Bioinformatics, 39(1), 2023, btac823
https://doi.org/10.1093/bioinformatics/btac823
Advance Access Publication Date: 22 December 2022
Original Paper

Databases and ontologies

PTMint database of experimentally verified PTM regulation on protein–protein interaction

Xiaokun Hong[1], Ningshan Li[2], Jiyang Lv[1], Yan Zhang [1], Jing Li [1]*, Jian Zhang [3]* and Hai-Feng Chen [1]*

[1]State Key Laboratory of Microbial Metabolism, Joint International Research Laboratory of Metabolic & Developmental Sciences, Department of Bioinformatics and Biostatistics, National Experimental Teaching Center for Life Sciences and Biotechnology, School of Life Sciences and Biotechnology, Shanghai Center for Systems Biomedicine, Shanghai Jiao Tong University, Shanghai 200240, China, [2]Department of Bioinformatics and Biostatistics, SJTU-Yale Joint Center for Biostatistics and Data Science, School of Life Sciences and Biotechnology, Shanghai Jiao Tong University, Shanghai, 200240, China and [3]Key Laboratory of Cell Differentiation and Apoptosis of Chinese Ministry of Education, Department of Pathophysiology, Shanghai Jiao-Tong University School of Medicine (SJTU-SM), Shanghai 200025, China

*To whom correspondence should be addressed.
Associate Editor: Peter Robinson

Received on May 25, 2022; revised on December 18, 2022; editorial decision on December 19, 2022; accepted on December 21, 2022

Abstract

Motivation: Post-translational modification (PTM) is an important biochemical process. which includes six most well-studied types: phosphorylation, acetylation, methylation, sumoylation, ubiquitylation and glycosylation. PTM is involved in various cell signaling pathways and biological processes. Abnormal PTM status is closely associated with severe diseases (such as cancer and neurologic diseases) by regulating protein functions, such as protein–protein interactions (PPIs). A set of databases was constructed separately for PTM sites and PPI; however, the resource of regulation for PTM on PPI is still unsolved.

Results: Here, we firstly constructed a public accessible database of PTMint (PTMs that are associated with PPIs) (https://ptmint.sjtu.edu.cn/) that contains manually curated complete experimental evidence of the PTM regulation on PPIs in multiple organisms, including *Homo sapiens*, *Arabidopsis thaliana*, *Caenorhabditis elegans*, *Drosophila melanogaster*, *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*. Currently, the first version of PTMint encompassed 2477 non-redundant PTM sites in 1169 proteins affecting 2371 protein–protein pairs involving 357 diseases. Various annotations were systematically integrated, such as protein sequence, structure properties and protein complex analysis. PTMint database can help to insight into disease mechanism, disease diagnosis and drug discovery associated with PTM and PPI.

Availability and implementation: PTMint is freely available at: https://ptmint.sjtu.edu.cn/.

Contact: haifengchen@sjtu.edu.cn or jian.zhang@sjtu.edu.cn or jing.li@sjtu.edu.cn

Supplementary information: Supplementary data are available at *Bioinformatics* online.

1 Introduction

P - a a a d f ca (PTM) a a b c e ca ce a e e a a . T e e a e e 400 PTM e , f c e a e e d ed, c d a (P), ace a (Ac), e a (Me), a (S), b a (Ub) a d c a (G c). M b ca ce a d a a a cc b e ac f e e (De La R a a d F a , 2010), c a e e a ed b PTM (See *et al.*, 2006). Ab a PTM a e c d ead e e e d ea e [c a A e e' d ea e (La *et al.*, 2008), ca ce (G *et al.*, 2013) a d ca d a c a d ea e (C *et al.*, 2012)] b e a e f c , c a e - e e ac (PPI).

T a d f PTM e f e e a a a e bee de - f ed e ad a ce e a ec e (MS) (C d a a d Ma , 2010; Ga a d C e , 2021; S e *et al.*, 2020). T e ab da PTM da a a e ed b c a a ab e e ce , c a P S eP (H bec *et al.*, 2015), P (Y *et al.*, 2019), P .ELM (D e *et al.*, 2011), dbPTM (L *et al.*, 2022), PLMD (X *et al.*, 2017) a d e e a da aba e, U (U P , 2012). H e e , e e f a e PTM e e , e ec a e PPI e a ed c a f .

