Celerino Abad-Zapatero, Med chem (Los Angeles) 2018, Volume 8
DOI: 10.4172/2161-0444-C1-038

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Are SAR tables obsolete?

The listing of the structures of compounds possessing biological activity (expressed as K_i, IC_{50} primarily) (structure-activity tables, SAR tables) for any drug discovery project is the core of any publication accross the medicinal chemistry scientific literature. It has been the standard way of reporting the progress of pharmaceutical discovery since the historical work of Erlich and coworkers in the early 1900'S. This summary was particularly important when the main variable driving drug discovery was potency. Nowadays, drug discovery teams have to examine a large number of variables simultaneously and pay a very close atention to the physico-chemical properties (primarly size, polarity/hydrophobicity) of the chemical entities being pursued. Presenting and summarizing all this information in an effective manner is of the utmost importance. 'Alternative variables combining the affinity of the ligands with relevant physico-chemical properties of the compounds have been introduced in various ways in the literature and are being cited in the literature, particularly as ligand efficiency indices. Controversy over the usage and utility of these variables to drive drug discovery is still prevalent in the community. The presentation will discuss certain formulations of 'Ligand Efficiency Indices' that permit the complete mapping of chemico-biological space (CBS) in efficiency planes (AltasCBS: https://www.ebi.ac.uk/chembl/atlascbs/), which allows a direct two-dimensional representation of the information presented in the SAR tables in a graphic manner. The proposed representation permits an easy and effective understanding of the multiparameter optimization variables involved, and intuitvely suggest the most efficient strategies to optimize the drug-like properties of the compounds.

Biography

Celerino Abad-Zapatero has completed his PhD as a Molecular Crystallographer at University of Texas at Austin and completed Postdoctoral work on virus and protein crystallography with Prof. M.G. Rossmann at Purdue University in the mid 1980s, solving the structure of the first icosahedral viruses. He worked for over 22 years at Abbott Laboratories employing and developing the tools of macromolecular crystallography for Structure-Based Drug Design (SBDD). His research is focused on the use of alternative variables, in particular ligand efficiency indices to optimize SBDD.

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