Main page

Platinum

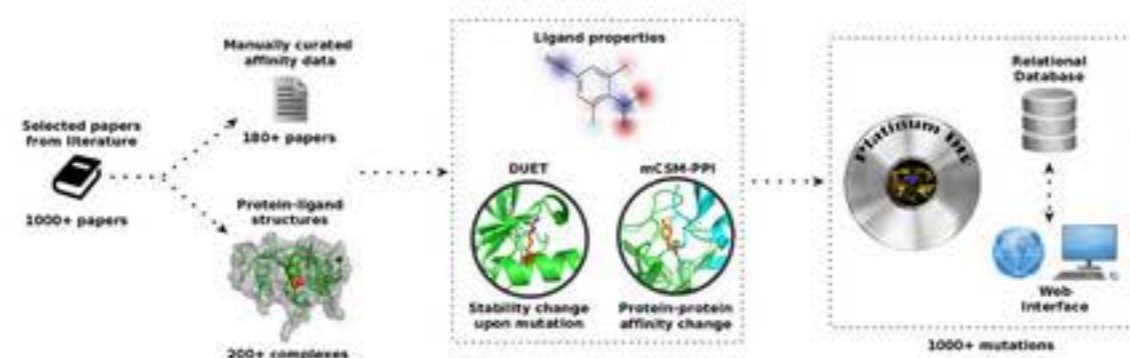*Protein-ligand affinity change upon mutation database*

Platinum: a large-scale structural database of experimentally measured effects of mutations on protein-ligand complexes

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High throughput sequencing initiatives are generating extensive data on non-synonymous single nucleotide polymorphisms (nsSNPs) in human and other genomes. The strong selective pressure imposed by small molecule drugs on many quickly evolving systems, including viruses, bacteria and human cancer, can cause the rapid development of resistance to these therapies.

In order to study and understand the impacts of missense mutations on the interaction of ligands with the proteome, as well as to guide protein engineering, we have developed **Platinum**. This manually curated, literature-derived database comprising over 1,000 mutations for the first time associates experimental information on changes in protein-ligand affinity with the three-dimensional structures of the complex. To minimise differences arising from experimental techniques and to be able to compare directly binding affinities, Platinum considers only changes measured by the same group and with the same amino-acid sequence used for structure determination, providing a direct link between protein structure, how a ligand binds and how mutations alter the affinity of the ligand for the protein.

We believe that Platinum will be an invaluable resource for understanding the effects of mutations that give rise to drug resistance, a major problem emerging in pandemics such those caused by the influenza virus, in infectious diseases such tuberculosis, in cancer and in many other life threatening illnesses.

About PLATINUM

PLATINUM is a manually curated, literature-derived database that associates experimental information on changes in protein-ligand affinity with the three-dimensional structures of the complex.

The current version of PLATINUM contains structural and affinity data reflecting the effects of mutations on protein-ligand complexes comprising:

- Over 1000 data points (approximately 80% of which are single-point mutations) with protein-ligand affinity data extracted from over 180 peer-reviewed manuscripts;

- More than 200 distinct ligands;

- Approximately 300 distinct PDB structures assigned to 140 different Uniprot entries.

Other information in the database include **ligand properties** and **predictions** of the effect of mutations on protein stability (calculated using DUET) and protein-protein affinity (calculated using mCSM-PPI).

Search page

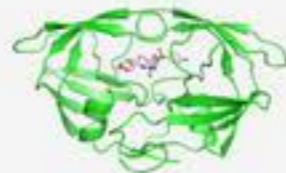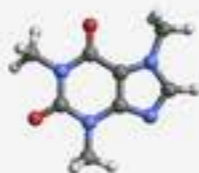# How to query the database:

The complete set of mutations, structural and affinity data in PLATINUM can be browsed by clicking in (1). Alternatively, users can search (2) for specific categories using the following criterium:

- Ligand type (3), classified according to **PDBeChem**;

- Organism category (4), which is broadly grouped by phylogenetic kingdoms;

- Mutation effect (5), to select mutations that either decrease or increase protein-ligand affinity;

- Protein classification (6), as assigned by the PDB;

- Experimental method (7), to choose how the affinities were determined;

- Structure resolution range (8), which allows you to select data based upon the resolutions of the complex structures.

- Mutation type (9), which allows you to view only single-point mutations;

- Affinity constant (10), which allows you to view only KD measurements;

After selecting the desired options you can submit your query (11).

Database page

Accessing the database

After clicking on **Browse** or performing a **Search** the database entries will be displayed in a tabulated format on this page.

The rows are coloured according to the effect of the mutation upon the binding affinity of the ligand. Red indicates that the mutant has a weaker affinity than the reference, while blue indicates that the mutant has stronger affinity.

Columns descriptions are available by hovering your cursor over the column headings (*tooltip function*). The headings of the hidden columns are coloured according to property they are linked to.

The information that is displayed can be adjusted according to your interests. Additional information regarding the following aspects can be shown or hidden:

- Residue properties **(1)**, when reference structure is available;

- Ligand properties **(2)**;

- Affinity experimental details **(3)** and

- Protein structural information **(4)**.

The number of records displayed per page can be selected at **(5)** and the filtered results can be downloaded as a comma-separated .csv file **(6)**, which can be easily imported by any spreadsheet program (*e.g.*, LibreOffice, Microsoft Excel, Numbers, etc.) or any text editor.

Database page

Filtering query results

Once a query result is displayed users can select subsets of mutations of interest by either using a global search **(1)** or a field-specific filtering tools.

The supported fields are:

- Protein name **(2)**;

- Mutation **(3)**;

- Ligand ID **(4)** and

- Uniprot ID **(5)**.

The column filtering fields also support regular expressions, and can therefore be used to build sophisticated selections.

For instance, the example shows the selection results considering the following options:

- Mutations affecting GDP binding (**Ligand ID: GDP**);

- For the *C. elegans* GDP-fucose protein O-fucosyltransferase 1 (**Uniprot ID: Q18014**) and

- Using a regular expression (**Mutation: A$**, which denotes "last character of the field is A") to filter only alanine scanning mutations.

Data page

Downloading the database

The data page **(1)** allows users to download the complete set of information available in PLATINUM:

- You can download PLATINUM as a single flat-file (comma-separated) by clicking on **(2)**.

- Additionally, you can also download the full set of processed protein-ligand complexes in PDB format **(3)**.

Contact page

Getting in touch

In case you experience any trouble using PLATINUM or have any suggestions or comments, please do not hesitate in contacting us (1) either via e-mail (2) or through the online form (3).