U da aba e ffe e 'PTM/P ce ' ec ec d e PTM e a d/ ce e e . H e e, e a e a d f e e e ced e ea c a d b e, a d a ac e f a f PTM e 3D c e . A e da aba e, P S eP (H bec *et al.*, 2015) de PTM effec PPI ba ed e a e L a a c f a e (Ba d *et al.*, 2009), c e ab c de c fa e e e . T da e, e e a a d e ce a e e e ed ed c e PTM f c . PTMf c ed c e PTM effec ba ed e c e a- e d a (Be a *et al.*, 2012). PTMc de ded a d ed c ed f c a a c a be ee PTM ba ed c- e e (M e *et al.*, 2015). A e d ffe e e d, e Mec eb e e ba ed e face a e- a (Be *et al.*, 2015) a d e e F dX f a e ba ed e ca f cef e d (Sc *et al.*, 2005), c e e- fac a PTM e ac ce, e .

W a e ab e c de a , e e e ed e PTM da aba e, a c e e e e e a e f ed PTM effec PPI , c a PTM e a d e , e ac e , de ec e d , a c a ed d ea e a d c - ca a . M e e , de fac a e e e a f PTM e , ec b ed e e e - e a e de ce e e ce a d c e a a . T da a- ba e be e f f e ea c e e e e a a PTM, PPI a d d ea e e e ce a d c e a ec .

2 Materials and methods

2.1 Data sources

T e f f e PTM da aba e c c a F e 1, c d da a c ec a d a a . We def ed e e a e f PTM PPI (Be *et al.*, 2015, 2017; L *et al.*, 2012; L *et al.*, 2021; See *et al.*, 2006; S e a d R ce 2009; Wa *et al.*, 2022): ( ) E a ce: I c ea e aff a d ( ) I b : Dec ea e aff . We e ac ed e f c a PTM e a da c- a ed e a e f U (U P , 2012), PTMD (X *et al.*, 2018), PTMf c (Be a *et al.*, 2012) a d P S eP (H bec *et al.*, 2015) da aba e . We a d aded e e e a e a e P bMed da aba e b ea c e f e- d a d e c b a : *Homo sapiens*, *Arabidopsis thaliana*, *Caenorhabditis elegans*, *Drosophila melanogaster*, *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe*, e , b d, a c a e, e ab e, e ac , e ac , b , d ab e, e e , d c a e, e, PTM, P , Ac, Me, S , Ub a d G c . T e , e c ec ed e f e f e ab e e a 3600 a e ca ef b a c e e e e e a e de ce, c c ded e a PTM e a d e , e ac e , de ec e d , a c a ed d ea e a d c - ca a . B ef , e e a ed e e a be ee PTM a d d ea e ba ed ce a a a d ea e d- e eac e a e. T e , ba ed e de ec e d f PPI , e e a ed e e e ac affec ed b PTM e f e . B e a , e e ab ed e e a a PTM, - e e ac a d d ea e .

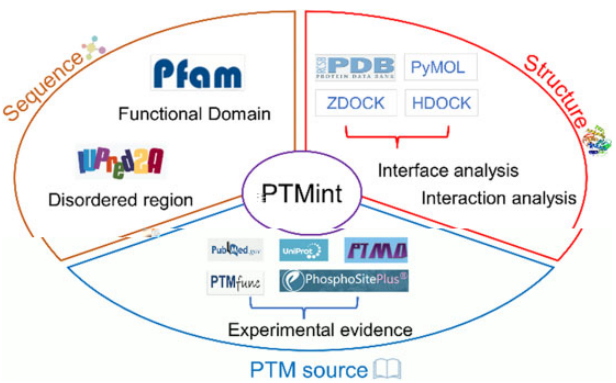

Fig. 1. T e e a de a d c c f PTM da aba e

2.2 Protein sequence analysis

We ea c ed e U da aba e (U P , 2012) b a a ca- ca e e e ce . A d e e e ce d (ea a d d ea f e e d e a d e PTM e) a a e ac ed. T e d de e c e e e ca c a ed b IUP ed2A (Me a *et al.*, 2018). P e e e ce e e a a ed Pfa da aba e b a f c a d a f a (M *et al.*, 2021).

