plasticity is therefore rapidly becoming a key goal in cancer research.

The clinic will benefit from the use of existing (targeted) drugs for a wider range of tumours that may arise from fortuitous off-target effects, as has been illustrated with the used of the BCR–ABL inhibitor imatinib against KIT-driven gastrointestinal stromal tumours[38]. In turn, this will encourage the pharmaceutical industry to dedicate resources for the development of drugs for rarer types of cancer that express a shared, prototypical cancer signature or a common mutated pathway. However, if RNA interference technologies can be effectively harnessed and delivered to patients, we may see alternatives to today's drug development approaches by global pharmaceutical companies, by enabling many more players to explore an unprecedented number of targets. As we more completely understand the various molecular requirements of any given cancer, we can more comprehensively focus on its various Achilles heels. Therapies will arise by homing in on the augmented reliance of the cancer cell on normal pathways, a phenomenon that is referred to as non-oncogene addiction[39], or on the need of a cancer cell to alter its metabolome so that energy production, macromolecule biosynthesis and redox reactions are balanced[40].

Our emerging capacity to replicate parts of the cancer ecosystem in genetically tailored and complementary *in vitro* and *in vivo* model systems will see a more systematic approach to comprehensively take advantage of synthetic lethal interactions. The power of this approach, most recently illustrated with PARP inhibitors in BRCA-mutant cancers[41,42], has proved to be very successful when it has been empirically exploited in the past. However, with the next decade generating an unprecedented number of new targets and experimental compounds, as well as treatment modalities, we may need to re-evaluate the current Phase III paradigm to maximize benefit for the patient.

K.V. Several areas of biology that have been underappreciated for years are now permeating the consciousness of all cancer researchers, and are likely to generate substantial advances in cancer treatment over the next 10 years. Examples include the importance of altered metabolism in the development and maintenance of malignancies[43] and the indisputable role of tumour cell interactions with the rest of the host in the form of stromal cells, angiogenesis, immune responses and so on[44]. Crucially, most of these discoveries came from basic molecular, developmental and cell research, and such fundamental science continues to inform many of the rationally designed therapies that are currently in clinical trials. It is vital that we are not tempted to divert funding away from basic research in the erroneous belief that we somehow know enough.

One unanticipated consequence of our recent technological advances — in particular the relative ease with which data on the genome, transcriptome, epigenome, proteome and metabolome can be gathered — is that we are in danger of drowning in information. It seems clear that biology must embrace mathematics, computing, informatics and data analysis in order to make sense of it all[30]. Above all, such analytical tools must always bear in mind that cancers, like all living systems, have not been designed but have evolved. Making sense of things in biology is challenging because cause and effect relationships can be difficult to discern or dissect, and because things can have function without an obvious purpose. There is a growing concern that the extent and nature of heterogeneity within cancers may simply defy rational explanation and explication. How can we make sense of data that not only document differences between individual cancers of the same type, but also changes within regions of the same cancer? The application of new technologies will help us to identify genes and epigenes that have an influence on cancer development, but integrating all of this information in a way that will be useful for making therapeutic decisions could prove difficult or perhaps impossible. One route through all of this information is to ask what is common to cancers, rather than what makes them all individual and unique. Finding common vulnerabilities to target for the treatment of multiple cancer types would make for an extremely attractive and alternative way forwards.

Another area in which progress will hopefully be made is in expanding the repertoire of targets for new drug discovery. Although the concept of rationally designed therapies has been amply vindicated, the range of mechanisms by which such drugs function has been limited. Many of the most attractive

and validated targets, such as transcription factors, have been deemed undruggable — surely this needs to change? New approaches to developing drugs that do not depend on the established rules are beginning to bear fruit, and the concept that protein–protein interactions can be successfully modulated is gaining credence[45]. The ability to build drugs from small fragments will hopefully open the door to attacking the most logical weak spots in cancers. Furthermore, the discovery of microRNAs and other non-coding RNAs may lead to completely novel ways of thinking about how to design new cancer therapies. Conversely, our expanding knowledge of cancer cell biology — such as the role of changes in metabolism — may allow us to use existing drugs that are currently used to treat other diseases for the treatment of cancer.

There is cause to hope that the use of rational combinations of targeted therapies will become routine in cancer care over the next 10 years, bringing more effective and less toxic treatment options. But maybe the best prediction is that new advances will be unpredictable, and in 10 years time we can again look back and wonder at the unimaginable progress that has been made.

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Competing interests statement
The authors declare no competing financial interests.

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