

Posttranslační modifikace a jejich význam

C2138 Pokročilá bioinformatika, jaro 2022

Proteom a proteomika

- **Proteom** – soubor všech forem proteinů existujících v buňce (organismu, biologickém vzorku) v určitém čase a za určitých podmínek.
- **Proteomika** – studium proteomů.
- **Proteomika** – věda zabývající se komplexní analýzou proteinů (identifikace, exprese, charakterizace).
- **Proteomika** – analýza proteinů ve velkém rozsahu (struktura, funkce, interakce).
- **Proteomika** – vyžaduje separační techniky, hmotnostní spektrometrii, bioinformatiku, databáze genů a proteinů.

Proteom a proteomika

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Množství kovalentních forem proteinů přesahuje množství proteinů predikovaných z DNA (genom).
Proteomy jsou složitější než **genomy**.
1 genom – mnoho proteomů.
- **1 gen může být exprimován ve více než 20 různých variantách proteinu. Například α 1-antitrypsin se může vyskytovat ve 22 různých formách.**
- **25 000 genů – 0,5 - 1 milion proteinů.**



Proteom a proteomika

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Proteomy jsou složitější než **genomy**.
1 genom – mnoho proteomů.
- Navýšení kódovací kapacity genomu: **alternativní sestřih, posttranslační modifikace (PTM)**.



Posttranslační modifikace

- **Posttranslační modifikace** – kovalentní modifikace proteinů po transkripci DNA a translaci RNA.
Posttranslační modifikace – probíhají i u prokaryot
Posttranslační modifikace jsou prováděny **enzymy**. Enzymy rozeznávají specifické signály – aminokyselinové sekvence v proteinech. Identifikace těchto sekvenčních motivů umožňuje predikci PTM.
Člověk: 500 proteinkinas, 150 proteinfosfatas, 500 proteas.
5 % genomu vyšších eukaryot – zapojení do PTM.
- **Klasifikace posttranslačních modifikací** – typ modifikované aminokyseliny, podle modifikujícího enzymu, reverzibilita modifikací.

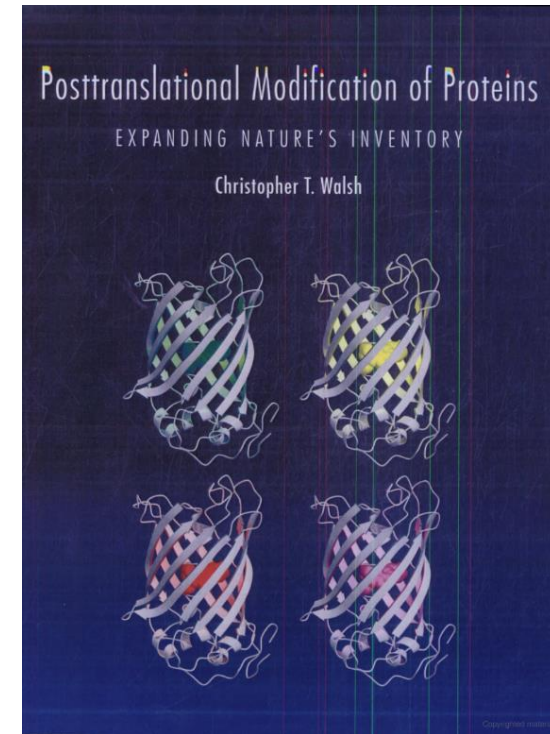
Posttranslační modifikace - typy

Table 1: Posttranslational protein modifications at the side chains.^[a]

Residue	Reaction	Example
Asp	phosphorylation	protein tyrosine phosphatases; response regulators in two-component systems
	isomerization to isoAsp	
Glu	methylation	chemotaxis receptor proteins
	carboxylation	Gla residues in blood coagulation
	polyglycination	tubulin
	polyglutamylolation	tubulin
Ser	phosphorylation	protein serine kinases and phosphatases
	O-glycosylation	notch O-glycosylation
	phosphopantetheinylation	fatty acid synthase
	autocleavages	pyruvamide enzyme formation
Thr	phosphorylation	protein threonine kinases/phosphatases
	O-glycosylation	
Tyr	phosphorylation	tyrosine kinases/phosphatases
	sulfation	CCRS receptor maturation
	<i>ortho</i> -nitration	inflammatory responses
	TOPA quinone	amine oxidase maturation
His	phosphorylation	sensor protein kinases in two-component regulatory systems
	aminocarboxypropylation	diphthamide formation
	N-methylation	methyl CoM reductase
Lys	N-methylation	histone methylation
	N-acylation by acetyl, biotinyl, lipoyl, ubiquityl groups	histone acetylation; swinging-arm prosthetic groups; ubiquitin; SUMO (small ubiquitin-like modifier) tagging of proteins
	C-hydroxylation	collagen maturation

Cys	S-hydroxylation (S-OH)	sulfenate intermediates
	disulfide bond formation	protein in oxidizing environments
	phosphorylation	PTPases
	S-acylation	Ras
	S-prenylation	Ras
Met	protein splicing	intein excisions
	oxidation to sulfoxide	Met sulfoxide reductase
Arg	N-methylation	histones
	N-ADP-ribosylation	G _{5a}
Asn	N-glycosylation	N-glycoproteins
	N-ADP-ribosylation	eEF-2
	protein splicing	intein excision step
Gln	transglutamination	protein cross-linking
Trp	C-mannosylation	plasma-membrane proteins
Pro	C-hydroxylation	collagen; HIF-1 α
Gly	C-hydroxylation	C-terminal amide formation

[a] No modifications of Leu, Ile, Val, Ala, Phe side chains are known. A more extensive list can be found in reference [3].



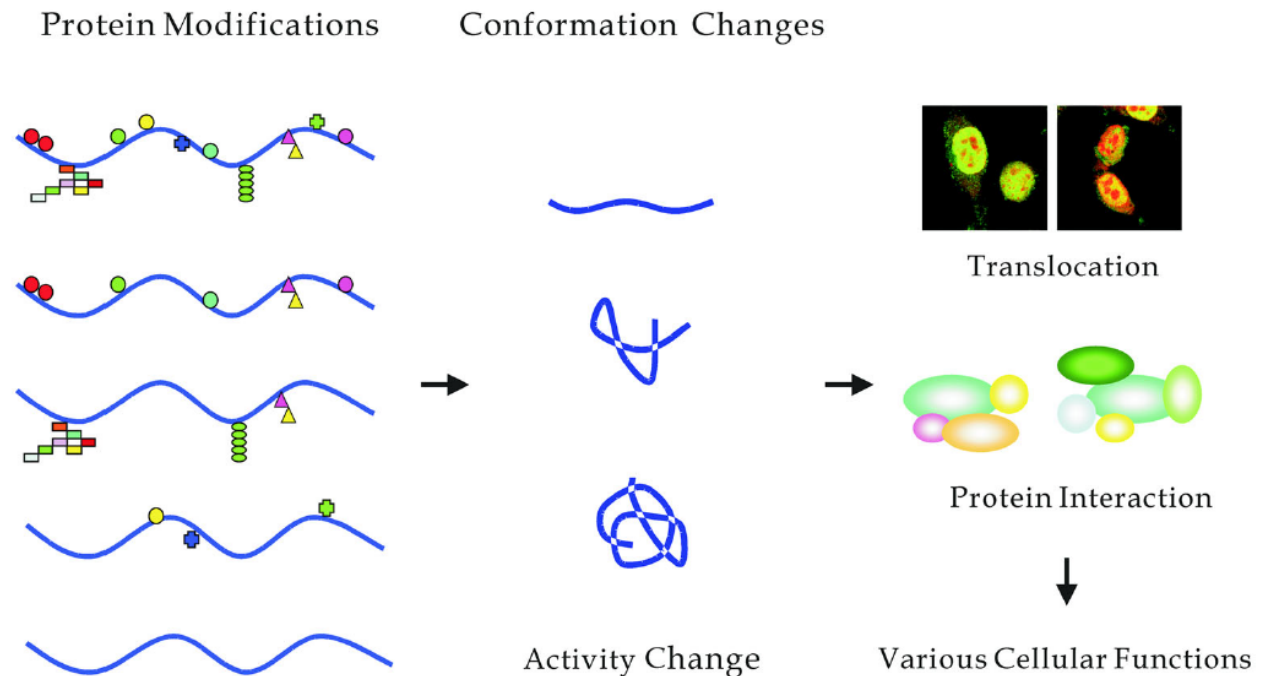
Protein Posttranslational Modifications: The Chemistry of Proteome Diversifications