2.3 Protein structure

F d d a e , e d aded e f - e e c e b f A aF d P e S c e Da aba e (A aF d DB) (Va ad *et al.*, 2022). If e e e a - e a 2700 a ac d , e ed A aF d (e 2.1.2) (J e *et al.*, 2021) ed c e d a c e f - e e , e ec e . F e c e e , a e a ed e e ce e e a ed e PDB da aba e (Be a *et al.*, 2000) b a a a dbaa e- a e f 10^{-4}. T e PDB e e e e ec ed acc d e f c e a: ( ) T e PTM e e ed e c e . ( ) T e e a e f ac ed e e ce a a e a e e . ( ) T e ac ed c e e c a e e efe ed. D e e ed c a c e , a a e ca e f e e d c a e f ed b ec a d c- f a e . ZDOCK a fa F e a f -ba ed d c ced e f d e a ea c e f a b e b d de e a a a a d a a ace be ee - e a d e a a e eac e a e e -ba ed c f c (P e ce *et al.*, 2014). HDOCK e b d d c a f e a e de a d f ee d c ba ed e d c a a d a e e de be e e e b d e e f a d e e d c (Ya *et al.*, 2020). P MOL e f ec a d c ba ed e a e a e , c a e e e e f e d c de f e a e a e c e (DeLa , 2010). F de , e ed P MOL (e 2.4.1) b a c e c e ba ed PDB e a e c e. F ec a d c , e ed ZDOCK (e 3.0.2) a d HDOCK (e 1.1) b XL-MS da a (c -) e a e c a f b ed e a e a d ed c ed d a d a e ac ded b IN c da aba e (Me e *et al.*, 2013) a e d c c a . F e e e d c e ded b a f a e , e - f ed e c e e e c e e f a e a e f a d c c e c e.

2.4 Interaction analysis

I e ac a e a a d ed - e f a e (C e a d L , 2007; Wa *et al.*, 2014). T e d b c e ac (HP) def ed e e a ce e f de c a f d b c e d e a e a c ed 6.5 A. T e c a e c a e e ac 11 A a a e e e / a d-b d f ee e e (Q *et al.*, 2010). T , e d a ce be ee e a ce e f c a e e d e e a 11 A, c a c de ed a e e c - a c e ac (ELE). A d e b d (HB) e c e def ed e e d a ce f a ea a e a 3.5 A a d e b d a e a e a 120°. We ed e I e faceRe d e . P c c ea ed b Ve ee J (:// . /) f c e e faceRe d e a a . B ef , P c e c e e ece f e ac c a a d e ca c a e e d ffe e ce be ee e c e -ba ed acce b e face a ea a d e c a - -ba ed acce b e face a ea . If e a e ea e a c ff (e defa 1.0 A2), e e d e a ed a e fac a e d e. T e a e ce a a d ed f PTM e abe e fac a PTM e .

2.5 Secondary structure analysis

T b a e e f e ec da c e f c e c- e a d PTM e , e ec da c e c e a ca c a ed b D c a f P e Sec da S c e a (Kab c a d Sa de , 1983) acc d e e d e- ec f c HB e

ec da c e (π- e , 3, (10)- e , α- e , β-b d e, β- ee , , be d a d c). F f ca , e a e c a f ed f e : ( ) He : π- e , 3, (10)- e a d α- e ; ( ) S ee : β-b d e a d β- ee ; ( ) T : ; ( ) L : be d a d c .

2.6 Score calculation

A e 20 ba c a ac d e , e a ac d a e f e e PTM- d f ed, c a Se e (S), T e e (T), T e (Y), L e (K) a d A e (R). Se e a d T e e ca be d f ed b P a d G c . A d L e ca be d f ed b - e d f ca , c a Ac, Me, S a d Ub. T a e e - a e a e f PTM PPI e *in vivo*, e d ced e a ce c e f PTM e .

T a ce c e a e acc f e be f PTM e a d e ac e a d ca c a ed E a (1).

$$\mathrm{Sc}\ \ e = 2 \sum(\mathrm{PTM}\ \ \mathrm{N}). \quad (1)$$

I c N e be f e c ec f c PTM e e a e .

A d e Sc e ca be a ed E a (2).

$$\begin{aligned} &\mathrm{N}\ \ a\ \ ed\_c\ \ e = 1 - 1/\mathrm{Sc}\ \ e \\ &\mathrm{N}\ \ a\ \ ed\_c\ \ e \in [0.5, 1) \end{aligned} \quad (2)$$

T e a ed_c e ef ec e e a e a ce f ec f c e a PTM e , c c ea e a e be f PTM e e ac e c ea e.

