

POSTER PRESENTATION

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Activity-difference maps and consensus similarity measure characterize structure-activity relationships

José L Medina-Franco^{1*}, Austin B Yongye¹, Jaime Pérez-Villanueva², Richard A Houghten¹, Karina Martínez-Mayorga¹

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Dual and triple activity-difference (DAD/TAD) maps are two- and three- dimensional representations of the pairwise activity differences of compound data sets, respectively [1]. These maps are valuable tools for the systematic characterization of structure-activity relationships (SAR) of compounds data sets screened against two or three targets [2]. Adding pairwise structural similarity information into the DAD/TAD maps readily reveals *activity cliff* [3] regions in the SAR for one, two or the three targets. In addition, pairs of compounds in the smooth regions of the SAR and scaffold hops are also easily identified in these maps. Herein, we describe DAD and TAD maps for the systematic characterization of the SAR of data sets screened against three molecular targets. Several 2D and 3D structure representations were used to characterize the SAR in order to reduce the well-known dependence of the activity landscape on the structural representation [4,5]. Systematic analysis of the DAD and TAD maps reveals regions in the landscape with similar SAR for two or the three targets as well as regions with inverse SAR, i.e., changes in structure that increase activity for one target, but decrease activity for the other target. Focusing the analysis on pairs of compounds with high structure similarity revealed the presence of single-, dual- and triple-target activity cliffs, i.e., small changes in structure with high changes in potency for one, two or the three targets, respectively. Triple-target scaffold hops are also discussed.

Author details

¹Torrey Pines Institute for Molecular Studies, Port St. Lucie, Florida, 34987, USA. ²Department of Biological Systems, UAM-X, Mexico City, 04960, Mexico.

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* Correspondence: jmedina@tpims.org

¹Torrey Pines Institute for Molecular Studies, Port St. Lucie, Florida, 34987, USA

Full list of author information is available at the end of the article