PRISMOID: a comprehensive 3D structure database for post-translational modifications and mutations with functional impact

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Abstract

Post-translational modifications (PTMs) play very important roles in various cell signalling pathways and biological process. Due to PTMs' extremely important roles, many major PTMs have been studied, while the functional and mechanical characterization of major PTMs is well-documented in several databases. However, most currently available databases mainly focus on protein sequences, while the real 3D structures of PTMs have been largely ignored. Therefore, studies of PTMs 3D structural signatures have been severely limited by the deficiency of the data. Here, we develop PRISMOID, a novel publicly available and free 3D structure database for a wide range of PTMs. PRISMOID represents an up-to-date and interactive online knowledge base with specific focus on 3D structural contexts of PTMs sites and mutations that occur on PTMs and in the close proximity of PTM sites with functional impact. The first version of PRISMOID encompasses 17,145 non-redundant modification sites on 3,919 related protein 3D structure entries pertaining to 37 different types of PTMs. Our entry web page is organized in a comprehensive manner, including detailed PTM annotation on the 3D structure and biological information in terms of mutations affecting PTMs, secondary structure features and per-residue solvent accessibility features of PTM sites, domain context, predicted natively disordered regions and sequence alignments. In addition, high-definition JavaScript packages are employed to enhance information visualization in PRISMOID. PRISMOID equips a variety of interactive and customizable search options and data browsing functions; these capabilities allow users to access data via keyword, ID, and advanced options combination search in an efficient and user-friendly way. A download page is also provided to enable users to download the SQL file, computational structural features, and PTM sites' data. We anticipate PRISMOID will swiftly become an invaluable online resource, assisting both biologists and bioinformaticians to conduct experiments and develop applications supporting discovery efforts in the sequence-structural-functional relationship of PTMs and providing important insight into mutations and PTM sites interaction mechanisms. The PRISMOID database is freely accessible at http://prismoid.erc.monash.edu/. The database and web interface are implemented in MySQL, JSP, JavaScript, and HTML with all major browsers supported.

1. Introduction

The relatively modest number of human genes (~25,000) does not reflect the downstream proteomic complexity that is necessary for development and sustaining life. This essential complexity is achieved through a number of factors, such as protein post-translational modifications (PTMs), alternative splicing [1], intrinsic disorder [2, 3], etc. PTMs exhibit tremendous chemical diversity and dynamics, playing fundamental roles in various cell signalling pathways, fundamental cellular and biological processes. For example, phosphorylation, one of the most studied PTMs [4], is involved in regulation of protein degradation [5], signal transduction [6], protein-protein interaction [7], and signalling pathways [8]. Glycosylation, another important PTM, has been proved to play a crucial role in protein folding, trafficking [9-11], subcellular localization, and degradation [12, 13]. Other PTMs, such as lysine PTMs, are key for protein stability [14], transcription [15], cellular metabolism [16], DNA repair and replication [17] etc. Likewise, due to the fundamental importance of PTMs in cell biology, a number of aberrant PTM sites, which are often introduced by mutations, are highly relevant to various human diseases, including somatic cancers [18-20]. Altogether, it is critical to identify and characterize PTMs and their functional roles, which can in turn help elucidate the pathogenesis of PTMs' related diseases.

A key step to understand mechanisms and functional roles of PTMs is to identify the sequences/structures of their natural substrates and the corresponding PTM sites. Given the fact that PTMs are strongly associated with mutations and diseases, significant efforts have been placed in using advanced high-throughput experimental techniques, such as mass spectrometry (MS) or MS-based techniques, to detect PTMs of proteins in proteomics data [21]. Therefore, large-scale modified proteomics data have been archived in recent years. To date, over 660 PTM types have been discovered (http://www.uniprot.org/docs/ptmlist.txt).

Several popular online databases have been developed, to collectively deposit and provide access to different types of experimentally validated PTMs data for public use. These databases include PhosphoSitePlus [22, 23], dbPTM [24, 25], SysPTM [26, 27], PLMD [28], Phospho.ELM [29], and UniProt [30]. PhosphoSitePlus was built by manually collecting and organizing data from

various PTMs and model organisms, though primarily phosphorylation, ubiquitination and acetylation, from mainly human and mouse proteins. dbPTM has been maintained over 10 years, and integrates multiple PTMs information, including functional and structural knowledge of PTMs; dbPTM also stores drug binding data that shows associations to PTM sites. SysPTM contains both PTM data from public databases and MS experimental data from the literature. We note Pfam domains, KEGG pathways, and Gene Ontology information are also integrated into SysPTM. PLMD is a lysine-specific PTM database, and it encompasses 20 types of lysine PTMs in both eukaryotes and prokaryotes. Phospho.ELM is a phosphorylation-specific database, designed to provide general and kinase-specific phosphorylation sites collected from scientific literature and phosphoproteomic experiments. Lastly, UniProt is one of the largest and most regularly updated databases available, providing comprehensive annotations on protein sequences, functions and other relevant biological information. Currently, the UniProt database contains the information of over 660 types of PTMs.

These online resources collect protein sequences with experimentally validated post-translational modification sites, where the positions of PTM sites on sequences have also been documented. These publicly available online resources not only help biologists to conduct valuable experimental analyses, but also provide bioinformaticians with a wealth of resources to build novel prediction tools for studying sequences and functions of PTMs. All these, together, speed up PTMs' research process.

