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The changing landscape of cancer drug discovery: a challenge to the medicinal chemist of tomorrow

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Since the development of the first cytotoxic agents, synthetic organic chemistry has advanced enormously. The synthetic and medicinal chemists of today are at the centre of drug development and are involved in most, if not all, processes of drug discovery. Recent decreases in government funding and reformed educational policies could, however, seriously impact on drug discovery initiatives worldwide. Not only could these changes result in fewer scientific breakthroughs, but they could also negatively affect the training of our next generation of medicinal chemists.

Synthetic organic chemistry is the foundation of cancer drug discovery. Its significant contributions began with chemotherapy, and synthetic chemistry has continually adapted to embrace innovative techniques and methodologies central to cancer therapy development. Cancer drug development began with an observation that mustard gas, employed in chemical warfare during World Wars I and II, destroyed lymphatic tissue and bone marrow formation. The observations made by Drs Gilman, Goodman and co-workers laid the foundation for conducting the first clinical trials with nitrogen mustards (β-chloroethylamines) in 1942 at Yale-New Haven Hospital, but a report of the clinical results was only made public four years later, because of the cloak of secrecy during World War II [1,2]. An array of DNA alkylating agents ensued, which paralleled an increased understanding of DNA in the 1950s. Several other agents subsequently emerged, such as the vinca alkaloids and purine/pyrimidine synthesis inhibitors [3]. These advances were, to a large extent, driven by the National Cancer Institute (NCI), enabling the assessment of primarily cytotoxic agents. By the 1970s, the importance of natural product-based early drug discovery had been realised [3]. Unfortunately, the synthesis of many of these frequently promising, novel agents was often too complex and too expensive to allow progression into early stage clinical trials. This situation facilitated a paradigm shift whereby natural product screening was implemented into stage discovery initiatives, providing an opportunity to identify natural products as *bona fide* lead compounds. These leads were then subsequently developed into truncated molecules, which were more amenable to synthesis.

More recently, advances in organic chemistry have successfully enabled the complete synthesis of many complex natural products, a milestone that has dramatically improved the ease with which chemists can now deal with the complexity of many of these naturally derived architectural structures. Organic chemistry has also been instrumental in the development of drug delivery and prodrug strategies, which have focused on the development of tumour-selective therapeutics with reduced side-effect profiles [4,5]. Furthermore, organic chemistry continues to respond to the molecular biology, high-throughput revolution of anticancer drug discovery, through the development of combinatorial, parallel and diverse oriented methodologies.

Today, the emergence of the genomics era is once again changing the landscape of drug discovery through a wealth of convergent data that has caused many to speculate on an expanding druggable genome [6] and epigenome [7,8]. A better understanding of the

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molecular abnormalities in malignant cells has provided an opportunity to rationally design mechanism-based drugs, molecular-targeted therapies that act selectively on these malignant cells and thus mitigate serious toxicity concerns. If, however, cancer research scientists are to continue this forward momentum, the success in the development of imatinib and other kinase inhibitors must be taken into account, given that it is in drugging the cancer kinome that scientists have accrued the greatest knowledge and experience. Continued success will require an improved understanding of the issues that were overcome, the lessons that were learned and the application of this knowledge to other molecular targets and therapeutics [9].

It is apparent that changes in our understanding of the molecular basis of cancer drug discovery pose significant challenges to medicinal chemists and other scientists working at the chemistry–biology interface. The role of the medicinal chemist in drug discovery has transformed significantly during the past half-century: from relying on validation data from *in vivo* studies to one in which high-throughput *in vitro* screening approaches are now the crucial drivers of validation [10–12]. Changes to the landscape of drug discovery have been more profound over the past five years, presenting additional and unforeseen challenges and opportunities to synthetic and medicinal chemists as was recently highlighted at the 2009 joint conference between the American Association for Cancer Research (AACR) and the American Chemical Society (ACS) in New Orleans, USA. This was the second conference focused on 'Chemistry in Cancer Research', with the aim of providing a forum for research discussions amongst chemists and others with cancer research interests. A report from the first meeting was published [13,14], describing recent trends in cancer-related drug discovery, including proteomics, chemical biology of carcinogenesis, structural biology, modelling and bioinformatics. Whereas the inaugural meeting covered a broad range of chemistry disciplines, the second Chemistry in Cancer Research Working Group (CICR) hosted conference was focused more on synthetic organic chemistry in support of cancer target identification, validation, lead discovery and optimisation.

