nature chemical biology

Come together

The third *Nature Chemical Biology* symposium brought together nearly 200 scientists to explore the frontiers of chemical biology and drug discovery.

In the past decade, chemical biology has expanded to embrace increasingly diverse research areas at the interface of chemistry and biology. *Nature Chemical Biology* has strived to highlight this aspect of chemical biology by publishing papers that apply chemical and biological approaches to achieving a greater mechanistic understanding of biological systems. The field also offers small molecules and tools that can be used to manipulate chemical and biological systems with unprecedented molecular precision. Given these basic and applied aspects, chemical biology has naturally resonated with fields that rely upon integrated chemical and biological insights. No field has been more affected than drug discovery.

This synergy was highlighted at the third *Nature Chemical Biology* symposium entitled "Chemical Biology in Drug Discovery" (http://www.nature.com/natureconferences/nchembio2009), held on 19–20 September 2009 at the Royal Sonesta Hotel in Cambridge, Massachusetts. The symposium was organized by Joanne Kotz (*Nature Chemical Biology*), Paul Workman (Cancer Research UK Centre for Cancer Therapeutics at The Institute of Cancer Research), Giulio Superti-Furga (Center for Molecular Medicine, Austrian Academy of Sciences) and Brian Shoichet (University of California, San Francisco). The two-day symposium, complete with autumnal views of the Charles River, featured four thematic sessions and a poster session that spurred lively discussion of how chemical biology is poised to transform the drug discovery process, both in academia and in the pharmaceutical industry.

In the opening address of the conference, Paul Workman explored the challenges facing the pharmaceutical industry and highlighted the many innovative approaches that chemical biologists have to offer. Inspired by the recent release of the digitally remastered oeuvre of the Beatles, Workman noted that many of the characteristics that engendered the success of the 'Fab Four'—"talent, technology and culture"—will similarly be critical elements for the future success of the pharmaceutical industry. In addition to these broader sociological themes, Workman highlighted several areas where chemical biology could lead to major advances in pharmaceutical science—themes that were elaborated on in the talks, posters and discussion that followed: identifying and expanding druggable targets, understanding 'chemical space' and developing integrated tool sets for drug discovery.

Because current drugs are directed at a small number of pharmacological targets, understanding 'target space' and expanding the 'druggable genome' are important priorities for sustaining drug discovery efforts and opening new therapeutic areas. Chemical biologists, especially those in academia, have opportunities to look beyond what is currently considered druggable toward less explored systems that are likely to yield new classes of 'chemically tractable' targets and novel types of therapeutic scaffolds. Robust validation of biological targets is also essential for the success of drug development and requires a mechanistic understanding of targets, their associated pathways and the full molecular impact of the molecules that are perturbing them. These challenges are familiar to chemical biologists, who excel at identifying the target(s) of small molecules within cells and who bring a mechanistic mindset to the analysis of pathways and compound specificity.

Charting and navigating 'chemical space'—the potential universe of chemical structures—presents a second important challenge. Current drugs and chemical probes occupy a tiny volume of presumed chemical space, so access to more diverse classes of chemical scaffolds will almost certainly be needed. Key steps will include defining chemical space more precisely and developing methods for guiding the choice of biologically active scaffolds and compounds within the chemical universe. In parallel, the vast majority of potential compounds in chemical space have never been synthesized, and approaches such as diversity-oriented synthesis, target-directed synthesis and metabolic engineering offer ways to explore chemical space more broadly. However, identifying the optimal intersections between chemical space and the parallel universe of target space remains a central challenge for lead identification. In light of these complexities, chemical biologists need to continue their efforts to develop new chemical scaffolds in uncharted chemical territory.

Chemical biology will unquestionably offer new technologies for drug discovery and will provide tools for drug development, including visualization, drug delivery and diagnostics approaches. The sophistication of these methods is evolving rapidly, which enables their application in biological systems of increasing complexity. However, as discussed throughout the conference, to be maximally effective, these molecular tools must be combined with systems-based approaches to provide a more complete view of the complex pathways involved in drug discovery efforts. Omic experiments provide a global snapshot of systems operating in context, and computational approaches for analyzing these experimental data sets are powerful tools for constructing models that can be probed further with molecular methods.

Though the symposium focused primarily on the ways that chemical biology will shape the science of drug discovery, it was clear that chemical biologists, who are equipped with a substantial toolbox of 'pathfinder compounds', chemical methods and other technologies, represent a new generation of talented interdisciplinary scientists who will bring fresh insights to the drug discovery culture. Pharmaceutical companies should make every effort to integrate chemical biology programs and scientists into their portfolios to promote innovation in chemical biology for drug discovery.

A primary aim of the *Nature Chemical Biology* symposium series has been to nucleate discussions among scientists who share common interests but approach these scientific areas from different perspectives or with divergent tools. We look forward to bringing together other groups at the frontiers of chemical biology, and we welcome suggestions for future symposium topics. ■