However, there are few databases have been developed for systematically archiving and conveniently accessing 3D structural data of PTMs. PhosphoSitePlus provides 3D structure views in the current version, while this only focus on limited entries. PTM-SD [31] is a protein structure database focus on PTMs, which contains 11,677 entries, while PTM-SD only focus on the protein structure information of PTMs, other important information such as disorder information associated with the PTM site and PTM-associated disease mutations is not provided. In addition, PTM-SD only present the automatic produced figures of the protein 3D structure, the interactive visualization of protein 3D structures is not provided. The latest version of dbPTM provides the related PDB (Protein Data Bank) ID of PTM proteins, but the corresponding positions of PTM sites position on PDB structures are not available. Furthermore, dbPTM does not provide a download function for

PTM related PDB information. Recently, Gao *et al*. [32] developed BioJavaMolFinder, a software designed to identify protein modifications stored in 3D structures within the PDB database. BioJavaMolFinder scanned PDB database and identified the proteins with modification, and provided the results on the PDB website. However, BioJavaMolFinder solely focuses on modification residues in PDBs, while the relationships among protein sequence-structure-function are not provided. More recently, Ledesma *et al*. developed YAAM for yeast amino acid modifications, which maps PTM sites in 680 protein 3D structures. On the whole, there is a generalized lack of user-friendly tools for both biologists and bioinformaticians to investigate the sequence-structural-function information of PTM proteins from existing protein sequence-based databases, limiting research efforts. For instance, although there are many bioinformatics prediction tools based on protein sequence data to investigate PTMs [4, 33-37], there are few prediction studies using PDB structures to build prediction models [38-40]. This is mainly due to the fact that the process of mapping from protein sequences to protein structures is quite time-consuming and operationally complex.

To bridge the existing knowledge gap, we developed a new web-based database, PRISMOID (PRoteIn Structure MOdIfication Database) to provide a comprehensive annotation of PTM sites in real 3D structures. We extracted experimentally validated PTMs information from several currently available protein sequence-based databases, and subsequently mapped the PTM sites to the corresponding 3D structures. We then filtrated the blast results and stored these results in PRISMOID. Aside, it has been reported there are 21% disease-related amino acid substitutions associated with missense single nucleotide variants (SNVs) are located in PTM sites [41]. Accordingly, we additionally extracted and collected PTM-associated disease and population mutations from ActiveDriverDB [41] database, so as to facilitate the investigation of structural properties of PTMs and to encourage construction of bioinformatics tools with structural features. To this effect, we also calculated secondary structure based features and residue accessibility features of PTM sites using DSSP [42] and NACCESS [43] software, respectively.

With all the above in consideration, PRISMOID provides users with the protein domain context, sequence-structural alignment and protein disorder information in each entry page. Moreover, to facilitate users' access to data of interest, keyword/ID search, advanced combinatorial

schemas search and “browse” functions are provided. PRISMOID also allows users to download the SQL file, the results files calculated from DSSP and NACCESS, and PTM annotation files in the download page.

2. Materials and Methods

2.1 PTM data collection

Figure 1 (**A**) shows the flowchart of PRISMOID steps, including data collection and processing. There are three major steps involved in entry collection and processing, described in what follows.

First, we extracted, manually checked and integrated 37 types of PTM annotation data from six major online, public available PTM databases, including PhosphoSitePlus [22], dbPTM [24], SysPTM [26], PLMD [28], Phospho.ELM [29], and UniProt [30]. We only considered and integrated experimentally validated PTM sites data for PRISMOID; accordingly, all PTM sites labelled as computational PTM annotations were discarded. For UniProt data, we only considered PTMs with ECO code ECO:0000269 (https://www.uniprot.org/help/evidences), which means the data is manually curated and involving published experimental data.

Secondly, all the remaining protein sequences with PTM sites were mapped to the PDB database [44] using PSI-BLAST [45] against PDB sequence database (pdbaa) with the e-value of 10^{-3} and three iterations.

Finally, the mapped PDB entries were selected according to the following criteria:

(1) With 100% sequence identity; only PDB sequences aligned with the entry protein sequences with 100% sequence identity were retained.

(2) X-ray resolution structures only; thus, nuclear magnetic resonance (NMR) and electron microscopy (EM) structures were excluded.

(3) PDB chains with missing atoms were removed.

(4) For each query blast sequence, the PDB chain with more PTM sites that can be aligned was selected;

(5) For protein sequences with more than one mapped PDB structure, the structure with the highest resolution was selected.

After these five steps, a total number of 17,145 PTM sites on 3,919 PDB chains for 37 types of PTMs were extracted and stored into PRISMOID. The statistics of each type of PTM data are shown in **Table 1**. A discussion of the statistical analysis is included in Section 3.1.

[Table 1]

[Figure 1]

2.2 PTM-associated Mutation collection

Single amino acid variants (SAVs) are the most abundant form of known genetic variations associated with human disease [46]. It is reported that about 60% of Mendelian diseases are caused by amino acid substitutions [47]. A potential effect of SAVs on protein function is the disruption of PTMs [48]. For example, the potential for phosphorylation sites to be affected by amino acid variants is high and there have been numerous examples of diseases associated naturally occurring variants that impact the phosphorylation status of proteins [49]. We have combined mutations associated with various diseases (including but not limited to cancer) and population variants affecting PTMs from ActiveDriverDB, which is a comprehensive collection of annotations of disease and population mutations contained in TCGA. The collected mutations were then mapped to the entries in PRISMOID. Please refer to **Figure 2** (C) “Mutations affecting PTM sites” panel.

2.3 3D structure-based features calculation

Previous studies have shown that 3D structure-based features play an important role in improving the predictive performance of PTM sites [38, 50]. Therefore, we calculated two commonly used protein 3D structure features, secondary structure features and solvent accessible area features by using DSSP [42] and NACCESS [43], respectively. The result files can be downloaded from the

download web page of PRISMOID ((http://prismoid.erc.monash.edu/pdb/download) please refer to **Figure 1 (B)**).

2.3.1 Secondary structure features

Different types of features were extracted from the DSSP calculation result files for each PTM site, including secondary structure, bond angles (virtual bond angle, *KAPPA*), torsion angles (virtual torsion angle, *ALPHA*; IUPAC peptide backbone torsion angles, *PHI PSI*), atom coordinates (C_α atom coordinates, *X-CA Y-CA Z-CA*), and the number of water molecules (*ACC*) features. There are eight features for each PTM site shown on the corresponding entry page.

2.3.2 Solvent accessible area (ASA) features

Since solvent accessible area (ASA) has been widely used in many bioinformatics fields, including hot spots identification [51], catalytic sites prediction [52], and glycosylation sites prediction [38], etc. Here, we employed the NACCESS program to calculate ASA features. The resulting file of NACCESS contains two types of ASA features, absolute ASA features and relative ASA features. Each type includes five different features: all-atoms, total-side, main-chain, non-polar, and all-polar ASA features. Thus, there are totally 10 ASA features for each PTM site. Please refer to the "Secondary structure and accessibilities features" panel of Figure 2 (C).