Christopher T. Walsh,* Sylvie Garneau-Tsodikova, and Gregory J. Gatto, Jr.

DOI: 10.1002/anie.200501023

Posttranslační modifikace - význam

- Ovlivňují **3D a 4D strukturu** proteinů, **aktivitu a funkci** (rozpustnost, stabilita, interakce, vypnuto/zapnuto).
- Mohou ovlivňovat **lokalizaci** proteinu v buňce (prenylace a jiné – připojení hydrofobní skupiny umožňuje lokalizaci do membrány).
- Tvorba disulfidických můstků může být nezbytná pro správné **sbalení** proteinů.
- Význam pro **imunitní systém** – glykosylace.

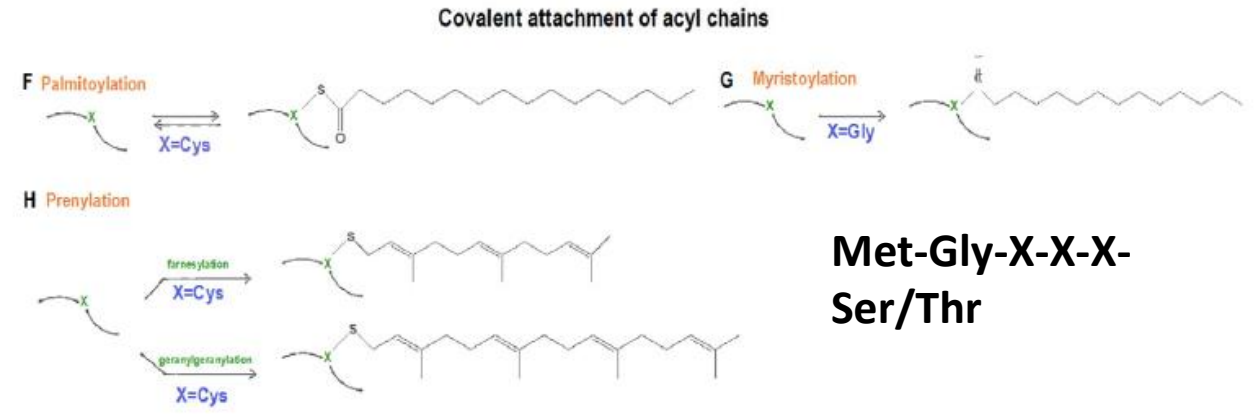


Post-translational Modifications and Their Biological Functions:
Proteomic Analysis and Systematic Approaches

Posttranslační modifikace - příklady

- Kovalentní připojení malé molekuly (funkční skupiny):
- Fosforylace (serin, threonin, tyrosin, histidin, arginin, lysin), aktivace/inhibice enzymů. **Nejstudovanější PTM.**
- Glykosylace (N-glykosylace, O-glykosylace, GPI kotva, C-mannosylace).
- S-nitrosylace (cystein). **Neenzymatické připojení NO. Vazba je labilní, náročná experimentální identifikace!**

- Kovalentní připojení acylových řetězců:



- Kovalentní připojení malých proteinů:
- Ubikvitinace (lysín). Regulace odbourávání proteinů, regulace funkce proteinů.

Protein post-translational modifications: *In silico* prediction tools and molecular modeling

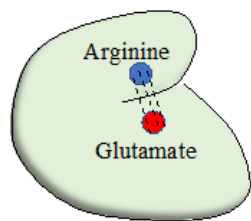
Martina Audagnotto*, Matteo Dal Peraro*

Institute of Bioengineering, School of Life Sciences, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland
Swiss Institute of Bioinformatics (SIB), Lausanne, Switzerland

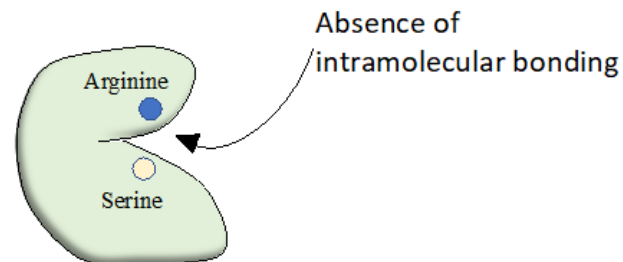
Posttranslační modifikace - příklady

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- Fosforylace (serin, threonin, tyrosin, histidin, arginin, lysin), aktivace/inhibice enzymů. **Nejstudovanější PTM.**

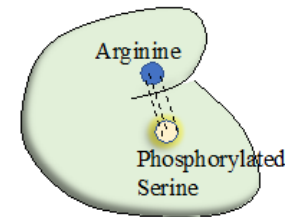
- Ovlivňují **3D a 4D strukturu** proteinů, **aktivitu a funkci** (rozpuštěnost, stabilita, interakce, vypnuto/zapnuto).



