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Guest Editorial

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This Highlight Issue of *Biological Chemistry* covers various aspects of today's drug discovery process at the interface between chemistry and biology, and provides an outlook on future research directions, methods and emerging trends. This collection of eight articles provides an overview of some of the diverse academic research interests in this field.

In recent decades, drug discovery has made tremendous progress thanks to innovative technologies and developments. Chemical biology research, including proteomics, imaging, small molecule probes and bioorthogonal chemical approaches, has certainly made a notable contribution to these positive developments. Chemical reactions to tag proteins in the complex environment of a cell are undoubtedly invaluable to drug discovery. Michael Taylor's review article describes recent advances in this field with particular emphasis on photochemical protein modifications (Taylor 2022). Paul Ebensperger and Claudia Jessen-Trefzer take up another interesting aspect of artificial protein chemistry. In their article "Artificial metalloenzymes in a nutshell" recent approaches to artificial metalloenzymes are discussed and their potential applications in biorthogonal chemistry with new-to-nature reactions and biocatalysis are presented (Ebensperger and Jessen-Trefzer 2022). Another example of selective chemistry in biological systems is the paper by Congzhen Shen and colleagues in this issue. In their short communication, the authors describe the development of fluorescent turn-on probes for precise thiol profiling in living cells and tissues, an important aspect in cancer diagnosis and therapy (Shen et al. 2022).

Novel platforms for the identification of new target proteins for pharmaceutical intervention and hit compounds that bind to proteins of interest are additional key aspects of Chemical Biology in the drug discovery process. In this context, Wang and coworkers describe a yeast three-hybrid system to identify the protein targets of small molecules, while addressing the challenge of compound uptake into yeast cells (Wang et al. 2022). Additionally, Rothweiler, Brennan and Huber review the potential of covalent fragment screening to identify hit compounds on the example of the ubiquitin system with important implications in manipulating cell homeostasis and targeted protein degradation (Rothweiler et al. 2022).

It is not only the development of new tools of the trade, but also a growing understanding of chemical processes in cells that is driving drug discovery. In their article on personalized cancer care, Anna Milton and David Konrad discuss the mechanisms underlying cancer progression and therapy resistance, focusing on the epithelial-mesenchymal transition and H_2O_2 signaling (Milton and Konrad 2022). Finally, two articles of the Highlight Issue address the important challenge of antibiotic development. In her article "Rational approaches towards inorganic and organometallic antibacterials" Janine Hess presents new research and ideas on inorganic and organometallic compounds as alternatives to classical antibiotics (Hess 2022). Furthermore, Deepti Sharan and Erin Carlson profile the selectivity of different β-lactams for individual members of the penicillin-binding protein family in *Streptococcus pneumoniae* and, in this way, lay the foundation for specifically studying individual members of this important antibiotic target family (Sharan and Carlson 2022).

Taken together, we hope that this Highlight Issue gives the interested reader a glimpse into the diverse applications of Chemical Biology in the drug discovery process and, in this way, helps to stimulate new developments in this exciting field of research.

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