2.4 Database access and download functionality

To obtain a database with abundant data, it is essential to apply a good search algorithm to provide users with more efficient and convenient access. As shown in the "Search function" panel of **Figure 1** (**B**), PRISMOID provides searching the entries in various ways, based on users' favour. The entries can be searched through three different methods, including ID search, Keyword search, and Advanced search. The Advanced search method in PRISMOID allows multiple search schemas specific to different types of data combined, e.g. PTM types and PDB ID, or PDB Chain, UniProt Acc and X-Ray resolution range. The search function is described in detail in Section 3.1, and an example is given to illustrate the usage of the advanced search function.

PRISMOID also allows users to explore data embedded in the database through the "Browse" page. **Figure 2** (**B**) illustrates an example of how to explore the data this way. When users click the "Browse" icon on the top page, the web page redirects them to "Browse" page, which displays a table with four columns including type (e.g. Acetylation), PTM type (e.g. Acetylation_A), target Amino acid (e.g. Alanine), and the number of entries (e.g. 65). The table lists all the PTM types stored in PRISMOID, as shown in the left sub-figure of **Figure 2** (**B**). Then, when users click the PTM type (e.g. Acetylation_A), the web page redirects them to the browse page of this PTM. There users find a three-column table that includes database ID (e.g. DBP1340), PDB chain (e.g. 3NSL:A), and protein name (e.g. Protein S100-A3). Please refer to the right sub-figure of **Figure 2** (**B**) for more details. Both the "Search" results page and "Browse" page allow results to be sorted, thereby enabling users to easily find the information they need, immediately.

[Figure 2]

PRISMOID also provides the download function to facilitate users download of PTMs data in PRISMOID. As shown in the "Download page" panel of **Figure 1** (**B**), PRISMOID allows users to download the SQL file of the database, calculated DSSP feature files, calculated NACCESS feature files, and PTM sites data. These files can greatly facilitate bioinformaticians in their efforts to build machine-learning based bioinformatics methods for predicting PTMs sites straight from the protein structure level.

2.5 Implementation

The information stored in PRISMOID resides in a MySQL relational database consisting of 49 tables. All the routines in PRISMOID were written in the Java programming language. A highly user-friendly web front-end to the data was implemented using the jQuery framework. The basic operations of web interfaces are supported by JavaScript and jQuery, and the web page frame was built utilizing the bootstrap framework (https://getbootstrap.com/). Apache Tomcat 7 resides on a Linux server handles serving request of data from users, utilizing SSM (Spring, SpringMVC and MyBatis)

framework for data searching, operation, web page hopping and viewing. The Linux server equipped with an 8-core CPU, 30 GB hard disk and 6 GB memory.

For the statistics page, the ECharts (https://ecomfe.github.io/echarts-doc/public/en/index.html) package [53] was used to achieve a user interactive pie charts display of statistical results. PRISMOID provides 11 different statistical results; users can view different statistics' pie charts by selecting the different statistical methods from the drop-down menus. Additionally, when users move the mouse over a sector of a pie chart, the corresponding statistical results are displayed right where the cursor points. By default, the pie chart shows the statistical results of the top-five types. However, users can select the types to be displayed by clicking the legend on the left.

For the entry page, 3Dmol.js [54] was employed for protein 3D structure visualization. 3Dmol.js is a high-performance, pure object-oriented JavaScript library, enabling interactive visualization of protein 3D structures. We opted to use 3Dmod.js because it does not need to install browser plug-ins or Java. In PRISMOID, each entry is a specific PDB chain. Therefore, only the corresponding chain of the PDB structure is displayed, and the PTM sites on the chain are labelled at the corresponding positions. Please refer to the "PTM information and 3D structural visualization" panel in **Figure 2** (**C**), where the PTM site is labelled at position 2 of the chain A as "ALA 2". A Scalable Vector Graphics (SVG) library, the Protein Feature view (http://andreasprlic.github.io/proteinfeatureview/), was applied to show variation data, Pfam domains, functional sites and some basic structural information. This visualization library enables users to quickly identify PTMs that lie within functional domains and to visualize the topology of the PTMs. The "Protein feature view" panel in **Figure 2** (**C**) illustrates this function. The RCSB-sequence viewer plug-in (https://github.com/biojava/rcsb-sequenceviewer) was also employed to generate the sequence view picture of the PDB chain. The sequence view shows the protein modification generated by BioJavaMolFinder, PDB chain sequence and secondary structures from DSSP. In addition, we also extracted the protein disorder figures from the disordered protein predictions database D2P2 [55]. An example of the sequence view and protein disorder pictures are shown in the "Disorder and Sequence view pictures" panel in **Figure 2** (**C**). Lastly, Alignment-To-HTML [56] was used for inter-

active visualization for the sequence alignments between the PDB chain sequence and the corresponding UniProt sequences.

3 Results and Discussion

3.1 Search functionality

As we discussed in section 2.4, PRISMOID provides several search algorithms, enabling users to get easy, comprehensive access to data. Here we introduce the search function of PRISMOID in detail, and present a specific example to show how to use the advanced search function.

PRISMOID data can be searched by three different search methods. The first method is the ID search, where the users can search PRISMOID entries by using a PDB ID (e.g. '3NSL'), UniProt ACC (e.g. 'P33764') or Database ID (e.g. 'DBP1340'). The second method is the keyword search, where users can search entries by entering a protein name or gene name. For these two search methods, a corresponding 'Example' button is provided, to guide users to conduct a search. With the click of the 'Example' button, users can automatically get an example for a search with ID/keyword. The third method is the Advanced Search. There are five different query schemas in the Advanced search field, including (i) PTM types, (ii) PDB IDs, (iii) Chain IDs, (iv) UniProt ACCs; and (v) range of X-Ray resolution. Users can search with individual schema or combinations of multiple schemas by selecting the search schema in the dropdown list of the 'Advanced search' menu and using the "Add Search Schema" button to search with multiple search schemas. **Figure 2** (**A**) illustrates an example using the combination of PTM types ("Acetylation_A" was selected) and X-ray resolution range (1 to 1.5 were filled) to conduct the search.

