

Finding and Applying Multi-Parameter Rules to Guide Successful Drug Discovery

Written by Matt Segall

Monday, 24 March 2014 15:25 - Last Updated Wednesday, 30 August 2017 15:59

Matt Segall gave this presentation at the International Symposium on Compound Design Technologies held in Tokyo and Osaka, Japan on 19 and 20 March 2014.

Abstract

A high quality drug must exhibit a balance of many properties, including potency, ADME and safety. These are often expressed as property 'rules' that a compound must meet in order to progress. Applying these rules effectively in drug discovery is challenging due to the complex, often conflicting property requirements they reflect, combined with uncertain data because of experimental variability or predictive error. We will discuss how methods known as multi-parameter optimization (MPO) [1] are currently being applied to quickly target compounds with the best chance of success, while avoiding missed opportunities.

But, how do we know what the appropriate profile of property criteria might be to efficiently identify successful leads and candidate compounds for a specific project? The property criteria will depend on the ultimate goal of the project, e.g. therapeutic indication and route of administration, and are typically chosen based on the subjective opinion of the project team. However, analysis of historical data can help to guide the determination of the most appropriate profile, which can then be used prospectively to prioritise new compounds. We will describe how new methods, known as rule induction [2], can guide this process to identify multi-parameter rules that distinguish successful compounds for a chosen objective. The resulting rules are interpretable and modifiable, allowing experts to understand and adjust them based on their knowledge of the underlying biology and chemistry. Furthermore, the importance of each criterion can be identified, allowing the most important data to be prioritized to make effective compound prioritization decisions.

References: [1] M.D. Segall. Multi-Parameter Optimization: Identifying high quality compounds with a balance of properties. *Curr. Pharm. Des.* (2012) 18(9) pp. 1292-1310; [2] I. Yusof, F. Shah, N. Greene and M.S. Segall. Finding the Rules for Successful Drug Optimization. *Drug. Discov. Today* (2014) (in press).

You can download this presentation as a [PDF](#).