**LSP-OptimalKinase library**

The LSP\_OptimalKinase library is a collection of kinase inhibitors in the public domain that were selected based on criteria described in Moret et al. (2019)[link to <https://www.cell.com/cell-chemical-biology/fulltext/S2451-9456(19)30073-X#secsectitle0010>

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| Figure 1 – Illustration of the compound selection procedure for a query target “BRAF” based on selectivity score and clinical phase. In this case, all compounds shown belong to tier A as they either have MS selectivity or are clinically approved drugs. |

]. The library was developed with the aim to have a pair of inhibitors for each kinase with the members of the pair structurally distinct but similar in selectivity for the intended kinase, along with all approved drugs or clinical candidates that show affinity for said particular kinase (**Figure 1**). Being structurally distinct has the advantage that the inhibitors are the most likely to have orthogonal target affinity spectra (TAS) and phenotypic fingerprint (PFP). To assess whether two compounds are similar in selectivity, we discretized the selectivity of compounds into four qualitative levels; most selective (MS), semi selective (SS), poly selective (PS) and unknown (UN).

The library is dividable into different tiers: Tier A is the minimal library and contains only those compounds (1) binding the specified list of genes with MS selectivity and (2) FDA-approved drugs binding more strongly than the affinity cutoff (which did not result in library redundancy). Tier B adds compounds with SS selectivity that target genes not covered by MS selectivity plus all compounds that bind the genes of interest and are in clinical development (clinical phases I–III). Tier C adds compounds from PS and UN specificity classes to maximally cover the user-specified list.

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| Figure 2 - Number of kinases inhibited at a specified selectivity class based for the LSP-OptimalKinase library. The highest selectivity achieved for each of the 545 human kinases is shown. | Figure 3 - Clinical grade compounds in the LSP-Optimal Kinase library by tier. |