Advances in synthetic organic chemistry

The identification of new, highly specific small-molecule ligands for biological targets remains a significant challenge in drug discovery. As the past decade has clearly demonstrated, the crucial issue for enhancing the rate at which such molecules are discovered depends upon our ability to improve the quality of compound collections utilised in our initial screens, thereby establishing areas of chemical space for further enhancement and refinement, and subsequently establishing the target(s) these molecules can modulate. Speakers at the conference addressed these issues in the context of improving our general understanding of key biological processes and their application to novel therapeutic opportunities in cancer. Derek Tan (Memorial Sloan-Kettering Cancer Center) discussed how the pharmaceutical industry has focused primarily on a relatively small set of 'druggable' targets and explained how this has resulted in the exploration of an increasingly narrow region of chemical space that is appropriate for these targets. For instance, a recent study identified just 207 current human targets for small-molecule drugs [15], yet this figure corresponds to approximately 1% of the human genome [16]. Even more striking is the fact that half of all drugs target only four protein classes. In light of this information, Dr Tan discussed how sequencing the human genome has opened the door to investigating a vast array of exciting new targets. The question, however, is to determine which molecular classes are optimal for interacting with them, given the documented trend that conventional libraries of drug-like substances from commercial suppliers often fail to provide useful probes amenable to hit-through-lead optimisation for these targets. Dr Tan described how a programme utilising knowledge of natural product structures (which have been evolved over millennia to interact with biomolecules), combined with new synthetic methods to fashion arrays of natural product-like structures rapidly, could potentially provide novel small molecules that would extend 'chemical space' and deliver novel lead structures for biological investigations against these new targets [17]. Scott Snyder (Columbia University) continued this theme for deciding which molecules should be incorporated in a potential screening library by noting that nature makes several unique and structurally diverse compound collections from simple building blocks as a first line, immune-like, chemical response to the invasion of a foreign pathogen. Synthetic chemists have not determined how to prepare these diverse structures (termed oligomeric natural products) in a controlled manner, thereby preventing their effective use as probes, since they are often difficult to isolate in pure form from nature in any quantity. Dr Snyder went on to illustrate a new strategy that has enabled the controlled synthesis of several architecturally complex molecules derived from both resveratrol and rosmarinic acid, one that required the identification of a building block that diverged significantly from nature's starting material, but that could be converted into each family member in just a few synthetic steps [18].

Michael Foley (Broad Institute) shared his thoughts on the sheer number of challenges that the chemistry community faces in developing effective hits and leads against such new targets, in particular transcription factors, regulatory RNAs and protein/protein interactions, targets often described as 'undruggable.' Although he pondered openly whether chemists were equipped to develop drugs against such targets, which would clearly lead to improvement in treatment outcomes for cancer patients in the future, he provided several promising case studies that suggested that chemists are moving in the right direction. He cautioned that the next several years would be crucial for establishing proof-of-concept. Finally, building on the concept of small-molecule discovery within this expanding 'druggable' genome, Alan Rigby (Beth Israel Deaconess Medical Center, Harvard Medical School) presented his laboratory's efforts to target protein–protein and protein–DNA interaction interfaces using *in silico* structure- and ligand-based small-molecule discovery partnered with nuclear magnetic resonance (NMR) spectroscopy. This target-specific, computer-aided drug design (CADD) approach allows one to rapidly interrogate these and/or other novel interaction interfaces, thereby identifying chemotypes of interest whilst triaging other compounds early in a rapid, iterative discovery cycle. The concept of selectively targeting and inhibiting the interfaces of protein–protein and/or protein–DNA complexes represents an exciting therapeutic opportunity for reprogramming specific pathways or programmes of gene expression that are dysregulated in cancer, inflammation and other complex disease states where there

remains considerable unmet therapeutic need. Given the importance and commercial promise of these 'non-traditional' interfacial targets, several groups have successfully identified hit compounds that disrupt the protein–protein interfaces within the dimer (homodimer and heterodimer) family of transcription factors, and Dr Rigby expanded upon these studies by demonstrating that it might be possible to target directly the transcription factor–DNA interface and in doing so selectively inhibit the expression of genes downstream of these specific transcription factors.