2.7 Database and web interface implementation

T e eb e face e e e ed H e Te Ma La a e (HTML), Ja aSc (JS) a d Ca cad S e S ee . A d e eb f a e a ed b B a 4 f a e . F e e, 3D . a e ed a e e 3D c e (Re a d K e , 2015). A d e PPI e a a a- ed a d a ed b EC a (L *et al.*, 2018). Be de , a f e a d ab e e eb e e e ef ed P .

3 Results

3.1 Database and content

T e c e e f PTM c a 2477 - ed da PTM e 1169 e affec 2371 e e a 357 d ea e . U da aba e de e 425 ec d f PTM ef- fec PPI a d 322 f c a PTM e . PTMD da aba e de e 45 ec d f PTM effec PPI a d 34 f c a PTM e . A d P eP de ea c e efe e ce e a e ba ed e . I e e a e (E a ce a d I b), 'E a ce' a a b e , e a PTM e d c ea e PPI (Tab e 1). I e , e 1 f a PTM e e a e be P (87%) (F . 2A). T e a e a PTM e a e Se e (S), T e e (T) a d T e (Y), c a e a c a e f 87.20% (F . 2B).

A S e e a Tab e S1, f a e e e e a e f e d e a PTM e , 15.82% ca e e e - e e face , e a a e f - e fac a e

Table 1. Summary of PTM effects on PPIs

PTM e	PTM e	E a ce	I b
P a	S, T, Y	2157	968
Ace a	K	170	86
Me a	K, R	81	19
S a	K	53	26
Ub a	K	60	11
G c a	S, T	5	0

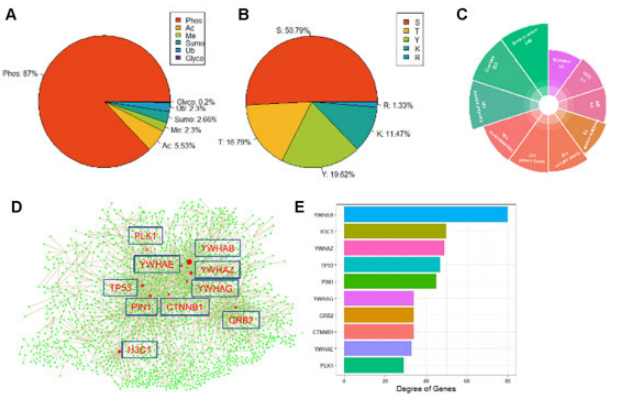

Fig. 2. T e da a e PTM da aba e. S a ca a a e e f PTM e (**A**) a d PTM e (**B**). (**C**) T 10 d ea e affec ed b PTM. (**D**) PTM-a c- a ed PPI e . T 10 e e e de ee e e ed PPI (D) a d a ed ba (**E**)

ca a e a e ec a e ac ; 36.61% ca be f d e f c a d a , ca e a b ca e f PTM d a e f c . I e e f ec da c- e, PTM e e d ca e e e a e a c- ed e (He , S ee a d T) (Tab e S2). Ba ed e f c e ca c a , e c e f PTM e (f ac : 74.54%) 0.5, c d ca e e d f ed b e e f PTM, ca d a e e PPI e c ec ed da a. A d e K10 e f H3C1 e e e e c e f 0.97. Ac f K10 ca e a e f e d f- fe e PPI, c d BAZ1B, BRD7, CHD4, CRH a d TRIM33. I add , e Me f K10 ca e a e 14 d ffe e PPI , c d AGO3, CBX1, CBX3, CDYL, CDYL2, CHAMP1, CHD4, DCAF8, HSFY1, KAT5, MAD2L2, POGZ, UHRF1 a d ZNF470.

T f e de a d e c c a ac e c f PTM- d f ed e a d e ac e , e e a e e e ed e c a f ca acc d e b ca f c (S e e a Tab e S3), a e e a d a - e , e e e e PTM a c a e e e e b - ca ce e a d a a a . I e da aba e, e e a e a 2960 c e c e c 360 c e (f ac : 12.16%) c e f PDB e e e a c e, 203 c e (f ac : 6.86%) f de (P MOL) a d 2397 (f ac : 80.98%) c e f ec a d c (ZDOCK a d HDOCK). Acc d e d c ed e (XL-MS a d d a d a e ac), eac c e a a ed a c f- de ce a e (H , Med L), 32.26% f c e e 'H ' 'Med '.