Searched results will be shown in a table on a separate webpage. The table will contain six columns, showing basic information of searched queries, including PDB ID, chain ID, PTM positions in PDB chain, the UniProt accession number (Acc), PTM positions in UniProt sequence, organism, PTM type, gene name, PDB resolution, and protein name (as shown in **Figure 2** (**A**)). Moreover, detailed information of each entry can be browsed in a new webpage by clicking the

PDB Chain in the result table. For each entry, there are eight major types of information provided, including protein 3D structure visualization, PTM information, mutations affecting PTM sites information, secondary structure based features calculated by DSSP, relative accessibilities features calculated by NACCESS, protein feature view, sequence alignment, disorder picture, and protein sequence view. To provide a demonstration of the annotation information for each entry in PRISMOID, 'PDBChain=3NSL:A' (PRISMOID ID='DBP1340') was used as an example query. The resulting page with annotation information is shown in **Figure 2** (**C**).

3.2 Database contents

With the data contained in PRISMOID, we conducted a statistical analysis of the PTM information distribution across the top eight species with the largest number of entries/PTM sites. Two bar charts (**Figure 3** (**A**) and (**B**)) show statistical results of the eight species with the largest number of entries (PDB chain) and PTM sites, respectively. The most abundant source with 11,560 PTM sites on 2,171 PDB chains was Human, followed by *E. coli* with 2,246 PTM sites on 549 entries, Yeast with 922 PTM sites on 275 entries, and Mouse with 877 PTM sites on 219 entries.

[Figure 3]

Two pie charts in **Figure 3** (**C** and **D**) indicate the distribution of entries and PTM sites of the eight largest number of PTM types, respectively. In general, the top eight largest types of PTM are the same, but the order is not exactly the same, in terms of the number of PTM proteins (entries) and the number of PTM sites. For example, the top two PTM types in terms of the number of proteins and PTM sites are the same, i.e. Phosphorylation and Acetylation respectively. There are 1736 phosphorylated proteins with 4312 phosphorylation sites and 1123 acetylated proteins with 3578 acetylation sites. The third largest type in terms of the PTM proteins number is Glycation (1050), while the third largest type in terms of the PTM sites number is Malonylation (3540).

[Figure 4]

The bar chart in **Figure 4** illustrates the number of PTM sites associated with mutations. There are three types of mutations, including somatic cancer mutations, inherited disease mutations, and population mutations. **Table 2 and Supplementary Table S1** list the cancer types and disease types of somatic cancer mutations and disease mutations, respectively.

The top three types of PTMs associated with three types of mutations are the same. They are: (i) Phosphorylation with 3987 cancer mutations, 3832 disease mutations, and 1127 population mutations; (ii) Ubiquitylation with 3723 cancer mutations, 3284 disease mutations, and 914 acetylation mutations; and (iii) Acetylation with 897 cancer mutations, 278 disease mutations and 197 population mutations.

4. Conclusions

PRISMOID is a freely available web-based resource providing 3D structure information of protein post-translational modification sites. PRISMOID retrieves comprehensive PTM information from six major protein sequence-based PTM databases. The collected protein sequences with PTM sites were then mapped to protein 3D structures. PRISMOID not only includes PTM sites data but also integrates and annotates the disease/cancer/population mutation affecting the PTM sites. Other information, such as protein secondary structure properties, solvent accessibility area features, protein disorder region, and protein domain context, etc., were also collected and annotated in PRISMOID. The annotations of 3D structural features of PTM sites in PRISMOID can effectively guide the design of experimental efforts such as crystallization and mutagenesis to interrogate the functional roles of PTM sites.

PRISMOID combines the strength of Java, Spring, SpringMVC, MyBatis, and JavaScript to achieve user-friendly interface design and efficient data query/display. Multiple data querying methods and data browsing pages enabled in PRISMOID can be explored, with a number of options. PRISMOID is also equipped with several bioinformatics plug-ins such as 3Dmol.js, Protein Feature view, and RCSB-sequence viewer to better visualize the comprehensive annotation data contained in PRISMOID. As new datasets accumulate rapidly, as well as computational resources, it is essen-

tial to maintain the database current. Thus, we plan to develop a website background management system to facilitate timely and automatized updates of the database at least once every six months. In the future, we will incorporate additional information such as PTM crosstalk patterns into PRISMOID. A straightforward mechanism of two PTM sites to be associated in a cross-talk pattern is based on their spatial proximity [57, 58]. Accordingly, the 3D structural information can be used to calculate the spatial distance between any two PTM sites and help identify potential PTM cross-talk pairs. In addition, it has been reported that some PTM sites tend to be located in disordered regions [59]. In view of this, PRISMOID has included the predicted disorder annotations for all related entries by providing the link to the D2P2 database [55]. In an upgraded version of PRISMOID in the future, we aim to collect the reliably annotated disordered region information from multiple disordered region databases (including D2P2 and others) and map the disordered region to the PDB structures of proteins with PTM sites to enable users to perform an in-depth analysis of the potential association between PTM sites and disorder regions. Taken altogether, we anticipate that PRISMOID will become a useful resource for both experimental and computational analyses of protein post-translational modifications.

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Key Points

- PRISMOID is a novel freely available web-based resource providing 3D structure information of a wide range of protein post-translational modification sites.
- The first version of PRISMOID encompasses 17,145 non-redundant modification sites on 3,919 related protein 3D structure entries pertaining to 37 different types of PTMs.
- The entry web page of PRISMOID is organized in a comprehensive manner, including detailed PTM annotation on the 3D structure and biological information in terms of mutations affecting PTMs, secondary structure features and per-residue solvent accessibility features of PTM sites, domain context, predicted natively disordered regions and sequence alignments.
- PRISMOID equips a variety of interactive and customizable search options and data browsing functions; these capabilities allow users to access data via keyword, ID, and advanced options combination search in an efficient and user-friendly way. A download page is also provided to enable users to download the SQL file, computational structural features, and PTM sites' data.