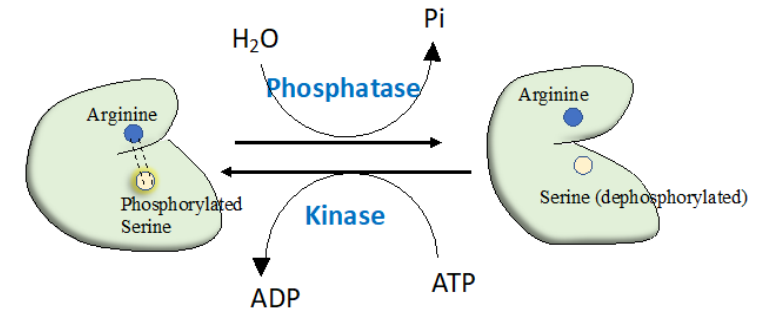
1
Ion pair formation between Arginine and Glutamate stabilizes the fold



2
Substitution of Glutamate with Serine leads to loss of intramolecular bonding and loss of functional fold



3
Phosphorylated Serine can substitute for Glutamate and ion pair forms again stabilizing the proteins conformation



Posttranslační modifikace - význam

Table 1 Golgi PTMs and associated diseases. This table summarizes all the human disorders linked to Golgi PTMs presented in this review

Affected gene	Protein	Affected PTM	Disease	Major clinical manifestations	Gene OMIM entry	Disease OMIM entry
MAN1B1	α 1,2 mannosidase	glycosylation	MAN1B1-CDG	severe mental retardation, delayed speech	604346	614202
SLC35A1	CMP-sialic acid transporter	glycosylation	SLC35A1-CDG	seizures, intellectual disability, ataxia, bleeding	605634	603585
SLC35A2	UDP-galactose transporter	glycosylation	SLC35A2-CDG	intellectual disability, seizures, skeletal abnormalities	314375	300896
SLC35A3	UDP-GlcNAc transporter	glycosylation	Arthrogyposis, mental retardation and seizures	autism spectrum disorder, hypotonia, epilepsy, and arthrogyposis	605632	615553
SEC23B	Sec23 homolog B	glycosylation	Dyserythropoietic anemia, congenital, type II	erythroblastic anemia: splenomegaly, gallstones, and iron overload potentially with liver cirrhosis or cardiac failure.	610512	224100
TRIP11	Golgi microtubule associated protein 210	glycosylation	Achondrogenesis type 1A	severe chondrodysplasia, lethal before or shortly after birth	604505	200600
UBE3A	Ubiquitin ligase E3A	glycosylation	Angelman syndrome	intellectual disability, seizures, lack of speech, and characteristic abnormal behavior	601623	105830
COG2	Component of oligomeric Golgi complex 2	glycosylation	COG2-CDG	microcephaly, developmental delay, intellectual disability, seizures, facial dysmorphism, liver dysfunction	606974	no entry yet
SLC33A1	Solute carrier family 33 (acetyl-CoA transporter), member 1	acetylation	Spastic paraplegia-42	spastic gait, increased lower limb tone, weakness and atrophy of the lower limb muscles, pes cavus	603690	612539
CHST3	Chondroitin 6-O-sulfotransferase	sulfation	Spondylo-epiphyseal dysplasia with joint dislocations	unusual skeletal dysplasia	603799	143095
CHST6	Corneal N-acetylglucosamine-6-O-sulfotransferase	sulfation	Macular corneal dystrophy type II	progressive corneal opacification and reduced corneal sensitivity	605294	217800
CHST8	GalNAc-4-O sulfotransferase I	sulfation	Peeling skin syndrome	general skin peeling	610190	270300
CHST14	Dermatan sulfate GalNAc-4-O sulfotransferase I	sulfation	Ehlers-Danlos syndrome musculocontractural type 1	craniofacial dysmorphism, congenital contractures of thumbs and fingers, clubfeet, severe kyphoscoliosis	608429	601776
ARSE	Arylsulfatase E	sulfation	Chondrodysplasia punctata 1	stippled epiphyses, brachytelephalangy, nasomaxillary hypoplasia	300180	302950
PAPPS2	PAPS synthase	sulfation	Brachyolmia type 4	short-trunk stature, rectangular vertebral bodies, precocious calcification of rib cartilages, short femoral neck. Early death for severe cases.	603005	612847
SLA26A2	Sulfate anion transporter	sulfation	Achondrogenesis type 1B	severe chondrodysplasia, early death of respiratory failure	606718	600972
			Atelosteogenesis type 2	pulmonary hypoplasia, lethal in infants	606718	256050
			Epiphyseal dysplasia multiple 4	joint pain, scoliosis, malformations of the hands, feet, and knees	606718	226900
			Diastrophic dysplasia	scoliosis, clubfeet, malformed pinnae with calcification of the cartilage, cleft palate in some cases	606718	222600
GNTPG	N-acetylglucosamine-1-phosphotransferase gamma subunit	phosphorylation	Mucopolidosis III gamma	short stature, skeletal abnormalities, cardiomegaly, and developmental delay	607838	252605

Posttranslační modifikace - význam

Table 1 (continued)

Affected gene	Protein	Affected PTM	Disease	Major clinical manifestations	Gene OMIM entry	Disease OMIM entry
GNTPAB	N-acetylglucosamine-1-phosphotransferase alpha and beta subunits	phosphorylation	Mucopolipidosis II and III	Hip dislocation, gingival hyperplasia, thoracic deformities and hernia soon after birth. Delayed psychomotor development. Same clinical features for mucopolipidosis III as described just above.	607840	252500 252600
IMPAD1	Golgi-resident PAP phosphatase	phosphorylation	Chondrodysplasia with joint dislocations	short stature, chondrodysplasia with brachydactyly, congenital joint dislocations, micrognathia, cleft palate, and facial dysmorphism	614010	614078
INPP5E	Inositol polyphosphate-5-phosphatase	phosphorylation	Morn syndrome	Mental retardation, truncal obesity, retinal dystrophy, and micropenis	613037	610156
		phosphorylation	Joubert syndrome 1	Heterogenous: hypoplasia of the cerebellar vermis with the characteristic neuroradiologic molar tooth sign, dysregulation of breathing pattern and developmental delay.	613037	213300
AKAP9	A-kinase anchor protein 9	phosphorylation	Long QT syndrome-11	recurrent syncope, seizure, or sudden death	604001	611820
FAM20C	Golgi kinase (family with sequence similarity 20, member C)	phosphorylation	Raine syndrome	neonatal osteosclerotic bone dysplasia, increased ossification of the skull	611061	259775
CAMKMT	Calmodulin-lysine N-methyltransferase	methylation	2p21 deletion syndrome	cystinuria, neonatal seizures, hypotonia, severe somatic and developmental delay, facial dysmorphism	609559	606407
MBTPS2	Site-2 protease	proteolytic cleavage	IFAP syndrome with or without BRESHECK syndrome	ichthyosis follicularis, atrichia, and photophobia	300294	308205
			Olmsted syndrome, X-linked	periorificial keratotic plaques and bilateral palmoplantar transgredient keratoderma	300294	300918
			keratosis follicularis spinulosa decalvans, X-linked	keratosis pilaris, progressive cicatricial alopecia of the scalp, eyebrows, and eyelashes	300294	308800
ZDHHC8	Zinc finger, DHHC-type containing 8	palmitoylation	Schizophrenia susceptibility	hallucinations and delusions, inappropriate emotional responses, disordered thinking and concentration, erratic behavior	608784	181500
ZDHHC9	Zinc finger, DHHC-type containing 9	palmitoylation	X-linked mental retardation (Raymond type)	general intellectual limitations associated with impairments in adaptive behavior	300646	300799
ZDHHC15	Zinc finger, DHHC-type containing 15	palmitoylation	X-linked mental retardation-91	general intellectual limitations associated with impairments in adaptive behavior	300576	300577
PPT1	Palmitoyl-protein thioesterase 1	palmitoylation	Neuronal ceroid lipofuscinosis 1	Heterogenous: progressive dementia, seizures, and progressive visual deficiency. The cellular phenotype includes intracellular accumulation of autofluorescent lipopigment storage material.	600722	256730

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OMIM® - Online Mendelian Inheritance in Man®

Welcome to OMIM®, Online Mendelian Inheritance in Man®. OMIM is a comprehensive, authoritative compendium of human genes and genetic phenotypes that is freely available and updated daily. The full-text, referenced overviews in OMIM contain information on all known mendelian disorders and over 15,000 genes. OMIM focuses on the relationship between phenotype and genotype. It is updated daily, and the entries contain copious links to other genetics resources.