Chemical biology to the fore

Exciting new directions in chemical biology were presented in talks given by Brett Stockwell (Columbia University), Steven Hall (Lync Pharma) and Benjamin Cravatt (Scripps Institute). Dr Stockwell provided the participants with insight into the use of 'combinatorial chemical genetics'. This is a systematic application of multiple chemical or mixed chemical and genetic perturbations, aimed at gaining insight into biological systems, as well as facilitating biomedical discoveries [19]. Dr Stockwell described a profiling approach where he sought potent compounds acting through novel cell-death mechanisms with the exciting prospect of not only revealing effective new drugs, but also exploring the fundamental mechanisms governing cell mortality. Dr Cravatt discussed investigations into the use of 'activity-based proteomics' developed by his laboratory to map vital biochemical pathways. He argued that although general biomarkers and targets for the diagnosis and treatment of cancer exist, there is a need to use more global technologies to measure protein levels and their corresponding activities as part of their discovery and validation. Dr Cravatt presented highlights of his research focused on a chemical strategy that he referred to as activity-based protein profiling (ABPP), which utilises active site-directed probes to profile the functional state of the enzyme being studied, and included examples from his work on serine hydrolases and metalloproteinases [20,21]. Dr Cravatt explained that ABPP probes label active enzymes, but not their inactive precursor or inhibitor-bound forms and, therefore, report on the major post-translational events that regulate enzyme function *in vivo*. Dr Hall described the efficacy of an unbiased screening method that enabled the parallel screening of small molecules across hundreds of targets from dozens of different gene families. This method, a derivative of the work by Haystead and colleagues [22] involved the identification of an ATP-based affinity resin that served as a capture mechanism for all purine-binding proteins. This was a powerful demonstration of how a single screen can be used to interrogate a chemical library against the entire superfamily of purine-binding proteins. Dr Hall further supported the rigour and applicability of this approach detailing its importance in the identification of the novel HSP90 inhibitor, SNX-5422 (currently in Phase 1 clinical trials) [23].

John Westwick (Odyssey Therapeutics) discussed how drugs frequently possess 'hidden phenotypes' that result from unexpected or unintended activities, owing either to their binding to unknown targets or to unknown interactions between the intended drug target and its effect on other biochemical pathways. Such unanticipated activities might either be harmful, leading to toxicity or beneficial, as is the case for many inhibitors with demonstrable poly-pharmacology [24]. He explained how new and potentially useful properties of drugs are often discovered serendipitously, and that the mechanisms through which these drugs produce their biological effect are often unknown. Dr Westwick presented a strategy for identifying hidden drug phenotypes using high-content cellular analysis of changes in protein–protein interactions to probe individual steps in signal transduction pathways [24]. He described how this strategy not only reproduced known structure–function relationships for a series of drugs and their targets but also commented on the predictive power of this strategy, correlating novel phenotypes with mechanism of action data not previously described.

Patrick Zarrinkar (Ambit Biosciences) described the potential of a single screen termed 'KinomeScan' to enable high-throughput kinase profiling. The KinomeScan assay panel currently includes more than 400 assays representing approximately 80% of the human protein kinome and has become instrumental in specificity profiling of novel kinase inhibitors [25]. Hence, kinase profiling of compound libraries reveals the complete kinase interaction potential of a library, as well as the detailed relationship between chemical structure and kinase interaction patterns.

Innovations in drug delivery

Anticancer drugs generally affect all types of rapidly proliferating cells and consequently their therapeutic indices are rather narrow. Harsh side effects are typically observed and clinical doses are often determined empirically on the basis of severe toxicity. However, in an effort to enhance drug selectivity and simultaneously reduce unwanted toxicity (i.e. improve the therapeutic index), some have focused on the development of specific drug delivery systems. Karen Petrak recently contemplated whether such approaches would serve to create 'ideal drugs' in *Drug Discovery Today* [26]. At the time, the conclusion was that the development of macromolecular, target-specific drug-carrier systems had not yet been validated at the clinical level, despite significant pre-clinical advances in these drug delivery technologies. Nonetheless, there have been scientific advances in drug delivery methodology over the past few years in areas such as (i) nanocarrier technology, and (ii) high affinity cell-targeting ligands in the form of monoclonal antibodies, peptides and vitamins. Both approaches continue to be evaluated for their ability to enhance the activity of certain anticancer agents, and examples of both were presented.

