Integrating Chemical and Biological Data for Drug Design and Mode-of-Action Analysis

Andreas Bender

University of Cambridge, UK

More and more chemical and biological information is becoming available, both in public databases as well as in company repositories. However, how to make use of this information in chemical biology and drug discovery settings is much less clear. In this work, we will discuss how chemical and biological information from different domains – such as compound bioactivity data, pathway annotations from the bioinformatics domain, and gene expression data – can be used for a variety of purposes, such as the mode-of-action analysis from phenotypic readouts,[1,2] anticipating compound toxicities in early discovery, and for designing and selecting compound with the desired bioactivities.[3,4] We will show that cheminformatics algorithms trained on large chemogenomics databases can be employed to support target deconvolution in high-content screening as well as organism-based screens using e.g. Xenopus laevis[2] as well as phenotypic data obtained from rat models. When anticipating compound adverse compound properties early on, we will show than gene expression data can be used for this purpose; however, how to generate and analyze data is very much case-dependent. Relating to compound design and selection, we can employ both bioactivity-driven approaches as well as gene expression based resources, and examples of both will be presented. Hence, overall, while the chemical and biological data available currently is very diverse, we are able to show that it can already be used successfully for understanding the mode of action of compounds, anticipating their toxicities early on in discovery, and designing and selecting novel chemical matter to modulate biology.

1. Koutsoukas A, Simms B, Kirchmair J, Bond PJ, Whitmore AV, Zimmer S, Young MP, Jenkins JL, Glick M, Glen RC, Bender A: J. Proteomics 2011, 74(12): 2554-2574.

2. Liggi S, Drakakis G, Hendry AE, Hanson KM, Brewerton SC, Wheeler GN, Bodkin MJ, Evans DA, Bender A: Mol. Inf. 2013, 32(11-12): 1009-1025.

3. Van Westen GJP, Wegner JK, IJzerman AP, van Vlijmen HWT, Bender A: MedChemComm 2011, 2(16): 16-30.

4. Van Westen GJP, Hendriks A, Wegner JK, IJzerman AP, van Vlijmen HWT, Bender A: PLoS Comp. Biol. 2013, 9(2): e1002899.