**SUPPLEMENTARY TABLES**

**Supplementary Table 1. Similarity Matrices of the DNF and single-layer taxonomies (based on the CTRPv2 drug sensitivity dataset). (A)** Similarity Matrix of the fused DNF taxonomy (**B)** Similarity Matrix of the Perturbation layer **(C)** Similarity Matrix of the Sensitivity layer (**D)** Similarity Matrix of the Structure layer. **(and based on the NCI60 drug sensitivity dataset). (E)** Similarity Matrix of the fused DNF taxonomy (**F)** Similarity Matrix of the Perturbation layer **(G)** Similarity Matrix of the Sensitivity layer (**H)** Similarity Matrix of the Structure layer.

**Supplementary Table 2**. **Statistical comparison of the DNF taxonomy against single datasets taxonomies, using one-sided superiority tests.** Comparisons were conducted for both DNFs generated using the CTRPv2 or the NCI60 datasets. Reported scores pertain to comparisons conducted using both drug benchmarks (Drug-target information as well as ATC).

**Supplementary Table 3. Drug communities identified from the DNF taxonomies.** **(A)** List of identified communities using the community detection algorithm against the DNF generated using CTRPv2. Exemplar drugs for each community are identified, along with the number of drugs in that community. The list of drugs pertaining to each community is indicated. Drug populations are coloured to indicate communities that have at least 2 drugs with a known mechanism of action (total 139 drugs for CTRPv2, green), and those communities where drugs are unlabeled or unclassified (orange). **(B)** Refined list of identified communities generated using CTRPv2, comprising communities that have at least two drugs with a known mechanism of action. Exemplar drugs for each community are identified, along with the number of drugs in that community. The list of drugs pertaining to each community is indicated. **(C)** Summary of Functional Drug Classes Identified Using DNF. **(D)** Summary of communities generated from CTRPv2/L1000 integrative layers showing positive controls cases with at least 2 drugs sharing a mechanism of action from the same community. **(E)** List of identified communities using the community detection algorithm against the DNF generated using NCI60. Exemplar drugs for each community are identified, along with the number of drugs in that community. The list of drugs pertaining to each community is indicated. Drug populations are coloured to indicate communities that have at least 2 drugs with a known mechanism of action, and those communities where drugs are unlabeled or unclassified (orange). **(F)** Refined list of identified communities using the community detection algorithm generated using NCI60, selected for communities that have at least two drugs with a known mechanism of action. Exemplar drugs for each community are identified, along with the number of drugs in that community. The list of drugs pertaining to each community is indicated.

**Supplementary Table 4. Enrichment of DNF drug communities.** List of enrichments of drug communities from DNF generated using CTRPv2 sensitivity against drug target **(A)** and ATC classes **(B)** and generated using NCI60 sensitivity against drug target **(C)** and ATC classes **(D).**

**Supplementary Table 5. Comparison of predictive value of DNF versus published methods. (A)** Similarity matrix used in benchmarking of SuperPred (based on the CTRPv2 drug sensitivity dataset). **(B)** Similarity matrix used in benchmarking of SuperPred (based on the NCI60 drug sensitivity dataset). **(C)** Similarity matrix used in benchmarking of the Iskar algorithm. **(D)** Similarity matrix used in benchmarking of the Iorio algorithm. **(E)** Similarity matrix used in benchmarking of the Drug E-Rank algorithm (CTRPv2). **(F)** Similarity matrix used in benchmarking of the Drug E-Rank algorithm (NCI60).