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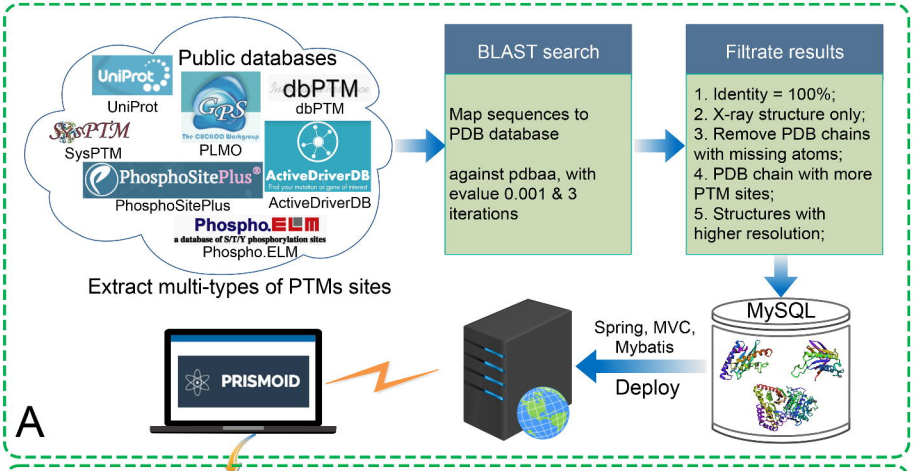
FIGURE LEGENDS

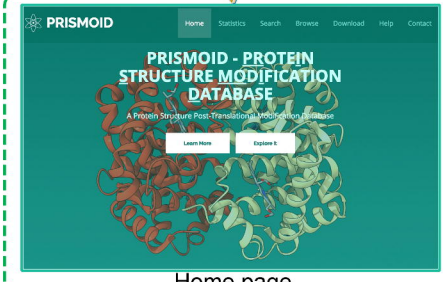
Figure 1. (**A**) PRISMOID data collection and processing flowchart; (**B**) Sample web interfaces. There are four major web pages in PRISMOID: "Home" page, "Search" page, "Statistics" page, and "Download" page.

Figure 2. Two different methods for data accessing in PRISMOID. **(A)** An example showing how to use the advanced function of PRISMOID. Here, two different search schemas were combined, PTM types (Acetylation A is selected) and the range of X-ray resolution (between 1 and 1.5); (**B**) An example illustrates how to explore the PTM data through the Browse webpage (Acetylation A and PDB chain 3NSL:A is selected); (**C**) Typical search result webpage using the PDB chain 3NSL:A as an example. The entry webpage consists of six major sections showing detailed information: PTM information and 3D structural visualization, mutations affecting PTM sites information, protein feature view, secondary structure and accessibilities features, disorder and sequence view pictures and sequence alignment.

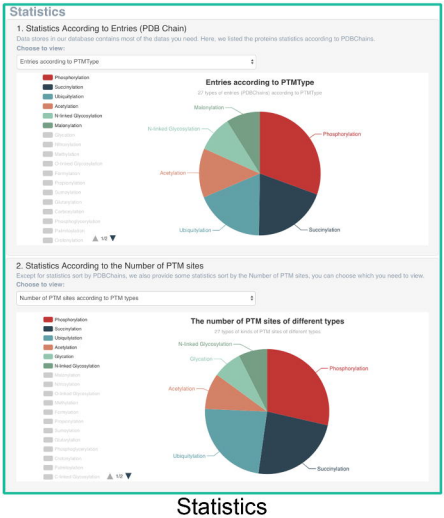
Figure 3. Statistical analysis results in terms of species and PTM types. (**A**) Statistical results of the entries (PDB chains) from the eight largest species, including *Homo sapiens*, *Escherichia coli*, *Saccharomyces cerevisiae*, *Mus musculus*, *Mycobacterium tuberculosis*, *Rattus norvegicus*, *Bos taurus*, and *Thermus thermophiles*; (**B**) Statistical analysis of the PTM sites from the eight largest species; (**C**) Distributions of eight largest PTM types in terms of the number of PTM entries; and (**D**) Distributions of eight largest PTM types in terms of the number of PTM sites.

Figure 4. The top three PTMs in terms of the number of PTM sites associated with mutations. There are three types of mutations, including somatic cancer mutations, inherited disease mutations, and population mutations.

