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Discovery of bRo5 Drugs: Lessons from the Past and Progress toward Better Prediction of Oral Absorption

Abstract

Orally bioavailable beyond the rule of five (bRo5) drug space is potentially vast with great importance for targets not amenable to drugging with conventional small molecules in the areas of virology, oncology, disruption of protein-protein interactions and protein degradation, among others. Understanding their oral absorption is important for preparing for yet to be discovered uses for bRo5 drugs. Prediction of which bRo5 compounds can be absorbed orally remains challenging, resulting in a high reliance on in vivo testing and an inefficient triage of chemical series to identify the most promising ones. AbbVie has a rich bRo5 dataset for retrospective analysis of bRo5 successes and failures that when taken together with human absorption data can shed new light on physicochemical property descriptors and assays that might be part of a more effective drug discovery toolbox for medicinal chemists. Aspects of our ongoing research will be described.

Bio

David DeGoey is a Senior Research Fellow at AbbVie. He received a B.S. degree in Chemistry from the University of Wisconsin Madison and earned a Ph.D. in Chemistry from Harvard University. He joined Abbott (now AbbVie) in 1995 where he has spent a large portion of his career in infectious diseases research working on the discovery of drugs in beyond rule of five chemical space to treat fungal, bacterial, and viral diseases, including HIV and hepatitis C. He co-led the medicinal chemistry team that discovered AbbVie's HCV NS5A inhibitors that are now approved for use in combination with other direct acting antivirals. He is currently part of the Centralized Medicinal Chemistry team at AbbVie, where he is responsible for lead optimization for projects across therapeutic areas.