GLOBAL SKIN HEALTH

MULTI-DIMENSIONAL COMPUTATIONAL PIPELINE FOR LARGE-SCALE DEEP SCREENING OF COMPOUND EFFECT ASSESSMENT: AN IN SILICO CASE STUDY ON CELL VITALITY-RELATED COMPOUNDS"

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In this study, we present a novel state-of-the-art computational pipeline for large-scale assessment of chemical compounds based on multiple dimensions – compound structural similarity, binding profiles and their network effects across pathways and molecular interaction maps. While both structure-based and docking-score based approaches are well suited for compound profiling, they are less robust in identifying holistic effect of the compounds over biological pathways. On the contrary, our pipeline demonstrates the effectiveness of incorporating the protein-protein interaction properties with docking profile towards generating testable hypotheses on the pharmacological landscapes as well as novel mechanisms of efficacy of compounds on phenomenological processes.

Further, we elucidate the application of the pipeline on a screen of cell vitality related compounds to cluster the candidates based on their structure, docking profile and network effects on molecular pathways associated with the vitality phenomenon, highlighting emergent insights on compounds' activities based on the multi-dimensional deep screen pipeline.

The major achievements of our work:
1. Construction of a deep-curated, literature-driven molecular-level, mechanistic map for vitality related pathways.
2. Application of the multi-dimension methodology on the classification and clustering of compounds in three dimensions- structure-similarity, binding profile, and network effect.
3. Comparative analysis of the clustering dimensions revealed the ability of the network-guided pipeline to identify novel cluster of compounds which differ in structure or binding profile, but may potential have similar effect signature at the network level (Rapamycin and Vitamin C for example).