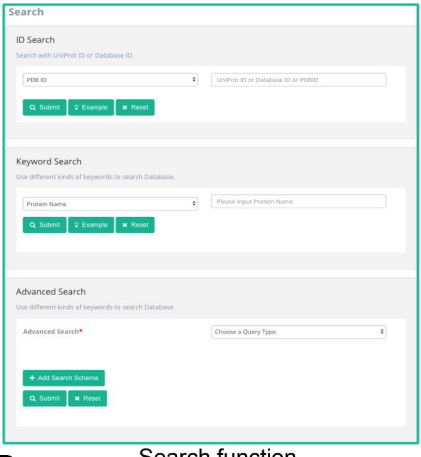




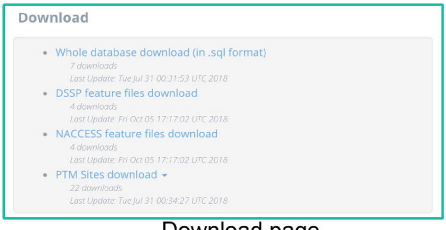
Home page



Statistics

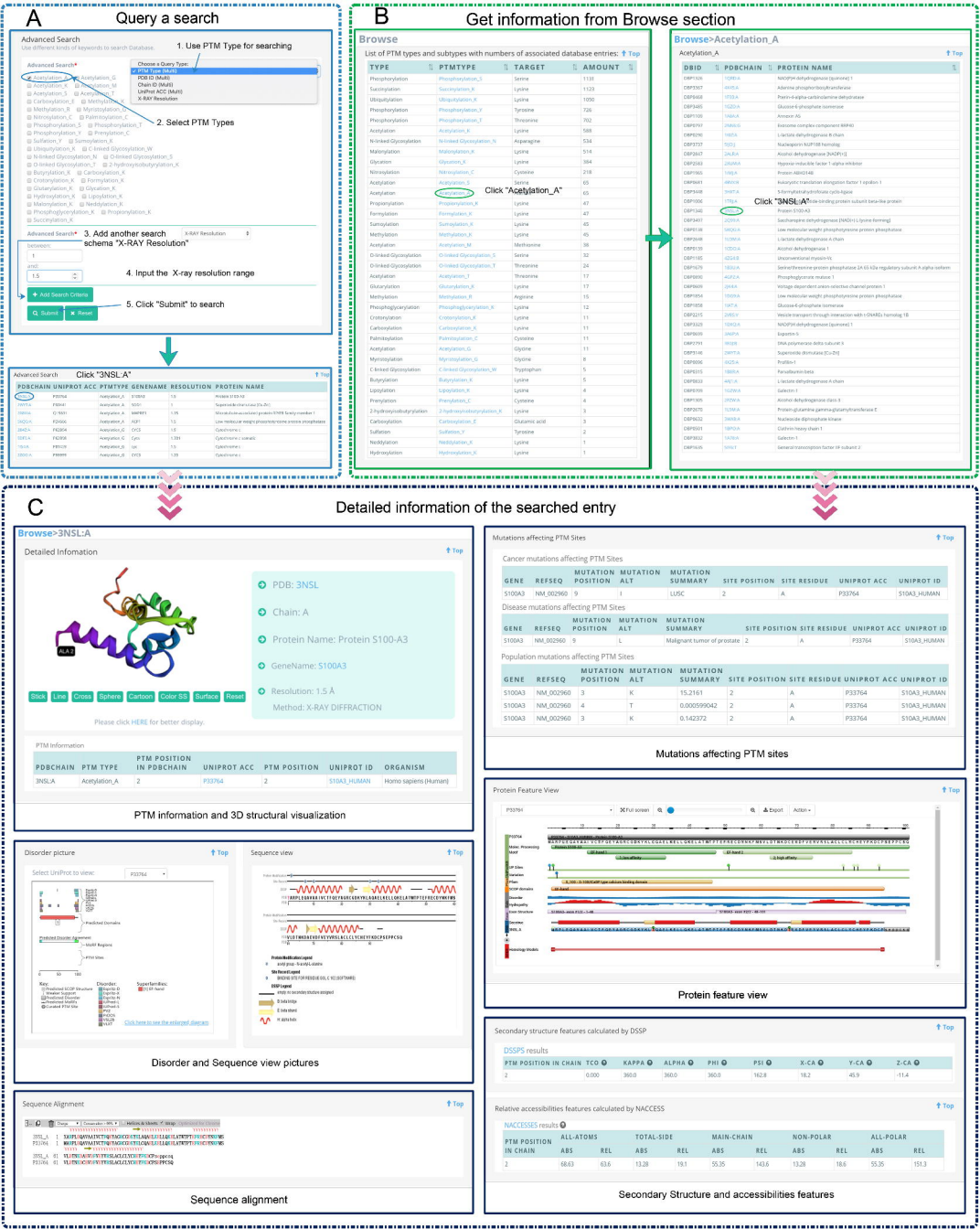


Search function



Download page

B


A
Query a search
Advanced Search
Use different kinds of keywords to search Database.
Advanced Search*
Acetylation_A
Acetylation_B
Acetylation_K
Acetylation_S
Acetylation_T
Carbonylation_K
Methylation_R
Nitrosylation_C
Phosphorylation_S
Phosphorylation_Y
Sulfation_Y
Ubiquitylation_K
N-linked Glycosylation_N
O-linked Glycosylation_S
O-linked Glycosylation_T
Butyrylation_K
Crotonylation_K
Glutarylation_K
Hydroxylation_K
Malonylation_K
Succinylation_K
Choose a Query Type:
PTM Type (Multi)
PDB ID (Multi)
Chain ID (Multi)
UniProt ACC (Multi)
X-RAY Resolution
1. Use PTM Type for searching
2. Select PTM Types
Advanced Search*
X-RAY Resolution
between:
1
and:
1.5
3. Add another search schema "X-RAY Resolution"
4. Input the X-ray resolution range
+ Add Search Criteria
Submit
Reset
5. Click "Submit" to search
Advanced Search
Click "3NSL:A"
Top
PDBCHAIN UNIPROT ACC PTMTYPE GENENAME RESOLUTION PROTEIN NAME
3NSL:A P33764 Acetylation_A S100A3 1.5 Protein S100-A3
3NSL:B P33764 Acetylation_A S100A3 1 Superoxide dismutase [Cu-Zn]
3NSL:C Q13501 Acetylation_A MAPRE1 1.35 Microtubule-associated protein RP/EB family member 1
3AQO:A P24666 Acetylation_A ACP1 1.5 Low molecular weight phosphotyrosine protein phosphatase
2B4Z:A P62994 Acetylation_G CYC3 1.0 Cytochrome c
3D8T:A P62936 Acetylation_G Cyc- 1.331 Cytochrome c somatic
1S6:A P81120 Acetylation_G Cyc 1.5 Cytochrome c
3D0C:A P99999 Acetylation_G CYC3 1.35 Cytochrome c
B
Get information from Browse section
Browse
List of PTM types and subtypes with numbers of associated database entries: Top
TYPE PTMTYPE TARGET AMOUNT
Phosphorylation Phosphorylation_S Serine 1131
Succinylation Succinylation_K Lysine 1123
Ubiquitylation Ubiquitylation_K Lysine 1050
Phosphorylation Phosphorylation_Y Tyrosine 726
Phosphorylation Phosphorylation_T Threonine 702
Acetylation Acetylation_K Lysine 588
N-linked Glycosylation N-linked Glycosylation_N Asparagine 534
Malonylation Malonylation_K Lysine 514
Glycation Glycation_K Lysine 384
Nitrosylation Nitrosylation_C Cysteine 218
Acetylation Acetylation_S Serine 65
Acetylation Acetylation_A 65
Propionylation Propionylation_K Lysine 47
Formylation Formylation_K Lysine 47
Sumoylation Sumoylation_K Lysine 45
Methylation Methylation_K Lysine 45
Acetylation Acetylation_M Methionine 38
O-linked Glycosylation O-linked Glycosylation_S Serine 32
O-linked Glycosylation O-linked Glycosylation_T Threonine 24
Acetylation Acetylation_T Threonine 17
Glutarylation Glutarylation_K Lysine 17
Methylation Methylation_R Arginine 15
Phosphoglycerylation Phosphoglycerylation_K Lysine 12
Crotonylation Crotonylation_K Lysine 11
Carbonylation Carbonylation_K Lysine 11
Palmitoylation Palmitoylation_C Cysteine 11
Acetylation Acetylation_G Glycine 11
Myristoylation Myristoylation_G Glycine 8
C-linked Glycosylation C-linked Glycosylation_W Tryptophan 5
Butyrylation Butyrylation_K Lysine 5
Lipoylation Lipoylation_K Lysine 4
Prenylation Prenylation_C Cysteine 4
2-hydroxyisobutyrylation 2-hydroxyisobutyrylation_K Lysine 3
Carboxylation Carboxylation_E Glutamic acid 3
Sulfation Sulfation_Y Tyrosine 2
Nedylation Nedylation_K Lysine 1
Hydroxylation Hydroxylation_K Lysine 1
Click "Acetylation_A"
Browse>Acetylation_A
Acetylation_A
Top
DBID PDBCHAIN PROTEIN NAME
DBP1526 1QR0:A NAD(P)H dehydrogenase (quinone) 1
DBP3537 4HVB:A Adenine phosphoribosyltransferase
DBP6668 1F5X:A Pteorin-4-alpha-carbinolamine dehydratase
DBP3485 1GZO:A Glucose-6-phosphate isomerase
DBP1100 1N8A:A Annexin A5
DBP6797 2NBB:D Exosome complex component RRP40
DBP8290 1H8D:A L-lactate dehydrogenase A chain
DBP3737 5JDJ:J Nucleoporin NUP188 homolog
DBP2867 2AJB:A Alcohol dehydrogenase [NADP(+)]
