

pdCSM-GPCR: predicting potent GPCR ligands

with graph-based signatures

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pdCSM-GPCR: In silico prediction of GPCR ligands

João Paulo L. Velloso, David B. Ascher & Douglas E. V. Pires

Abstract: The G protein coupled receptors superfamily is one of the most widely class of proteins screened for ligands. Despite the great effort directed towards the gpcr ligand discovery, many endogenous ligands still remain unknown (orphan receptors) and there are still leakage of safe and effective drug for many GPCR of medical interest. With recent advances in computational power, and machine learning algorithms, prediction of ligand affinity is getting more and more feasible. We take advantage of it to discover new ligands for GPCRs through assessment of ligand bioactivities. This can guide rational experimentation in finding and validating novel ligands for GPCRs.

Our approach is called pdCSM-GPCR, and relies on graph-based signatures. These encode distance patterns between atoms and are used to represent the small molecule and to train predictive models. Here we present a web server which provides a reliable and cost-free platform to rapidly screen ligands for GPCR.

Graph-based Signatures

Best Features

Auxiliary Features

Bioactivity

THE UNIVERSITY OF MELBOURNE Baker UFMG

Best viewed using Chrome on 1280x960 resolution and above

About pdCSM-GPCR

pdCSM-GPCR is a machine-learning platform to predict GPCR ligands, which relies on distance/pharmacophore patterns encoded as graph-based and auxiliary signatures. The platform is composed of 36 regression models, trained and tested on different experimental data sets encompassing a diverse and complementary set of GPCRs as follows:

- **Class A:** P08173, P08908, P08912, P0DMS8, P20309, P21452, P21917, P24530, P28335, P29275, P30542, P30968, P34995, P35346, P35348, P35372, P46663, P47900, P48039, P50406, P51677, Q8TDS4, Q8TDU6, Q96LB2, Q99500, Q99705, Q9H228, Q9HC97, Q9Y5N1, Q9Y5Y4;
- **Class B1:** P47871, Q16602;
- **Class C:** P41180, Q14416, Q14833;
- **Class F:** Q99835.

Submission page

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pdCSM-GPCR: In silico prediction of GPCR ligands

Please provide a set of molecules (SMILES format)

SMILES file (limited to 1000 molecules) 2 No file selected.

OR

SMILES strings 3

Select type of prediction 4

How to run a prediction

To run a prediction:

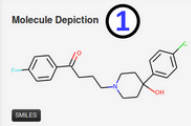
- Click on "Prediction" (1) to open the submission page.
- Provide either an input file with a list of molecules (2) in SMILES format (up to a maximum of 100 molecules) or supply a single SMILES string (3). Users are advised to use Canonical SMILES. Syntax non-compliant molecules will be ignored.
- The next step is to choose the type of prediction (4). Users can choose between running **All** receptors at once or running class **A**, class **B1**, class **C** and class **F** receptors separately, by clicking on its corresponding button.

Results page

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Pharmacokinetic Properties

Molecule Depiction (1)



SMILES

Molecule properties: (2)

| Descriptor | Value |
|------------------|---------|
| Molecular Weight | 375.671 |
| LogP | 4.3172 |
| #Rotatable Bonds | 6 |
| #Acceptors | 3 |
| #Donors | 1 |
| Surface Area | 157.952 |

Property (3)

| Property | Model Name | Predicted Value | Unit |
|------------|-------------------------------|-----------------|----------------------|
| Absorption | Caco2 | 1.09 | Numeric (log cm/s) |
| Absorption | Water solubility | -4.906 | Numeric (log mol/L) |
| Absorption | Intestinal absorption (human) | 91.125 | Numeric (% Absorbed) |
| Absorption | P-glycoprotein substrate | No | Categorical (Yes/No) |
| Absorption | P-glycoprotein I inhibitor | Yes | Categorical (Yes/No) |
| Absorption | P-glycoprotein II inhibitor | Yes | Categorical (Yes/No) |

Run another prediction

Results

For a **single molecule** prediction, your results can be displayed as follows:

- A **depiction** of the uploaded molecule will be shown in (1). Make sure the depiction is what you are expecting for your molecule.
- A list of **molecule properties** will be calculated and shown in (2).
- The prediction will be displayed in a tabular format as presented in (3). The information shown is the **Bioactivity** being predicted and the actual **predicted value** in μMolar .

Results for **multiple molecules** will be shown in a tabular format, without molecule depiction, which can be downloaded as a CSV file.

Contact page

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GPCR-CSM: contact

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Get in touch

Have you come across a problem on the website or have any requests or suggestions? Please report it here!

Name

Email address

(optional)

Getting in touch

In case you experience any trouble using pdCSM-GPCR or have any suggestions or comments, please do not hesitate in contacting us (1) either via e-mail or through the online form.