

Lipinski's rule-of-five analysis

Christopher Lipinski's rule-of-five analysis helped to raise awareness about properties and structural features that make molecules more or less drug-like. The guidelines were quickly adopted by the pharmaceutical industry as it helped apply ADME considerations early in preclinical development and could help avoid costly late-stage preclinical and clinical failures. The guidelines predict that poor absorption or permeation of a orally administered compound are more likely if the compound meets the following criteria:

- Molecular mass greater than 500 Da
- High lipophilicity (expressed as cLogP greater than 5)
- More than 5 hydrogen bond donors
- More than 10 hydrogen bond acceptors

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Dr. Chris Lipinski (TB Alliance) Honored by American Chemical Society for Rule of Five

Dr. Christopher Lipinski, member of the TB Alliance Scientific Advisory Committee and a retired Senior Research Fellow at Pfizer Global R&D Groton New London labs, has been honored for his groundbreaking "Rule of Five" by the American Chemical Society. On August 23rd, the ACS announced that Dr. Lipinski is the recipient of the 2005 E.B. Hershberg Award for Important Discoveries in Medicinally Active Substances.

Since its publication in 1997, The Lipinski rule of five has been a critical filter for drug development programs. A simple algorithm that helps identify successful drug candidates, the principles filter out molecules likely to have poor intestinal permeability or poor aqueous solubility, and hence poor oral absorption. This landmark contribution to drug development has influenced the way that the pharmaceutical industry approaches the development of orally active drugs. Drug discovery programs worldwide use the Rule as a filter in high-throughput screening libraries and the TB Alliance is applying Dr. Lipinski's Rule to its go/no-go decision-making process for its projects in the nitroimidazopyran and quinolone classes.

About Dr. Lipinski:

Dr. Lipinski joined Pfizer in 1970 supervising medicinal chemistry laboratories, discovering multiple gastrointestinal and diabetic clinical candidates. Since 1984, he has been an adjunct faculty member at Connecticut College in New London, Connecticut. Over the course of his distinguished career he has authored over 190 publications and invited presentations and has 17 issued US patents.

In 1990, he established a laboratory combining computations and experimental physical-property measurements and since 2001 has been a member of the Scientific Advisory

Committee of the TB Alliance, helping to guide the research and development of novel TB drugs. Dr. Lipinski obtained his Ph.D. from the University of California, Berkeley, and did his postdoctoral training at Caltech, supported by the National Institute of General Medical Sciences.

About the TB Alliance Scientific Advisory Committee:

The TB Alliance Scientific Advisory Committee was established to assist in evaluating proposals and projects under consideration for investment as part of its TB drugs portfolio. The Scientific Advisory Committee provides technical expertise on drug research, development, manufacturing, and distribution, as well as other medical and scientific issues.

The E.B. Hershberg Award for Important Discoveries in Medicinally Active Substances is sponsored by Schering-Plough Corp.

The Global Alliance for TB Drug Development is a public-private partnership driven to halt the rise and reverse the spread of the world's oldest infectious disease by developing new, faster-acting and affordable tuberculosis medicines.

(Source: TB Alliance website, <http://www.tballiance.org>)