C-2-04

Understanding polypharmacology and promiscuous chemotypes on LSKB

Atsushi Midorikawa midorikawa@w-fusion.co.jp,
Tetsuya Takasaki takasaki@w-fusion.co.jp,
Toshiro Kimura kimura@w-fusion.co.jp
Kozo Kawahara kkawahara@w-fusion.co.jp

World Fusion Co., Ltd., 2-15-15 Nihonbashi Ningyocho, Chuo-ku, Tokyo 103-0013, Japan

Keywords: knowledge, Open Data Source, Polypharmacology, Molecular Framework, Workflow

Toward disease related target, it is important to classify the drug target(genes/proteins) based on its function, and the subtype has often different ligand recognition.
Knowledge of SAR and related studies is used for recognition of ligand structures ; In many cases, we try to find common core and/or scaffold from the analysis and use the information.
Bajorath et al., reported promiscuous chemotypes by analysis of polypharmacology between drugs and targets, using the chemical structures, scaffolds and molecular frameworks[3]. And also a series of compounds, which have common scaffold, is specific toward a target class in same case and they describe the benefit of activity cliffs for the understanding SAR[1,2].

In the poster, Life Science Knowledge Bank(LSKB)[4] is well-organized database system storing the binary relationship each combination of the terms (Gene/Protein/Disease/Tissue/chemical) mined from Medline and extracted information from various Open Data Sources. And the well-organized compound structure database is also available in LSKB; the chemical contents is built as non-redundant (NR)chemical structures from PubChem[5], ChEMBL[6], ZINC[7] and ligand structures collection taken from PDB protein-ligand complexes (where the information extracted from PDB[8]). And it associates LSKB knowledge dataset. In LSKB version 4.2, compound databases stores 70M NR compounds and, molecular frameworks associated with each compounds.
The latest release provides protein classification i.e., EC number, GPCR, Kinase. and registration function of interest gene set in private experimental data. We show you the benefit of combination, LSKB and workflow tool Pipeline Pilot[9] by several instances for understanding polypharmacology and SAR Matrix generation.

[1] Hu, Y. and Bajorath,J., *Polypharmacology Directed Compound Data Mining: Identification of Promiscuous Chemotypes with Different Activity Profiles and Comparison to Approved Drugs*, J. Chem. Inf. Model. 2010, 50, 2112?2118
[2] Hu, Y. and Bajorath,J., *Molecular Scaffolds with High Propensity to Form Multi-Target Activity Cliffs*, J. Chem. Inf. Model. 2010, 50, 500-510
[3] Bemis, G.W. and Murcko,M. A., *The Properties of Known Drugs. 1. Molecular Frameworks*, J. Med. Chem. 1996, 39, 2887-2893
[4] World Fusion Co., Ltd., 2-15-15 Nihonbashi Ningyocho, Chuo-ku, Tokyo 103-0013, Japan
[5] http://pubchem.ncbi.nlm.nih.gov/
[6] https://www.ebi.ac.uk/chembldb/
[7] http://zinc.docking.org/
[8] http://www.rcsb.org/pdb/home/home.do
[9] Accelrys, 10188 Telesis Court, San Diego CA 92121, USA