T e 10 d ea e affec ed b PTM e e c ed a d F e 2C, c a c ded f ee e : ( ) ca ce : b ea ca ce (be : 340), ca ce (be : 323), ce ca ca ce (be : 302), e a c a (be : 136), ca ce (be : 127), c ca ce (be : 119), a e ca ce (be : 76) a d e a ce a ca c a (HCC) (be : 61); ( ) A e ' d ea e (AD) (be : 63); a d ( ) d abe e (be : 52). We a c c ed a PTM-a c a ed PPI e (F . 2D). N de de ee PPI e e e e c e de . T e e ed a e 10 e e e e de ee e e: YWHAB (de ee: 80), H3C1 (de ee: 50), YWHAZ(de ee: 49), TP53 (de ee: 47), PIN1 (de ee: 45), GRB2 (de ee: 34), YWHAG (de ee: 34), CTNNB1 (de ee: 34), YWHAE (de ee: 33) a d PLK1 (de ee: 29) (F . 2D a d E), e a e e e e e e d ea e- ce b ea d e a d a e .

3.2 Web search function

Q c ea c a d ad a ced ea c e e e e ed e e- a e a d 'Sea c ' a e, e ec e e . O e e a e, e e ca d ec ea c e da aba e b e d (c a Ge e, U , PTM, Effec a d O a) (F . 3B). S e e f - e c d , c a Ge e/U , O a a d PTM e ca

be ec f ed e ‘Sea c ’ a e (F . 3B). Ta ‘CTDP1’ e e a a e a e, e ea c ed e be a ab a f a, c d O a , Ge e, U , PTM, S e, AA, I _ , I _ e e, Effec , PMID a d De a (F . 3B). H e f U a d P bMed a e ded. A d e e f de a ed e ca be b c c e ‘S ’ b , e ec e (F . 3B).

T e ca e a e c f a ec (F . 3C), c d e e e (c a a , e a e, e c e a d e d a f a), e fea e (d- de a a), PTM PPI , e ac e , a ce c e f PTM e a d c e a a . I ‘PTM PPI ’ ec , c- e e e e a e de ce a d c e, e a a e e e- a ed (c a e e PTM e ca ed e e face e d a , c e), c ca be a ed ea c ed, ea . I ‘C e a a ’ ec , c e c e ca e f PDB da aba e (Be a *et al.*, 2000) a d ca ec a d c . A d PTM e a d e e e a ed e c e. A d e ca ea a a e a d c c e . F e, e e- ac (HB, HP a d ELE) ca c a ed b - e f a e (C e a d L , 2007; Wa *et al.*, 2014) a e a ab a f a . I e faceRe d e a a ca c a ed a a e e a a ca- f PTM e . ‘D ad’ f c a ded f e d ad e fea e a d a c e f a c ed f c e c e , e faceRe d e a d e ac . We a ded e e a e e a , c a U da aba e (U P , 2012), A aF d da aba e (Va ad *et al.*, 2022), Pfa da aba e (M *et al.*, 2021) a d P bMed da aba e b c c de ed .

3.3 Web browse function

T e PTM e a d e e e e ed a d a ed a abe ca de , c a e e c b a e e ed e (F . 3A).

3.4 Web download and help function

A da a e PTM da aba e ca be d aded e ‘D ad’ a e, c d PTM e e e a e de ce a d e c e f a . A d de a ed c e e a a ab e e ‘He ’ a e.

4 Discussion

T ed e, PTM da aba e e f c e e e da a- ba e f e e a e de ce f e PTM effec PPI , c c de c e e e e a ec d , c a PTM e a d e , e ac e , de ec e d , a c a ed d- ea e a d c- ca a , b a e a e e acc d e e ce a d c e a a (c a ec a d c a d e ac a a), e a ca .