This database was initiated in the early 1960s by Dr. Victor A. McKusick as a catalog of mendelian traits and disorders, entitled Mendelian Inheritance in Man (MIM). Twelve book editions of MIM were published between 1966 and 1998. The online version, OMIM, was created in 1985 by a collaboration between the National Library of Medicine and the William H. Welch Medical Library at Johns Hopkins. It was made generally available on the internet starting in 1987. In 1995, OMIM was developed for the World Wide Web by NCBI, the National Center for Biotechnology Information.

OMIM is authored and edited at the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, under the direction of Dr. Ada Hamosh.

NLM's Profiles in Science -- The McKusick Papers

Searching Online Mendelian Inheritance in Man (OMIM): A Knowledgebase of Human Genes and Genetic Phenotypes

Joanna S. Amberger¹ and Ada Hamosh

McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21287, Tel. 410-955-0313, Fax. 410-955-4999

Abstract

Online Mendelian Inheritance in Man (OMIM) at OMIM.org is the primary repository of comprehensive, curated information on genes and genetic phenotypes and the relationships between them. This unit provides an overview of the types of information in OMIM and optimal strategies for searching and retrieving the information. OMIM.org has links to many related and complementary databases providing easy access to exploring more information on a topic. The relationship between genes and genetic disorders is highlighted in this unit. The basic protocol explains searching OMIM both from a gene then clinical features perspective. Two alternate protocols provide strategies for viewing gene-phenotype relationships as a gene map table and clinical features as a Quick View or Side-by-Side format. OMIM.org is updated nightly and the MIMmatch service, described in the Support Protocol, provides a convenient way to follow updates to entries, gene-phenotype relationships, and collaborate with other researchers.

OMIM databáze – geny a geneticky podmíněné choroby



<https://omim.org>

Posttranslační modifikace - význam

603585

CONGENITAL DISORDER OF GLYCOSYLATION, TYPE II_f; CDG2_F

Alternative titles; symbols
CDG II_f; CDGII_f

▼ Clinical Features

Willig et al. (2001) reported a 4-month-old boy who presented with a spontaneous massive bleed in the posterior chamber of the right eye along with cutaneous hemorrhages. Laboratory studies showed marked thrombocytopenia and neutropenia. The patient experienced multiple episodes of bleeding over the next 30 months, including severe pulmonary hemorrhage. He also had multiple recurrent bacterial infections. Bone marrow transplantation was performed at age 34 months, but the patient died of complications at age 37 months.

Macrothrombocytopenia with abnormal demarcation membranes in megakaryocytes and neutropenia with a complete lack of sialyl-Lewis-X antigen in leukocytes--a new syndrome?

Willig TB, Breton-Gorius J, Elbim C, Mignotte V, Kaplan C, Mollicone R, Pasquier C, Filipe A, Miélot F, Cartron JP, Gougerot-Pocidallo MA, Debili N, Guichard J, Dommergues JP, Mohandas N, Tchernia G. Blood. 2001 Feb 1;97(3):826-8. doi: 10.1182/blood.v97.3.826. PMID: 11157507 [Free article.](#)

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* 606672

GLYCOPROTEIN Ib, PLATELET, ALPHA POLYPEPTIDE; GP1BA

Alternative titles; symbols

GP Ib, ALPHA SUBUNIT
PLATELET GLYCOPROTEIN Ib, ALPHA POLYPEPTIDE
CD42B

▼ Biochemical Features

By detailed laboratory analysis of a patient with thrombocytopenia and recurrent infections, Willig et al. (2001) found markedly decreased amounts of platelet membrane GP Ib (see GP1BA, 606672) and undetectable sialyl-Lewis-X on the surface of neutrophils, suggesting a defect in the posttranslational modification of glycoproteins. Martinez-Duncker et al. (2005) noted that the plasma of the patient reported by Willig et al. (2001) showed a normal sialylation pattern of transferrin (TF; 190000) and other major serum glycoproteins. The phenotype was due to the lack of sialyl-Lewis-X, which has considerable roles in cell-to-cell interactions, such as infections and megakaryocytic immaturity, that were defective in this patient.

▼ Molecular Genetics

In a patient originally described by Willig et al. (2001), Martinez-Duncker et al. (2005) identified compound heterozygosity for 2 mutations in the SLC35A1 gene (605634.0001; 605634.0002). Martinez-Duncker et al. (2005) referred to this disorder as CDG type II_f.