Discussions at this meeting illustrated how progress towards better clinical efficacy is being achieved through novel drug delivery strategies. For example, Paul Wender (Stanford University) discussed his research on 'molecular transporters', that is compounds that enable or enhance the uptake of drugs or probes which themselves do not enter cells or do so poorly. Dr Wender's research presentation discussed nanotubes for protein delivery, nano-arginine (R9), as well as other guanidinium-rich transporters, that have the potential to treat multidrug-resistant tumours. Further improvement on nanotechnology-based carriers for imaging and cytotoxic agents was discussed by Tamara Minko (Rutgers University) and Jayanth Panyam (University of Minnesota). Dr Minko discussed the latest developments in the tumour-specific receptor-targeting of nanocarriers to enable higher tumour selectivity and imaging efficacy of multifunctional nanotherapeutics

[27]. Dr Panyam then described how multiple targeting ligand functionalisation could be accomplished using a single-step surface technique [28]. Peter Senter (Seattle Genetics) mentioned positive clinical outcomes following the use of monoclonal antibodies for the delivery of anticancer drugs, such as SGN-35, an anti-CD30–aurostatin conjugate and trastuzumab-DM1, an anti-Her2/neu-maytansine conjugate. Chris Leamon (Endocyte Inc.) later described how over-expression of the folate receptor on the cell membrane in many human cancers could be exploited to deliver both real-time radiodiagnostic imaging agents as well as pharmacologically active molecules. Emphasis was placed on the value of stratifying eligible (e.g. folate receptor positive) patients for the clinical testing of the targeted chemotherapeutics. He also conveyed encouraging results from Phase 1 clinical trials of the folate–*Vinca* conjugate EC145 (now in multiple Phase 2 trials), and commented that two additional folate-targeted agents, EC0225 and BMS-753493, have entered Phase 1 clinical trials [29]. Frederick Goldberg (AstraZeneca) gave several examples from the literature of targeted and non-targeted prodrug strategies that have positively impacted drug discovery programmes and ultimately led to the identification and validation of clinical candidates. Using the example of AZD1152, a selective Aurora B inhibitor, he focused on the potential benefits of such prodrug strategies to improve drug delivery and *in vivo* pharmacokinetics.

Medicinal chemistry and future challenges

It is evident from participation in the CICR-organised conference that synthetic organic chemistry remains a vital component to the advancement of cancer drug discovery, not only in its ability to provide/create novel 'hits' and 'leads', but also in enabling the interrogation of unchartered biological systems and newly discovered targets. The successful completion of the Human Genome Project provides a grand new challenge. If we are going to successfully leverage the wealth of this limitless 'omic' data it will require iterative and synergistic interactions between medicinal chemists and the broader research community for years to come. Decoding the information stored in the functional genome, including thousands of predicted gene products, will only be possible with new scientific tools and methods that are fit for purpose. Increasingly, small molecules are used as probes to study functions of proteins and cellular processes [30]. For the medicinal chemist to address such challenges, a range of new skills are required for successful drug discovery, in addition to basic knowledge of fundamental medicinal chemistry and an understanding of the biology that relates to and is causal in disease. 'Chemical genetics', for example, is increasingly providing scientists with a new set of complementary chemical tools to investigate biological systems [31,32]. As also highlighted at this meeting, chemical genetics uses small molecules to perturb the function of gene products (e.g. proteins), thereby facilitating the dissection of biological processes through refined chemical intervention [31]. Small molecules designed and synthesised in chemistry laboratories have been shown to be valuable for treating diseases and constitute many of the medicines marketed today [33]. Consequently, their effect on biomedical research during the past decade has been dramatic, providing both new tools for understanding living systems as well as enabling a didactic transition from biology to medicine [33–35]. The synergistic relationship between organic synthesis planning and methodology is even more significant as synthetic organic chemists tackle these new challenges [33]. Hambley and Hait recently emphasised that the search for new anticancer agents needs to continue on many fronts, and should not be focused on one strategy or traditional approaches alone [36]. As a consequence, there are multiple approaches to drug discovery with each necessitating a broader understanding of chemistry that can and should be implemented in the training and education of future chemists. This is important for the development of new scientific tools and methodologies that are being used to advance cancer research, whilst facilitating transfer of knowledge to the next generation of chemical investigators and students about the varied opportunities and power of innovative chemistry, which can be applied to important problems in the discovery and development of new cancer medicines today. Unfortunately these exciting new challenges are not being effectively addressed, as the training needs of synthetic and medicinal chemists of tomorrow are being negatively impacted by significantly reduced government budgets and reformed educational policy throughout the world.