DBP2263 2AUMA Hypoxia-inducible factor 1 alpha inhibitor
DBP1965 1M6J:A Protein ABHD14B
DBP8681 4WVW Eukaryotic translation elongation factor 1 epsilon-1
DBP5408 3HPT:A 5-formyltetrahydrofolate cyclo-ligase
DBP6506 1T9J:A Cell cycle-binding protein subunit beta-like protein
DBP1340 P33764 Protein S100-A3
DBP3497 2QR9:A Saccharopine dehydrogenase [NAD(+), L-lysine-forming]
DBP8138 5HC0:A Low molecular weight phosphotyrosine protein phosphatase
DBP3648 1U3W:A L-lactate dehydrogenase A chain
DBP8159 1ODO:A Alcohol dehydrogenase 1
DBP1185 4ZGB:B Uncharacterized myosin-VI
DBP5679 1B3U:A Serine/threonine protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform
DBP8890 4GFZ:A Phosphoglycerate mutase 1
DBP8609 2J4A:A Voltage-dependent anion-selective channel protein 1
DBP8564 1E0X:A Low molecular weight phosphotyrosine protein phosphatase
DBP1858 1AT1:A Glucose-6-phosphate isomerase
DBP2215 2VRS:Y Vesicle transport through interaction with t-SNAREs homolog 1B
DBP3325 1D4Q:A NAD(P)H dehydrogenase (quinone) 1
DBP8699 3A6P:A Exportin-5
DBP2791 1R5B Dna polymerase delta subunit 4
DBP3146 2WFT:A Superoxide dismutase [Cu-Zn]
DBP8096 6QZS:A Profilin-1
DBP8315 1BBR:A Parvalbumin beta
DBP5833 4AJ1:A L-lactate dehydrogenase A chain
DBP8709 1G2W:A Galectin-7
DBP1905 2RDW:A Alcohol dehydrogenase class II
DBP2875 1U3W:A Protein-glutamine gamma-glutamyltransferase E
DBP6632 3WKB:A Nucleoside diphosphate kinase
DBP8501 1BPO:A Clathrin heavy chain 1
DBP3832 1A78:A Galectin-1
DBP8635 5H6E1 General transcription factor IIF subunit 2
Click "3NSL:A"
C
Detailed information of the searched entry
Browse>3NSL:A
Detailed Infomation
Top
PDB: 3NSL
Chain: A
Protein Name: Protein S100-A3
GeneName: S100A3
Resolution: 1.5 Å
Method: X-RAY DIFFRACTION
Stick Line Cross Sphere Cartoon Color SS Surface Reset
Please click HERE for better display.
PTM Information
PDBCHAIN PTM TYPE PTM POSITION IN PDBCHAIN UNIPROT ACC PTM POSITION UNIPROT ID ORGANISM
3NSL:A Acetylation_A 2 P33764 2 S10A3_HUMAN Homo sapiens (Human)
PTM information and 3D structural visualization
Mutations affecting PTM Sites
Top
Cancer mutations affecting PTM Sites
GENE REFSEQ MUTATION POSITION MUTATION ALT MUTATION SUMMARY SITE POSITION SITE RESIDUE UNIPROT ACC UNIPROT ID
S100A3 NM_002960 9 I LUSC 2 A P33764 S10A3_HUMAN
Disease mutations affecting PTM Sites
GENE REFSEQ MUTATION POSITION MUTATION ALT MUTATION SUMMARY SITE POSITION SITE RESIDUE UNIPROT ACC UNIPROT ID
S100A3 NM_002960 9 L Malignant tumor of prostate 2 A P33764 S10A3_HUMAN
Population mutations affecting PTM Sites
GENE REFSEQ MUTATION POSITION MUTATION ALT MUTATION SUMMARY SITE POSITION SITE RESIDUE UNIPROT ACC UNIPROT ID
S100A3 NM_002960 3 K 15.2161 2 A P33764 S10A3_HUMAN
S100A3 NM_002960 4 T 0.000599042 2 A P33764 S10A3_HUMAN
S100A3 NM_002960 3 K 0.142372 2 A P33764 S10A3_HUMAN
Mutations affecting PTM sites
Protein Feature View
Top
P33764
Full screen
Export
Action
Protein Feature View
Disorder picture
Top
Select UniProt to view:
P33764
Predicted Domains
Predicted Disorder Agreement
Modif. Regions
PTM Sites
Key:
Disorder:
Superfamilies:
Click here to see the enlarged diagram
Sequence view
Top
Protein Modification Legend
Site Record Legend
DSSP Legend
Disorder picture
Sequence view pictures
Secondary structure features calculated by DSSP
Top
DSSPS results
PTM POSITION IN CHAIN TCO KAPPA ALPHA PHI PSI X-CA Y-CA Z-CA
2 0.000 360.0 360.0 360.0 162.8 18.2 45.9 -11.4
Relative accessibilities features calculated by NACCESS
Top
NACCESSES results
PTM POSITION IN CHAIN ALL-ATOMS TOTAL-SIDE MAIN-CHAIN NON-POLAR ALL-POLAR
ABS REL ABS REL ABS REL ABS REL ABS REL
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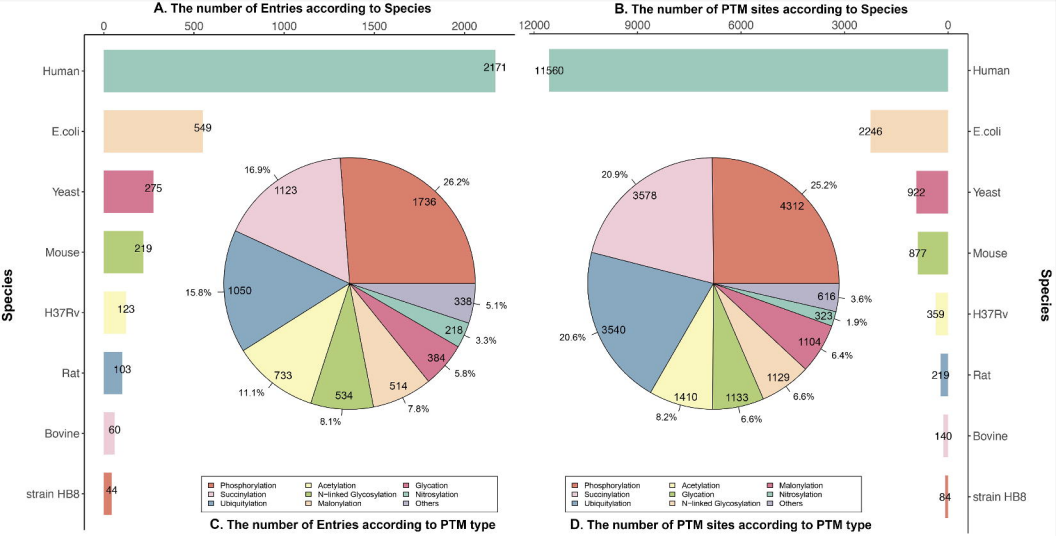
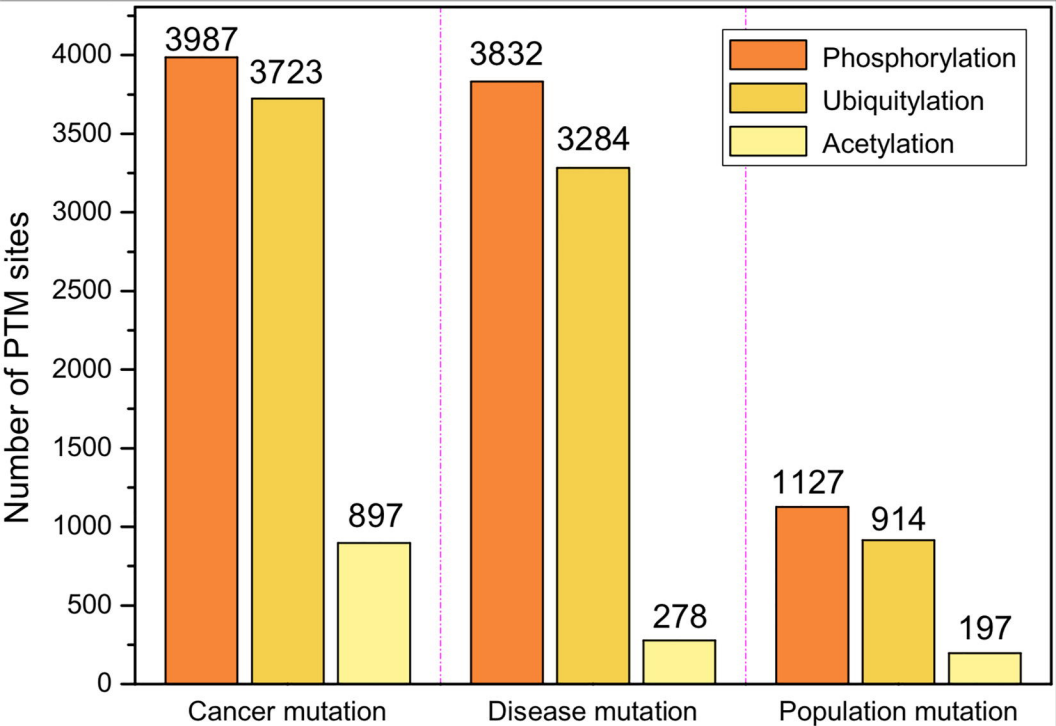
Secondary Structure and accessibilities features
Sequence Alignment
Top
Sequence alignment