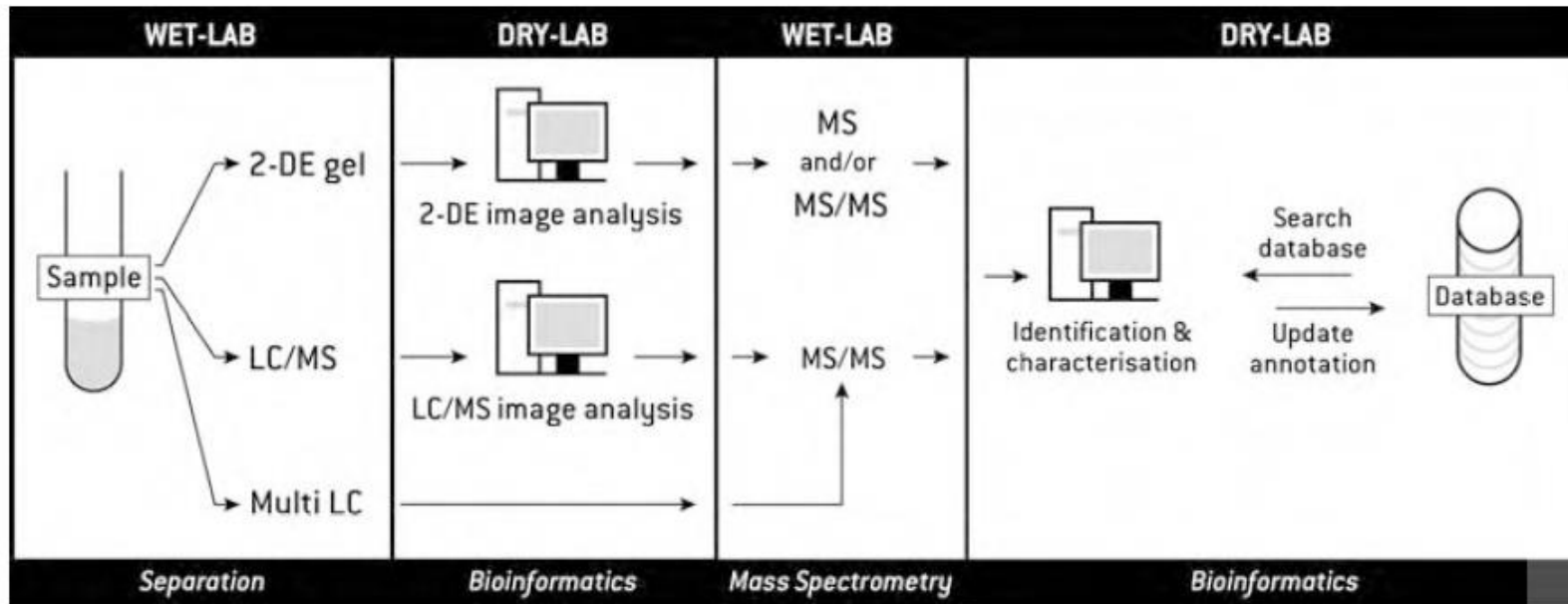
* 605634

SOLUTE CARRIER FAMILY 35 (CMP-SIALIC ACID TRANSPORTER), MEMBER 1; SLC35A1

The SLC35A1 gene encodes a CMP-sialic acid transporter located within the membrane of the Golgi apparatus. The transporter moves nucleotide sugars across the membrane for use in glycosylation reactions that take place within the Golgi department (Eckhardt et al., 1996).

Posttranslační modifikace a proteomika

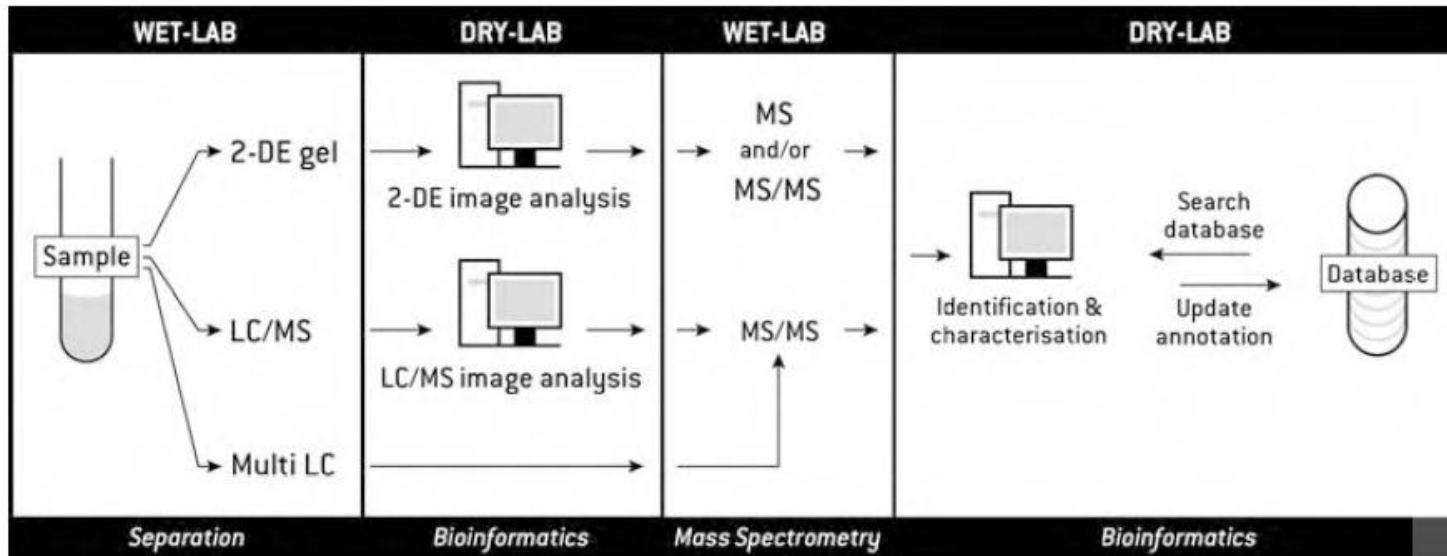
- **Proteomika** – vyžaduje separační techniky, hmotnostní spektrometrii, bioinformatiku, databáze genů a proteinů.
- **Proteomika** – diagnostika (markery), „drug targets“, zkoumání vlivu léčiv na organismus. Podmíněno schopností identifikovat, charakterizovat a kvantifikovat výskyt jednotlivých proteinů v komplexním vzorku.



Posttranslační modifikace

Experimentální identifikace

- Problémy při identifikaci posttranslačních modifikací:
modifikovaná je jen **frakce** proteinu (nízká koncentrace, nutné citlivé metody), kovalentní vazba PTM je **labilní** – nemusí vydržet zpracování vzorku a analýzu.
- **Identifikace a analýza PTM: kombinace separační metody a MS analýzy.**