Continuous investment needed

Training in medicinal chemistry as an academic discipline in the UK is largely through PhD studentships, with a small number of taught/research-based drug discovery courses available at MSc level. There are several key medicinal chemistry training centres around the country, funded by both government and charities, which provide an excellent opportunity for those able to obtain a studentship. Two recent key decisions by major funding bodies have, however, given rise to real concern throughout the UK cancer medicinal chemistry community. The EPSRC (Engineering and Physical Sciences Research Council) modified the rules regarding its First Grant Scheme. This scheme was set up specifically to give newly appointed academics assistance in obtaining EPSRC funding. Whereas a new limit of £125k should ensure that more grants are funded (previously no limit), a cap of two years funding means that it is no longer possible to apply for a PhD studentship via this scheme [37]. Cancer Research UK (CRUK) has also revised its regulations regarding PhD studentships, and only awards PhD studentships to five particular universities (http://www.science.cancerresearchuk.org/gapp/personalfund/phdstudentship/tcdb_medchem).

Changes to the UK funding landscape are also having an impact on attracting and training students in synthetic organic chemistry. Many medicinal chemists working in the biotech and pharmaceutical industries received their PhDs in organic synthesis, a consequence of the view that excellence in organic synthesis is a prerequisite for a successful medicinal chemistry career [38]. Obtaining funding for organic synthesis might become more challenging in the future, because of a shift away from 'responsive mode' applications; the success rate of EPSRC applications has dropped from approximately 25% to 10% (http://www.rsc.org/chemistryworld/News/2008/October/20100801.asp), and this coincided with a new policy to limit applications from persistently unsuccessful academics [39] (http://www.epsrc.ac.uk/ResearchFunding/Changes/ReducingPressure.htm). Restricting support is, however, likely to result in a reduction of the pool of potential answers/solutions to crucial problems, which arise from current and future challenges. This has led to concerns

within industry that a reduced emphasis on organic synthesis would negatively impact the quality of future generations of medicinal chemists. To balance these changes the EPSRC has initiated 'grand challenges', where money is available to address key priorities of future collaborative research, such as in human health. These funding policy changes present opportunities for academics that can adapt, and a probable consequence is an increased degree of collaboration between organic synthesis and other disciplines. Ultimately this might result in the establishment of highly collaborative centres focused on chemical biology, drug discovery and other disciplines that support this important thematic initiative. One concern that industry has with such collaborative centres is that the students might find it more difficult to acquire highly specialised physical and synthetic organic chemistry skills and/or tools that would allow them to compete in a highly competitive job market. If, however, these centres do provide a thorough educational opportunity these PhD students might prove to be highly qualified for a career in medicinal chemistry, where success in projects frequently relies upon the successful collaboration and integration of multiple disciplines.

Whilst the system for funding students is slightly different in the USA, similar challenges and obstacles remain for principal investigators and the students in their laboratories. Specifically, the National Cancer Institute, which is part of the National Institutes of Health (NIH) and the U.S. Department of Health and Human Services (DHHS), remains the principal agency for cancer research with other research grant support available from the Center for Disease Control (CDC) and Prevention and the Department of Defence (DOD) (http://www.cancer.gov/cancertopics/factsheet/NCI/research-funding). Given that the NCI is one of 27 Institutes and Centres that make up the NIH its annual operating budget, which is allocated by the US Congress has remained flat at approximately $4.8 billion (http://www.obf.cancer.gov/financial/bypass.htm); a number that has drastically lowered the funding payline with success rates for new Research Project Grants (better known as a RO1 grant) currently at or below 10% (http://www.report.nih.gov/reports.aspx?section=SuccessRates&title=Success%20Rate).
Whilst scientists earlier in their career are often supported for a period of three to five years through several financial mechanisms including foundations and academic departments, the current funding situation remains dichotomist given these significant federal budget constraints. Whilst there is an appreciated need to support those in the earliest stage of their career the risk-reward equation from the viewpoint of many of these funding agencies is one that does not currently support innovative or highly translational research programmes. Unfortunately, these programmes are often the foundation of budding young scientists in cancer research. Given the current fiscal concerns in the USA, the average age at which a scientist typically obtains their first significant federal grant has increased to approximately 40 years of age. Given this plight, how do these promising young scientists, in the early stages of their careers, generate the preliminary data needed to be competitive and where does the 'bridge funding' between a start-up package and obtaining their first RO1 grant come from? In spite of these dire numbers, there is now significant hope in the American Recovery and Reinvestment Act (ARRA), which has appropriated $10.4 billion to the NIH for research and related projects under President Obama. These monies include an estimated $1.3 billion to the NCI, which should improve the current funding landscape. Dr John Niederhuber, Director of the NCI, stated at the recent AACR 2009 Centennial meeting that he expects these and other monies to be used to support a 'marked increase in the number of principal investigators studying cancer, including first-time investigators' and that this funding will be used to support translational research by unifying 'the commitment and contributions of biologists, chemists, informaticians and clinical scientists' (http://www.cancer.gov/newscenter/pressreleases/AACRspeech2009QandA). Indeed, modern drug discovery should be a conversation and meeting of minds from a spectrum of disciplines with the medicinal chemist perhaps being involved at an earlier state of target validation.

