ALY 6080: Integrated Experiential Learning

Annotated Bibliography III

Submitted to

Bryce Allen

Submitted by

Md Tajrianul Islam

Date: Oct 10, 2020

Annotated Bibliography III

I. Summary

This is a summary of a peer reviewed paper about the polypharmacology browser: a web-based multi-fingerprint target prediction tool using ChEMBL bioactivity data. This paper will be helpful to understand the different processes we can follow in order to recommend a drug like small molecule that Silicon Therapeutics can allocate their resources to.

Many computational tools have been developed that exploit databases containing detailed structural information on the activity of small molecule drugs and their protein targets to predict the polypharmacology of any hit compound or drug candidate. A few online web-based tools have been accounted for as of late which foresee the potential focuses of a little particle by comparability to mixes of realized bioactivity utilizing atomic fingerprints (fps), anyway expectations for each situation depend on likenesses registered from just a couple of fps. Taking into account that auxiliary similitude and in this way the anticipated targets emphatically rely upon the technique utilized for correlation, it would be exceptionally alluring to foresee targets utilizing a more extensive arrangement of fps all the while.

Ligand-based methods using fp comparisons are particularly versatile because they are applicable to any biological activity. Although a portion of these ligand based instruments offer a choice of various fps, none of them allows the synchronous utilization of more than one fp. Considering the way that sub-atomic likeness and accordingly the anticipated targets unequivocally rely upon which fp is utilized for examination, it would be exceptionally alluring to foresee targets utilizing various fps at the same time, given that each fp would perform well exclusively in virtual screening and target forecast experiments. So their browser searches through 2.7 M ligand-target interactions extracted from ChEMBL 21 and generates a list of predicted targets, each linked to the lists of known actives used for the prediction. They analyzed ChEMBL

21 and constructed the target database containing 4613 groups of at least 10 bioactive molecules with documented activity against the same biological target. Briefly, target database was constructed as follows: initially all targets along with their ligands were retrieved from the ChEMBL version 21. For each target we retained the compounds having IC50, EC50, GI50, K i, K D, or potency value of ⩽10 μM or percent inhibition of >50%. All molecules were processed as non-stereo SMILES and ionized at pH 7.4 using an in-house developed Java program utilizing the JChem chemistry library from ChemAxon Pvt. Ltd. Finally, targets with at least 10 bioactive compounds were retained in database. They then performed enrichment studies of ligands against decoys in the directory of useful decoys and evaluated the average performance of 57 different combinations of the scaled fingerprints in terms of area under the curve (AUC) and enrichment factor at 1% screening in the receiver operator characteristic (ROC) curves (data not shown). We selected the four fusion fingerprints Ffp1–Ffp4 due to their good performance in this enrichment study and computed the corresponding Ffp1–4 values for the 871,673 ChEMBL compounds.

II. References

1. https://jcheminf.biomedcentral.com/articles/10.1186/s13321-017-0199-x