PPARγ AGONISTS DATASET version 1: INFORMATION REGARDING THE DATASET AND METHODOLOGY FOR ITS DEVELOPMENT

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1 Dataset content (field descriptions*)

1.1 2D connection table of the ligand named by its InChi key.

1.2 SMILES code of the ligands(Open Babel v. 2.3.2 generated "inchified" SMILES).

1.3 IUPAC names of the ligands.

1.4 Trivial name of the ligand (where present in the sources).

1.5 PDB complex and ligand codes (for the complexes deposited in Protein Data Bank by the cited authors).

1.6 PDB code of the ligand found in Protein Data Bank (even if no complex(es) are deposited in Protein Data Bank by the cited authors).

1.7 Ligand name / notation in the data source.

1.8 Data source.

1.9 Binding affinity data (IC50), error, comments.

1.10 Transactivation activity data (EC50), error, comments.

1.11 Relative transactivation efficacy (% max), error, comments.

1.12 Reference compound used in the relative transactivation efficacy calculation.

1.13 Species and cell line used in the activity/efficacy determination.

1.14 Assay names.

1.15 Training/test set assignment for the compounds used in 3D QSAR modelling [Al Sharif et al., Application of molecular modelling in the Adverse Outcome Pathway framework: case study on ligand-dependent PPARγ dysregulation, 2015, in preparation]**.

2 Methodology details

2.1 Data collection: 452 structures from 32 papers were harvested; 18 of the sources deposited a single structure in Protein Data Bank (PDB), 2 – two structures, 1 – three structures, and 11 – no structure. These structures represent 439 different PPARγ ligands. Among them 5 are standards for full PPARγ agonists and there is more than one reported experimental measurement (rosiglitazone – 8; pioglitazone – 4; farglitazar – 2; ragaglitazar – 2; tesaglitazar – 2).

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* A dummy row was inserted in the beginning of the sdf file to ensure the correct field order and type in any opening software.

** Since the protonation states of the modelled ligands differ from that of the neutral forms presented in this dataset, for some structures two protonation states were shown to coexist and were considered as different ligands in the modelling study.

2.1.1 Ligands with correct IUPAC names available in the literature source (183): SMILES were generated through NCI/CADD SIR (http://cactus.nci.nih.gov) or University of Cambridge OPSIN (http://opsin.ch.cam.ac.uk) services.

2.1.2 Ligands without IUPAC names available in the source (231): SMILES codes were generated from similar structures that were modified accordingly; IUPAC names were obtained through ChemAxon's chemicalize.org service (http://www.chemicalize.org).

2.1.3 Ligands with available but incorrect/unresolvable IUPAC names (8) were processed according to 2.1.2.

2.1.4 Ligands with the PPARγ complexes deposited in PDB (27): ligand structures were extracted from the complexes, they were neutralized through the Wash procedure in MOE platform v. 2014.0901, (CCG Inc., http://www.chemcomp.com), and their stereochemistry was fixed where necessary.

2.2 Data refinement

2.2.1 All SMILES codes were converted to “inchified” SMILES by Openbabel 2.3.2 (http://openbabel.org, CLI parameters: -ismi -osmi -xl); InChi keys were generated and used as connection table names.

2.2.2 All binding affinity and transactivation activity data were converted to micromolar concentrations.

3 Data sources

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