PTM e e e c ed ec e ba ed a e a a d a a c e (C e , 2002; H e , 1995). A d e a e e a e d ffe e PTM e a ca a e , c a ca ce a d a (X *et al.*, 2022). F e a e, L e (K) ca e ec e be ace a ed, e a ed b a ed. Se e (S) ca be a ed c a ed. I add , e f d e ec f c PTM e a e f e e , ca e a e e e a - e c ec ed da a. F e a e, -S289 MDM4 ca a e d ce MDM4-MDM2 a d MDM4- 53 e ac- (W *et al.*, 2012). Be a2 e P T 758 ac a a - ec a c b f a b d a d e a ce e 14-3-3 e b d e e c a c d a (Ta a a *et al.*, 2008). F e e, 14-3-3 e , c c a a e -b d d a (PPBD), ca b d -T32 FOXO3 (S *et al.*, 2010), -S253 FOXO3 (S *et al.*, 2010), -T642 TBC1D4 (Ra *et al.*, 2006), -S939 TSC2 (Ca *et al.*, 2006), -S981 TSC2 (Ca *et al.*, 2006) a d -S99 BAD (P e *et al.*, 2009) e PI3K-A a a a . I de a e e e f e a e , a e a e f e e a e a ed acc d e a ce c e, c ca c- a ed b PTM e a d e c . H e c e ea e a e d ea e ce a d e a d a e . F e a e, e Y654 f CTNNB1 a a c e f 0.93, b P b I a b ffe ed a e a e c a e a e c c e d e e a (CML) (C cc a *et al.*, 2007), c a acc d PTM-a c a ed PPI e e (F . 2D a d E). Acc d e e (Be *et al.*, 2017; S *et al.*, 2001; S *et al.*, 2008), PTM e c ca ed e e face be ee e , ca e a e e e ac . We ed e e PTM e c ca ed e e face, ca a e- a ce b e ac . T e ef e, e a a ed a e c e a d e face a ac d . T e, b e fac a a d - e fac a e e e e a e (S e e a Tab e S1). F e a e, -Y47 Fe65 c ca e e

e d e a d e PTM e) c d be a a d c a e e .

D e e ed c a c e , e e a f a e a d eb- e e ffe e b ec a d c , c a ZDOCK (P e ce *et al.*, 2014), HDOCK (Ya *et al.*, 2020), C P (K a *et al.*, 2017) a d HADDOCK (a Z de *et al.*, 2016). I de e e e acc ac f d c e , a a e ca e f ec a d c a e f ed c b ed e e e a XL-MS da a (c -) a d ed c ed d a d a e ac . F e e, e a a a ed e e ac (HB, HP a d ELE) e e ea c e be e de a d e PTM e d ea e. C a e f e ac (c a HB, HP a d ELE) a d c e (c a a e , d de - - de , e ec a c e a a d d - a c c e a e) d ced b PTM ca e a PTM c d e a e PPI a d d ea e e (De a a d *et al.*, 2018; L a d J -B , 2017). T e ef e, da aba e de a a ab e c a ba f f e e a , c a ec a d a c a (MD) a d Ma a e de (MSM). F e e, de e e f a ec f c f cef e d f e a f e e c e (P a a *et al.*, 2020) d f ed b e PTM e c d be a a ab e e ea c f ed. A e a c- a e e e b a ed ba ed c ec ed da a (Tab e 1, S e e a Tab e S1 S3), b be e a b a ed d e e ed PTM e a d e - d ed e .

PTM da aba e ca be f e ed e f a ec . F , e c e e f e da aba e c a a de a a d PTM e . M e a a d PTM e be added. Sec d, add a c a , c a PTM- a e ed d , PTM e e a a , PTM-a c a ed a a a a d a c a be ee PTM a d a be e a ed. T d, e e ace e a ed c ed c e c e e e - e c e c e a e e ea ed e PDB da aba e. I e f e, e c a a a a d - da e e PTM da aba e, e e e a PTM e a e e ed e e a e.