In any event, for research to advance more quickly in the UK, USA and indeed worldwide, a closer relationship between academia and industry might become increasingly important, particularly within the fields of drug discovery and cancer research. As was recently discussed in this journal, new strategies are emerging as a result of re-focusing and restructuring of the drug discovery field, leading to a new 'front end' between pharma and academia which aims at more successfully taking new therapeutic entities through pre-clinical and clinical development to the market [40].

By addressing 'grand challenges' such as in healthcare and in setting up collaborative centres with a focus on drug discovery it might be that academia can benefit from advice and support from the pharmaceutical and biotech industries given their longstanding success in this field. During difficult economic times, however, many private sector companies are forced to reduce their R&D budgets. This is an opportunity for academics to fill an important innovation gap. In the business sector we are witnessing this change through the significant licensing as well as merger and acquisition activity that has been documented through numerous partnership deals between academic institutions and pharmaceutical companies.

The goals of academia and industry might become more closely aligned if, as suggested by the research councils of the UK, there is a shift in academia from fundamental/basic research towards knowledge transfer and innovation. The EPSRC, for instance, encourages the formation of partnerships between academia and industry through its postgraduate CASE awards, which already serve to strengthen the ties between the two. Industry also contributes in a positive manner to undergraduate teaching of medicinal chemistry in many universities through educational tools, including industrial case histories as well as more traditional academic lecturers. However, some people in industry have the opinion that many of the key skills and novel techniques that are a part of modern drug discovery in industry are lacking at undergraduate level [38]. The challenge for universities is to ensure that the medicinal chemistry content of their chemistry courses is relevant to modern drug discovery and to address the opportunity for greater collaboration between industry and academia. Given the importance of the early stage knowledge transfer and the development of these core competencies many institutions both in the UK and USA

have developed or are developing both undergraduate and graduate curricula with a focus on bioinformatics, biotechnology and the interplay between the two. Whilst concerns over course content are, however, important for attracting and educating skilful chemists [41], arguably the greater threat to medicinal and synthetic organic chemistry is funding. It is vital that both industry and academia work with public funding bodies to ensure that the core disciplines that will provide the next generation of innovative and skilled medicinal chemists are appropriately supported at the public, corporate and government level.

Conclusion and future prospects

Since the development of the first cytotoxic agents, synthetic organic chemistry has developed enormously. The synthetic and medicinal chemists of today are at the centre of drug development and are involved in most, if not all, processes of drug discovery. Cancer research is a multidisciplinary effort and the continuing need for excellent synthetic and medicinal chemists is imperative, not only to successful drug development, but also to the exploration of new targets using small molecules to probe cellular and molecular mechanisms.

The recent advances discussed at the joint AACR/ACS meeting have highlighted the need for synthetic and medicinal chemists to adapt to an ever-changing landscape of drug discovery. However, there is cause for concern. Declining government funding and reformed educational policy worldwide are likely to have serious implications for drug discovery educators and practitioners, which could widen the already significant gap between research scientists at the highest level and the education of students at undergraduate and postgraduate level. There is a real concern that the chemists of tomorrow will not possess the 'right' tools in the toolkit to be able to effectively interrogate and address the questions being asked by research scientists in academia and industry today. The challenges can only be met if the government agencies worldwide are willing to invest in the education of academics and students alike. The onus is also on academics to be able to adapt to the rapidly changing funding priorities. This is the only way that we can improve our knowledge, continue to be innovative and ultimately combat serious diseases such as cancer.

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