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Editorial overview: Toward smart medicines

Gonçalo J. L. Bernardes and Raphaël Rodriguez

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Gonçalo J.L. Bernardes
Department of Chemistry, The University of Cambridge, CB21EW Cambridge UK
Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Avenida Professor Egas Moniz, 1649-028, Lisboa, Portugal
e-mails: gb453@cam.ac.uk; gbernardes@medicina.ulisboa.pt

Gonçalo Bernardes is a Reader (associate professor) in chemical biology at the Department of Chemistry, University of Cambridge (UK). He is also the director of a pioneering research unit in chemical biology at the Instituto de Medicina Molecular (Lisbon, Portugal). After completing his DPhil in 2008 at the University of Oxford (UK); he undertook postdoctoral work at the Max-Planck Institute of Colloids and Interfaces (Germany) and at ETH Zürich (Switzerland). In addition, he worked as a group leader at Alfama Lda in Portugal. Gonçalo is the recipient of two European Research Council grants, including a starting grant and a proof-of-concept grant. He was also awarded the Harrison–Meldola Memorial Prize in 2016 and the MedChemComm Emerging Investigator Lectureship in 2018, both from the Royal Society of Chemistry. His research group interests focus on the use of chemical principles to tackle challenging biological problems for understanding and fighting cancer.

Chemical biology, a terminology coined early on in the mid-1940s in a correspondence from George Beadle to Linus Pauling, has been later defined as 'work in chemistry which is of biological interest — and to that work in biology in which the chemical approach is used to solve biological problems'. True to its roots, this issue illustrates the most recent advances in chemical biology spanning the many facets of this ever-growing field. Such advances include the invention of innovative therapeutic strategies, the understanding of the underlying mechanisms of these strategies, and the corresponding considerations in relevant biological contexts. Chemical biology contains powerful approaches to generate biologically active small molecules, to delineate how powerful tools can be used to probe and to manipulate cell biology providing the basis for therapeutic intervention, to create new chemistry-based methodologies for solving mechanisms of action, and to discuss particular biological contexts and models by which novel therapeutics can be evaluated and applied.

The science of 'molecular medicine' emerged in the late 1940s as a discipline seeking to identify fundamental molecular disease-causing errors and to develop the appropriate molecular intervention tools to correct these defects. Such a rich legacy has prompted the development of chemistry in a way that enables the systematic study of cell biology in an unbiased manner using biologically active small molecules, giving an extra dimension to chemical biology. Over the past decades, we have witnessed the prevalent role of small molecules in cell biology. Such contexts have raised the question of how to produce molecular regulators that can selectively act on each biochemical event effectively with spatial and temporal resolution — a rather challenging endeavor. To achieve this, this issue features long-lasting efforts toward generating structurally diverse and complex small molecules, some of which are inspired by natural products (Schreiber and Waldmann labs), to populate the biologically relevant chemical space. Then, we present recent examples of small molecules to alter or directly target protein–protein interactions in the context of chromatin biology, highlighting cases involving chromatin writers and readers (Margueron and Grandi labs). This is followed by a section on organometallic drugs and metal-based photodynamic therapies in the context of cancer research (Dyson and Gasser labs). Subsequently,

Raphaël Rodriguez
Chemical Biology of Cancer Laboratory, Institut Curie, CNRS, INSERM, PSL Université Paris, 75005 Paris, France
e-mail: raphael.rodriguez@curie.fr

Raphaël Rodriguez is a research director at the Centre National de la Recherche Scientifique (CNRS) and a senior principal investigator at Institut Curie where he holds the Marie Curie Chair of Chemical Biology. He was trained under the mentorship of Sirs Jack E. Baldwin and Shankar Balasubramanian at the University of Oxford and University of Cambridge, respectively. He is best known for his contribution to understanding the roles and regulation of iron homeostasis in cancer biology and for his development and use of small molecules to probe and manipulate biology. He is a recipient of a European Research Council consolidator grant, the Tetrahedron Young Investigator Award, the Lacassagne Prize from Collège de France, and the Charles Defforey Prize from Institut de France. He is a fellow of the Royal Society of Chemistry.

recent innovative chemical biology approaches based on chimeric molecules to target proteins for degradation and small-molecule mimics of RNA interference strategies are detailed (Winter and Disney labs). As if this was not enough to satisfy your curiosity and feed your insatiable appetite for novelty, methodologies to predict or identify functional biological targets and to characterize induced phenotypes are described (Bernardes, Castaldi and Rodriguez labs). Progress in design of de novo proteins for immunotherapy is discussed (Silva and Romano labs), which then leads to final contributions on the use of disease-relevant models, the targeting of specific tissues, and the manipulation of biological processes with small molecules (Superti-Furga and Castagner and Tate labs). With all of these impactful studies in mind, you will hopefully get a glimpse of the transformative impact of chemical biology on next-generation medicines.

Conflict of interest statement

The authors declare no conflict of interests.

Note added in Proof

The paper by Paola Grandi et al. will be published in the following issue. The Publisher apologises for any inconvenience.