BioNanoScience 2016 vol.6 N4, pages 464-472

Generative Topographic Mapping Approach to Modeling and Chemical Space Visualization of Human Intestinal Transporters

Gimadiev T., Madzhidov T., Marcou G., Varnek A.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2016, Springer Science+Business Media New York.The generative topographic mapping (GTM) approach has been used both to build predictive models linking chemical structure of molecules and their ability to bind some membrane transport proteins (transporters) and to visualize a chemical space of transporters' binders on two-dimensional maps. For this purpose, experimental data on 2958 molecules active against up to 11 transporters have been used. It has been shown that GTM-based classification (active/inactive) models display reasonable predictive performance, comparable with that of such popular machine-learning methods as Random Forest, SVM, or k-NN. Moreover, GTM offers its own models applicability domain definition which may significantly improve the models performance. GTM maps themselves represent an interesting tool of the chemical space analysis of the transporters' ligands. Thus, with the help of class landscapes, they identify distinct zones populated by active or inactive molecules with respect to a given transporter. As demonstrated in this paper, the superposition of class landscapes describing different activities delineates the areas mostly populated by the compounds of desired pharmacological profile.

http://dx.doi.org/10.1007/s12668-016-0246-5

Keywords

Cellular membrane transport proteins, Generative topographic mapping, Inhibition, Structure-activity models, Transport