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QSAR modeling and chemical space analysis of antimalarial compounds

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Abstract

© 2017, Springer International Publishing Switzerland.Generative topographic mapping (GTM) has been used to visualize and analyze the chemical space of antimalarial compounds as well as to build predictive models linking structure of molecules with their antimalarial activity. For this, a database, including ~3000 molecules tested in one or several of 17 anti-Plasmodium activity assessment protocols, has been compiled by assembling experimental data from in-house and ChEMBL databases. GTM classification models built on subsets corresponding to individual bioassays perform similarly to the earlier reported SVM models. Zones preferentially populated by active and inactive molecules, respectively, clearly emerge in the class landscapes supported by the GTM model. Their analysis resulted in identification of privileged structural motifs of potential antimalarial compounds. Projection of marketed antimalarial drugs on this map allowed us to delineate several areas in the chemical space corresponding to different mechanisms of antimalarial activity. This helped us to make a suggestion about the mode of action of the molecules populating these zones.

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Keywords

Antimalarial compounds, Chemical space, Generative topographic mapping (GTM), Mode of action, Quantitative structure–activity relationships (QSAR)

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