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The IUPHAR/BPS Guide to PHARMACOLOGY as an *in silico* resource for drug:target interactions to improve pre-clinical experimental design

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Introduction: Imperfect experimental design has been suggested to be a major source of variation in preclinical studies (1). A number of beneficial strategies for good experimental design were recently described in the British Journal of Pharmacology in 2015 (2). Good experimental design involves careful planning, not least in the correct choice of compounds and appropriate concentrations/doses. The International Union of Basic and Clinical Pharmacology (IUPHAR)/British Pharmacological Society (BPS) database, GuidetoPHARMACOLOGY.org (3) provides expert-annotated molecular interactions between endogenous receptor ligands, research compounds, drugs in current clinical use and their molecular targets.

Methods: GtoPdb is populated by records curated from pharmacology and medicinal chemistry journals (4). Updates are released quarterly, with ligands refreshed as PubChem updates. Quality is ensured, not only by molecular mappings curated at high stringency but also by our unique model of content selection proposed by ~90 NC-IUPHAR target class subcommittees of international experts collaborating with the in-house curators.

Results: The database has now accumulated over 14 000 quantitative datapoints (mainly IC_{50}, K_i or K_d values) between ~9000 ligands and 1500 human proteins (extending to 2000 including rodent species). This includes a proportion of unique content; of 6565 structures we submit to PubChem, 5206 are not in DrugBank and 1535 not in ChEMBL. In addition we have curated ligand binding interactions for ~70 human proteins that are neither in DrugBank nor ChEMBL. As an *in silico* resource, GtoPdb has a number of features that will assist experimental design:1) Coverage is small enough to be navigable but large enough (~9000 compounds) to cover clinical and experimental drugs 2) Translational aspects: a focus on human data, but with information from mouse and rat3) Curated lists of recommended tool compounds 4) Primary transduction mechanisms, expression data in model organisms and consequences of altering gene expression 5) Via the PubChem CID cross-references, over 75% of the small molecules have vendor links

Conclusion: The GuidetoPHARMACOLOGY database represents, therefore, an ideal first-stop shop for pharmacologists and other researchers to identify and plan to use compounds in their experiments, which in turn should allow an improved reproducibility.

References

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4 Southan C *et al*. (2016) *Nucleic Acids Res* 44**:** D1054-D1068