2-DE, 2D-PAGE

Dvourozměrná gelová elektroforéza

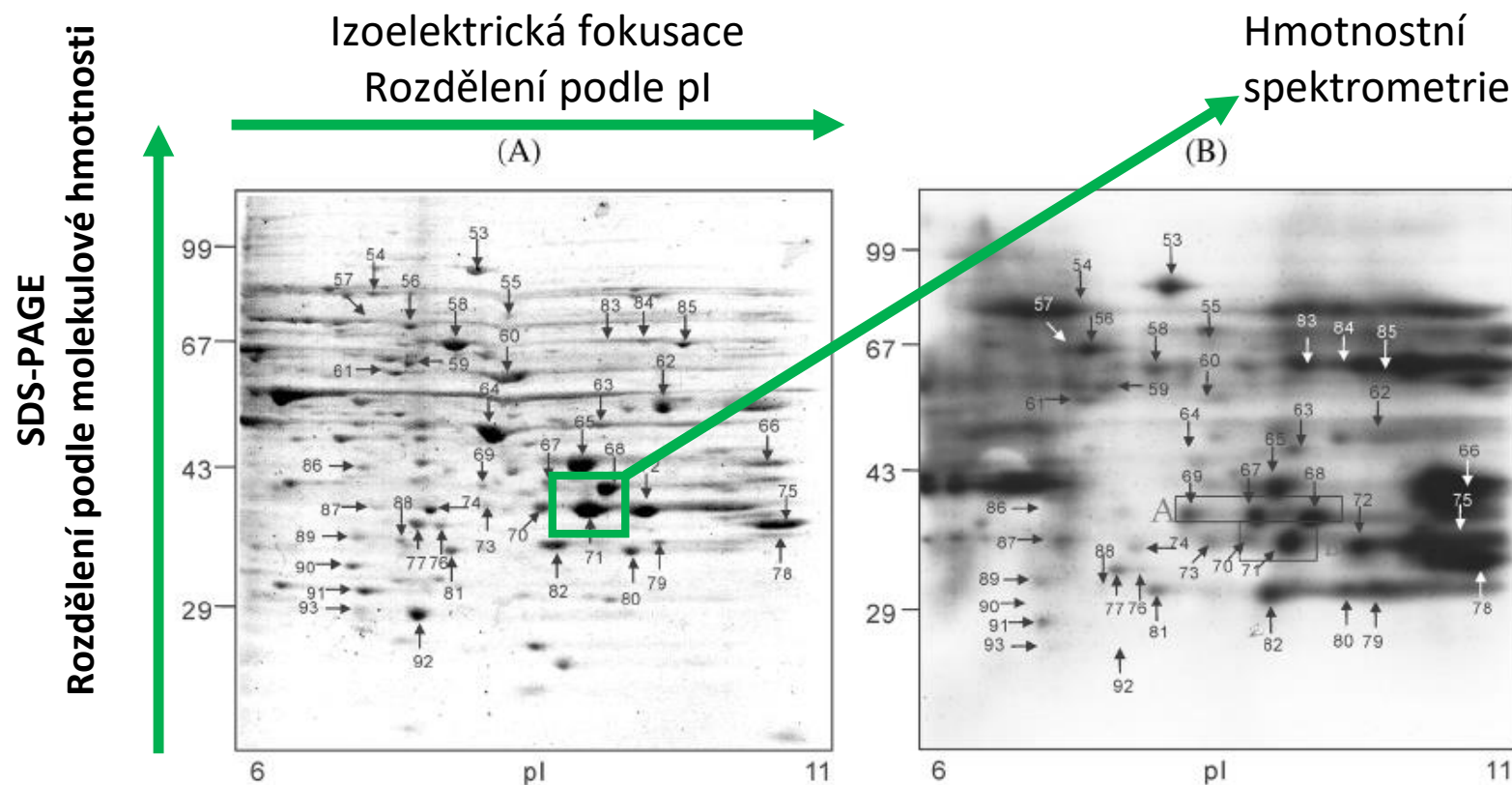


Fig. 2. Two dimensional gel images visualized by silver staining and immunostaining. (A, B) Silver stained 2D gel in pH range 6-11 of mouse fibrosarcoma cells (A), and western analysis of 2D gel with anti-phosphotyrosine antibody (B). Box A indicates the modifications of MAP kinase kinase (spot 67, 68, 69) and Box B presents the GAPDH (spot 70, 71). Adapted and reprinted with permission from Kim *et al.*, 2002.

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- Identifikace a analýza PTM: kombinace LC a MS analýzy.

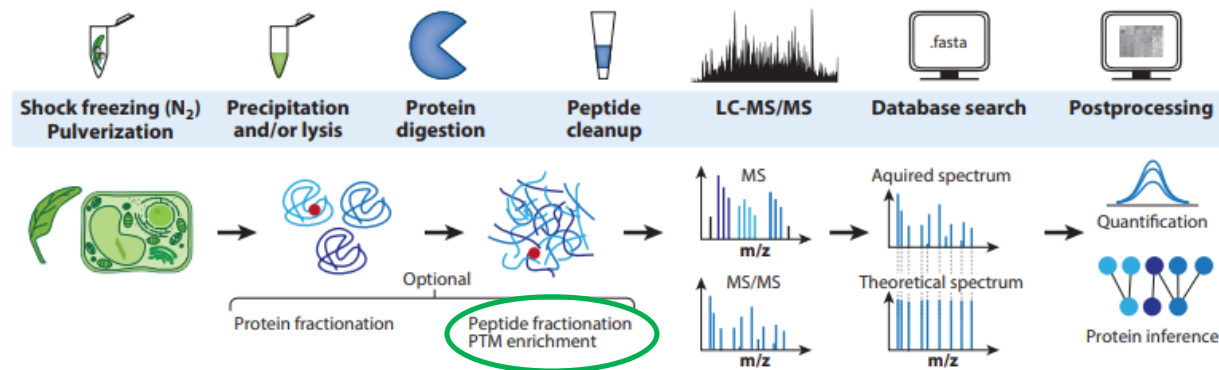


Figure 2

Generic workflow for proteomic sample preparation, data acquisition, and analysis. Proteins are extracted from whole-plant samples or enriched subfractions using optimized homogenization and protein extraction methods. Proteins are digested into peptides and measured on an LC-MS/MS system. Peptides are identified from MS/MS spectra by database matching and quantified based on the peak areas of intact peptide (survey MS spectra) or fragment ion signals (tandem MS spectra) provided by the mass spectrometer along the chromatographic time scale. Protein identity and quantity are then inferred based on peptide sequence assignments. Abbreviations: LC-MS/MS, liquid chromatography–coupled tandem mass spectrometry; MS, mass spectrometry; MS/MS, tandem mass spectrometry; m/z, mass-to-charge ratio; PTM, posttranslational modification.

Annual Review of Plant Biology
Plant Proteome Dynamics

Julia Mergner^{1,2} and Bernhard Kuster^{2,3}

¹Bavarian Center for Biomolecular Mass Spectrometry at Klinikum rechts der Isar (BayBioMS@MRI), Technical University of Munich, Munich, Germany; email: julia.mergner@tum.de

²Chair of Proteomics and Bioanalytics, Technical University of Munich, Freising, Germany; email: kuster@tum.de

³Bavarian Center for Biomolecular Mass Spectrometry (BayBioMS), Technical University of Munich, Freising, Germany

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Posttranslační modifikace

Predikce

- **Posttranslační modifikace** jsou prováděny enzymy. Enzymy rozeznávají specifické signály – aminokyselinové sekvence v proteinech. Identifikace těchto sekvenčních motivů umožňuje predikci PTM.
- **Problémy predikce:**
 - Může být **těžké** vytvořit „průměrný“ sekvenční motiv vhodný pro predikci.
 - Proteiny jsou modifikovány různými enzymy s různou specifitou.
 - **Vliv okolních aminokyselin** – ovlivnění náboje, hydrofility části proteinu v kontaktu s enzymem.
 - **Vliv 3D/4D struktury.**

**Prediction of Posttranslational Modification of Proteins
from Their Amino Acid Sequence**

Birgit Eisenhaber and Frank Eisenhaber

Post-translational modifications of proteins

DictyOGlyc	O-(alpha)-GlcNAc glycosylation sites (trained on Dictyostelium discoideum proteins)
NetAcet	N-terminal acetylation in eukaryotic proteins
NetCGlyc	C-mannosylation sites in mammalian proteins
NetCorona	Coronavirus 3C-like proteinase cleavage sites in proteins
NetGPI	GPI Anchor predictions
NetNGlyc	N-linked glycosylation sites in human proteins
NetOGlyc	O-GalNAc (mucin type) glycosylation sites in mammalian proteins
NetPhorest	Linear motif atlas for phosphorylation-dependent signaling
NetPhos	Generic phosphorylation sites in eukaryotic proteins
NetPhosBac	Generic phosphorylation sites in bacterial proteins
NetPhosYeast	Serine and threonine phosphorylation sites in yeast proteins
NetPhospan	Prediction of phosphorylation using convolutional neural networks (CNNs).
NetworKIN	In vivo kinase-substrate relationships
ProP	Arginine and lysine propeptide cleavage sites in eukaryotic protein sequences

DTU Health Tech

DTU - Technical University of Denmark



<https://services.healthtech.dtu.dk/>

Expasy

Swiss Bioinformatics Resource Portal



Sulfinator

Predict tyrosine sulfation sites in protein sequences

The Sulfinator is a software tool able to predict tyrosine sulfation sites in protein sequences. It employs four different Hidden Markov Models that were built to recognise sulfated tyrosine residues located N-terminally, within sequence windows of more than 25 amino acids and C-terminally, as well as sulfated tyrosines clustered within 25 amino acid windows, respectively. All four HMMs contain the distilled information from one multiple sequence alignment.