I c c , e de e ed PTM , a c e e e da aba e

M ,J. *et al.* (2021) Pfa : e e fa e da aba e 2021. *Nucleic Acids Res.*, **49**, D412 D419.
P a a,S. *et al.* (2020) De e e f a f ce e d f e a f e-c a e a d e - e c e e. *J. Chem. Theory Comput.*, **16**, 2494 2507.
P e ce,B.G. *et al.* (2014) ZDOCK e e : e ac e d c ed c f e - e c e e a d e c e . *Bioinformatics*, **30**, 1771 1773.
P e ,L. *et al.* (2009) Ide ca f e a e f e a a c e BAD: e-f ac f BAD e - a ed b a . *J. Biol. Chem.*, **284**, 28004 28020.
Q ,F. *et al.* (2010) I d ced c f a a e ec f RNA/U1A f d- . *RNA*, **16**, 1053 1061.
Ra ,G. *et al.* (2006) A e f 14-3-3 - a ed GLUT4 a - ca e ac e RabGAP AS160. *J. Biol. Chem.*, **281**, 29174 29180.
Re ,N. a d K e ,D. (2015) 3D . : ec a a a WebGL. *Bioinformatics*, **31**, 1322 1324.
Sc ,J. *et al.* (2005) T e F dX eb e e : a e f ce e d. *Nucleic Acids Res.*, **33**, W382 W388.
See ,B.T. *et al.* (2006) Read e d ca e ac d a . *Nat. Rev. Mol. Cell Biol.*, **7**, 473 483.
S ,W.X. *et al.* (2001) S c a a a f ade e b a fe - a e f *Saccharomyces cerevisiae*. *Biochemistry*, **40**, 10800 10809.
S ,A. *et al.* (2010) P e a a e 2A eac a e FOXO3a a d a c e a 14-3-3 a d AKT. *Mol. Biol. Cell.*, **21**, 1140 1152.
S ,C.Y. *et al.* (2008) Se e 88 a f e 8- Da d e c a 1 a ec a c f d e a a a d f c . *J. Biol. Chem.*, **283**, 4004 4013.
S e ,T.M. a d R ce,J.C. (2009) Ide ca a d c a ac e a f - a a a d ca - ec c b d e b a a a e e ed ca a . *Proc. Natl. Acad. Sci. USA*, **106**, 14808 14813.
S e ,J.J. *et al.* (2020) D ec e ce a a a ec e -ba ed e c . *Curr. Opin. Cell Biol.*, **63**, 20 30.
Ta a a,H. *et al.* (2008) Be a2 e a T 758 ac a a ec a c e a e 14-3-3 a d a b d . *Blood*, **112**, 1853 1862.
U P ,C. (2012) Re a e e ace a e e a e e- ce (U P). *Nucleic Acids Res.*, **40**, D71 D75.
a Z de ,G.C.P. *et al.* (2016) T e HADDOCK2.2 eb e e : e -F e d e a e de f b ec a c e e. *J. Mol. Biol.*, **428**, 720 725.
Va ad ,M. *et al.* (2022) A aF d e c e da aba e: a e e a d e c a c e a e f e - e e ce ace -acc ac de . *Nucleic Acids Res.*, **50**, D439 D444.
Wa ,C. *et al.* (2020) GPS 5.0: a da e e ed c f a e- ec c a e e . *Genomics Proteomics Bioinformatics*, **18**, 72 80.
Wa ,S. *et al.* (2022) U c e - a a a d ca -a c a ed e - e e ac . *Curr. Opin. Struct. Biol.*, **74**, 102352.
Wa ,W. *et al.* (2014) Ne f ce e d de ca d de ed e .) *Chem. Biol. Drug Des.*, **84**, 253 269.
W ,S. *et al.* (2012) Ca e a e 1a a e a e a MDMX a ec a e ac a e 53 b d . *Mol. Cell. Biol.*, **32**, 4821 4832.
X ,H. *et al.* (2018) PTMD: a da aba e f a d ea e-a c a ed - a - a a d ca . *Genomics Proteomics Bioinformatics*, **16**, 244 251.
X ,H.D. *et al.* (2017) PLMD: a da ed da a e ce f e e d - ca . *J. Genet. Genomics*, **44**, 243 250.
X ,P. *et al.* (2022) E c e a a a e-2 c ba a a d c c d e d ea e b e de e a d ca e e - a . *Cell Metab.*, **34**, 299 316.e6.
X e,Y. *et al.* (2005) GPS: a c e e e e e f a e ed c . *Nucleic Acids Res*, **33**, W184 W187.
Ya ,Y.M. *et al.* (2020) T e HDOCK e e f e a ed e - e d c . *Nat. Protoc.*, **15**, 1829 1852.
Y ,K. *et al.* (2019) P : a da aba e f e a d a c a . *Nucleic Acids Res.*, **47**, D451 D458.