A. The number of Entries according to Species
0
500
1000
1500
2000
Species
Human
E.coli
Yeast
Mouse
H37Rv
Rat
Bovine
strain HB8
2171
549
275
219
123
103
60
44
B. The number of PTM sites according to Species
12000
9000
6000
3000
0
11560
2246
922
877
359
219
140
84
C. The number of Entries according to PTM type
26.2%
1736
16.9%
1123
15.8%
1050
5.1%
338
3.3%
218
5.8%
384
7.8%
514
8.1%
534
11.1%
733
Phosphorylation
Succinylation
Ubiquitylation
Acetylation
N-linked Glycosylation
Malonylation
Glycation
Nitrosylation
Others
D. The number of PTM sites according to PTM type
25.2%
4312
20.9%
3578
20.6%
3540
3.6%
616
1.9%
323
6.4%
1104
6.6%
1129
6.6%
1133
8.2%
1410
Phosphorylation
Succinylation
Ubiquitylation
Acetylation
Glycation
N-linked Glycosylation
Malonylation
Nitrosylation
Others


Number of PTM sites
0
500
1000
1500
2000
2500
3000
3500
4000
3987
3723
897
3832
3284
278
1127
914
197
Phosphorylation
Ubiquitylation
Acetylation
Cancer mutation
Disease mutation
Population mutation