PeptideCutter

Potential cleavage sites in a protein



GlycoMod

Possible oligosaccharide structures on proteins from masses



Myristoylator

N-terminal myristoylation of proteins by neural networks.



FindMod

Potential PTMs and single amino acid substitutions

Expert Protein Analysis System

<http://www.expasy.org>

Post-translational modifications of proteins

DictyOGlyc	O-(alpha)-GlcNAc glycosylation sites (trained on Dictyostelium discoideum proteins)
NetAcet	N-terminal acetylation in eukaryotic proteins
NetCGlyc	C-mannosylation sites in mammalian proteins
NetCorona	Coronavirus 3C-like proteinase cleavage sites in proteins
NetGPI	GPI Anchor predictions
NetNGlyc	N-linked glycosylation sites in human proteins
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NetPhospan	Prediction of phosphorylation using convolutional neural networks (CNNs).
NetworkKIN	In vivo kinase-substrate relationships
ProP	Arginine and lysine propeptide cleavage sites in eukaryotic protein sequences

NetCGlyc - 1.0

C-mannosylation sites in mammalian proteins

The NetCGlyc 1.0 produces neural network predictions of C-mannosylation sites in mammalian proteins.

```
##gff-version 2
##source-version netCglyc-1.0b
##date 2007-03-14
```

```
##Type Protein
```

# seqname	source	feature	start	end	score +/-	?
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	21	21	0.269	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	38	38	0.459	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	41	41	0.639	W
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	44	44	0.484	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	72	72	0.221	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	115	115	0.285	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	207	207	0.228	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	244	244	0.246	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	299	299	0.160	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	317	317	0.203	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	410	410	0.243	.
Q6ZMM2_ATL5_HUMAN	netCglyc-1.0b	C-manno	454	454	0.227	.

Only the residues with scores higher than 0.5, marked with "W" are predicted as C-mannosylated.

Methodology article

Open Access

Coronavirus 3CL^{pro} proteinase cleavage sites: Possible relevance to SARS virus pathology

Lars Kiemer, Ole Lund, Søren Brunak and Nikolaj Blom*

Address: Center for Biological Sequence Analysis BioCentrum-DTU, Building 208 Technical University of Denmark DK-2800 Lyngby, Denmark

Email: Lars Kiemer - lars@cbs.dtu.dk; Ole Lund - lund@cbs.dtu.dk; Søren Brunak - brunak@cbs.dtu.dk; Nikolaj Blom* - nikob@cbs.dtu.dk

* Corresponding author

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Abstract

Background: Despite the passing of more than a year since the first outbreak of Severe Acute Respiratory Syndrome (SARS), efficient counter-measures are still few and many believe that reappearance of SARS, or a similar disease caused by a coronavirus, is not unlikely. For other virus families like the picornaviruses it is known that pathology is related to proteolytic cleavage of host proteins by viral proteinases. Furthermore, several studies indicate that virus proliferation can be arrested using specific proteinase inhibitors supporting the belief that proteinases are indeed important during infection. Prompted by this, we set out to analyse and predict cleavage by the coronavirus main proteinase using computational methods.

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<https://services.healthtech.dtu.dk/>

Posttranslační modifikace

**Experimentální
identifikace**

Predikce

Predikce PTM

Experimentální
identifikace/ ověření PTM.
Databáze PTM.
Databáze modifikovaných
proteinů.

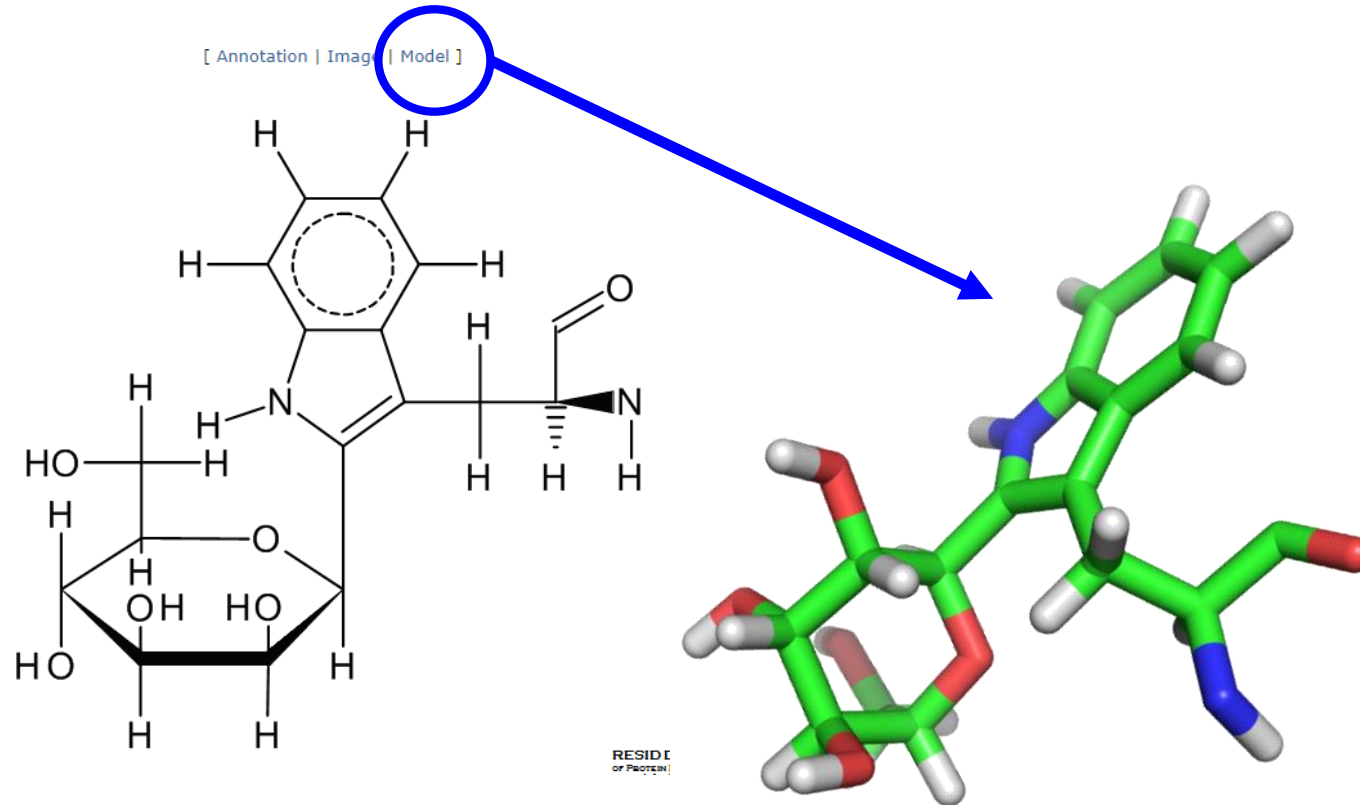
Vyhodnocování experimentálních dat

Predikce PTM na základě homologie.
Predikce na základě sekvenčních motivů.

