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Conference Report

DMCCB Basel Symposium 2018: Novel Chemical Space and Tools for Chemical Biology, Medicinal and Agrochemistry, Basel, 14th May 2018

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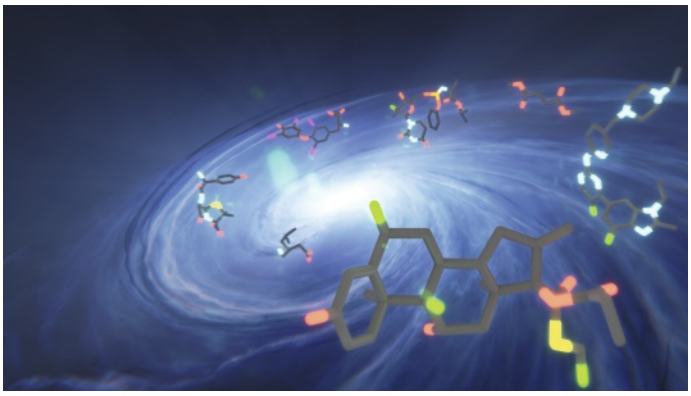

The 2018 DMCCB Basel symposium organized by the Swiss Chemical Society (SCS) focused on '*Novel Chemical Space and Tools for Chemical Biology, Medicinal and Agrochemistry*'. For the second time, the topic of the conference was selected by vote of the members of the medicinal chemistry and chemical biology division (DMCCB).

The conference opened with an enlightening lecture by ***Alleyn Plowright***, current Head of Integrated Drug Discovery at Sanofi Germany, titled '*Joining forces: application of Chemical Biology and Medicinal Chemistry to discover novel biological tools and utilise new therapeutic modalities*'. Sharing his experience in several major research projects, Plowright highlighted the importance of so-called 'new modalities' in drug discovery. These 'new modalities' include altered peptides which are used to address non-classical targets such as protein–protein interactions (PPIs). By introducing the example of a novel Melanocortin Receptor Agonist, he reminded the audience of the importance of factors such as chemical stability and cell permeability and the need to consider these aspects as early as possible in a drug discovery project.[1]

The second inspiring presentation, tackling the subject of structure-based drug discovery for GPCR targets, was given by ***Miles Congreve***, head of Drug Discovery and Senior Vice President of Heptares. GPCRs are an important class of drug targets with 116 drugs developed for 43 different GPCR targets in the past 20 years. However, for many years their intrinsic requirement for the membrane environment made the acquisition of their crystal structures notoriously difficult. The exciting recent developments in structural biology methods, such as the cryo-electron microscopy, made it possible to access several crystal structures of different GPCRs that previously resisted elucidation. Through different compelling examples, Congreve convincingly demonstrated the power of structure-based drug design (SBDD) and the use of new crystal structures of GPCRs co-crystalized with allosteric modulators to produce vastly improved drug candidates.[2]

Following the coffee break, the symposium continued with speakers from academia. ***Gisbert Schneider*** from ETH Zurich presented his vision of virtual drug design and new exciting ways to improve research efficiency by automation. In the first part of the presentation, Schneider introduced innovative chemoinformatics methods among which TIGER (Target Inference GEneratoR), which uses several self-organizing feature maps (SOMs) and machine learning to predict targets for a given active compound. The efficiency of the method was substantiated with different real-world examples as proof of concept. Going a step further, the second part of the presentation was dedicated to a new and impressive method for generation of *de novo* simple synthetic mimetics of complex natural products which still retain the biological activity using the software tool DOGS (Design of Genuine Structures). Beyond doubt, these methods and others alike will soon be part of every good drug discovery workflow.[3]

It is a well-known fact that RNA interference (RNAi) strategies are severely limited by the infamously poor bioavailability of oligonucleotides, including the therapeutically required siRNA. It is perhaps less known that this statement, which broadly applies to humans, does not necessarily apply to other species. In fact, as the audience could learn from the illuminating lecture by ***Jozef Vanden Broeck*** from University of Leuwen, some insect species are particularly prone to RNA interference. By comparing PK/PD data in different insect species, Vanden Broeck made a compelling case for the use of RNAi in insects as a method for pest control. He also introduced methods for mitigating poor oral bioavailability *in insecto* for the more refractory species. Elegantly, these methods rely themselves on RNAi.[4]

The symposium ended with the stimulating talk of ***David Spring*** from the University of Cambridge on drugging undruggable targets in the field of the notoriously challenging protein–protein interactions. Modulating PPIs has the potential to extend the range of druggable proteins and are therefore of particular interest in medicinal chemistry. Expanding on stapled peptides, Spring presented outstanding progress towards harnessing the promises of mastering PPIs for therapeutic applications. He also discussed the importance of using the right linker and showed that, under the right conditions, a very diverse range of peptide conformations can be stabilized opening the door to a wealth of new possible targets.[5]

Thanks to the excellent speakers and the high level and diversity of science presented, the 2018 DMCCB Basel symposium was a great success and met its goal of not only educating but inspiring the audience. The chemical space is expanding, and new tools are coming to exploit its full potential. These are truly exciting times for medicinal chemistry and chemical biology. The next DMCCB Basel Symposium will take place in early 2020. DMCCB members will be asked for input on possible topics for this symposium, watch out for polls on the DMCCB social media portals.

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