Posttranslační modifikace - databáze

List of SequenceSpecs

L-alanine
L-arginine
L-asparagine
L-aspartic acid
L-cysteine
L-glutamic acid
L-glutamine
glycine
L-histidine
L-isoleucine
L-leucine
L-lysine
L-methionine
L-phenylalanine
L-proline
L-pyrrolysine
L-selenocysteine
L-serine
L-threonine
L-tryptophan
L-tyrosine
L-valine



<https://pir.georgetown.edu/resid/>

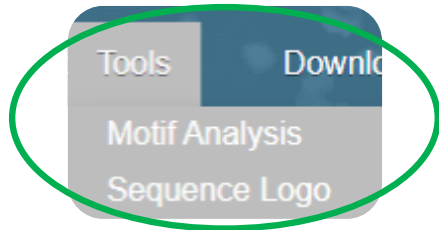
Posttranslační modifikace - databáze



<https://www.phosphosite.org/homeAction>

MODIFICATION SITE STATISTICS, NON-REDUNDANT:

Acetylation:	38,128
Caspase cleavage:	484
Di-Methylation:	2,854
Methylation:	226
Mono-Methylation:	15,170
N-Glycosylation:	6,400
O-Galnac:	2,101
O-Glcnac:	1,748
Phospho-Ser:	176,776
Phospho-Thr:	72,606
Phospho-Tyr:	44,849
Succinylation:	4,627
Sumoylation:	8,550
Tri-Methylation:	341
Ubiquitylation:	110,107



You searched for: **Sequence or motif: RX[ST]Q(3)**

Show Sequence Logo

Launch Motif Analysis

Download

30 6 records found. Displaying 1 of 1 Pages. << First < Previous | Next > Last >>

GENE	PROTEIN	ACC_ID	ORGANISM	MW_(DA)	RSD	SITE_GRP_ID	SITE_+/-7_AA
ABRAXAS2	ABRAXAS2	Q15018	human	46,901	T101-p	23104841	WYRFRRNtQQQMSYR
CRTC2	TORC2	Q53ET0	human	73,302	S447-p	23154638	GPADARRsQQQLPkQ
CSNK1G1	CK1G1	Q9HCP0	human	48,511	S361-p	4270552	HTHRDRP sQQQPLRN
NBN	NBS1	O60934	human	84,959	S447-p	36128582	Nk sKDRAsQQQQTNS
PRKDC	DNAPK	P78527	human	469,089	T2638-p	448712	VAGQIRA tQQQHDFt
PRKDC	DNAPK	P97313	mouse	471,471	T2634-p	448712	KPGQVRA tQQQYDFt

30 6 records found. Displaying 1 of 1 Pages. << First < Previous | Next > Last >>

Posttranslační modifikace - databáze



<https://www.phosphosite.org/homeAction>

MODIFICATION SITE STATISTICS, NON-REDUNDANT:

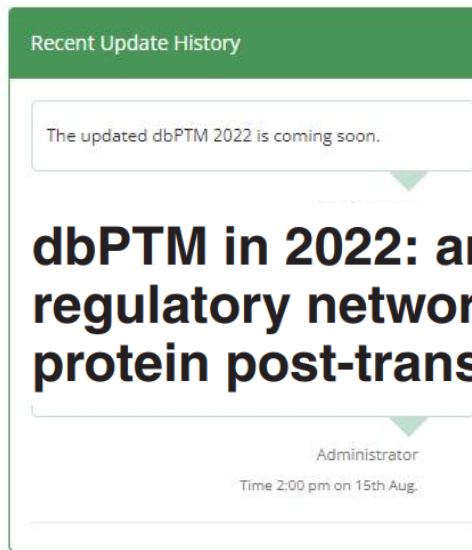
Acetylation:	38,128
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O-Glcnac:	1,748
Phospho-Ser:	176,776
Phospho-Thr:	72,606
Phospho-Tyr:	44,849
Succinylation:	4,627
Sumoylation:	8,550
Tri-Methylation:	341
Ubiquitylation:	110,107



		General statistics		
	Acronym	Number of covered organisms	Number of PTM types	Number of PTMs ^a
General database	dbPTM	More than 1000 organisms	130	S: ~908 900 P: ~557 700
	BioGRID	71 organisms	6	S: ~700 000 P: ~419 400
	Phosphosite Plus	26 organisms	7	S: ~483 700 P: ~20 200
	PTMCode v2	19 organisms	69	S: ~316 500 P: ~ 45 300
	qPTM	Human	10	S: ~296 900 P: ~19 600
	PLMD	176 organisms	20	S: ~285 700 P: ~53 500
	CPLM	122 organisms	12	S: ~189 900 P: ~45 700
	YAAM	<i>Saccharomyces cerevisiae</i>	19	S: ~121 900 P: ~680
	HPRD	Human	9	S: ~ 93 700 P: ~30 000
	PHOSIDA	9 organisms	3	S: ~80 000 P: ~28 700
	PTM-SD	7 model organisms	21	S: ~10 600 P: ~842
	WERAM	8 organisms	2	S: ~ 900 P: ~584

Post-translational modifications in proteins: resources, tools and prediction methods

Shahin Ramazi^{1,†} and Javad Zahiri^{1,2,3,*†}



dbPTM in 2022: an updated database for exploring regulatory networks and functional associations of protein post-translational modifications

2,235,664 Sites
Experimental PTM Sites

70+ PTM Types
Collecting PTM Types

40+ Databases
Integrated Databases

30+ Datasets
Benchmark Datasets

dbPTM: an information repository of protein post-translational modification

Tzong-Yi Lee¹, Hsien-Da Huang^{1,2,*}, Jui-Hung Hung¹, Hsi-Yuan Huang¹, Yuh-Shyong Yang^{2,3} and Tzu-Hao Wang⁴

<https://awi.cuhk.edu.cn/dbPTM/index.php>

Search: ricinus

ID	Organism	Protein Name	PTM
2SS_RICCO	Ricinus communis (Castor bean).	2S albumin	Show

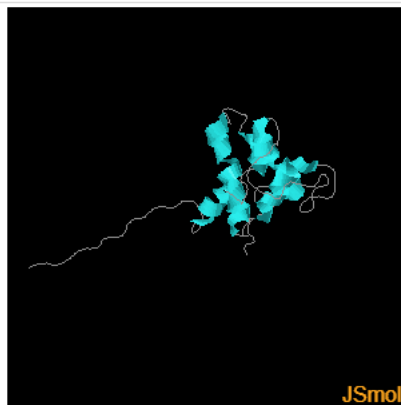
Showing 1 to 1 of 1 entries (filtered from 117 total entries)

2SS_RICCO - PTM Information in dbPTM

- Information
- Experimental PTM Sites
- Upstream Regulatory Proteins
- Interacting Proteins
- Disease-associated PTM Sites by SAP
- Drug & Disease Associations
- Literatures

Basic Information of Protein

UniProt ID	2SS_RICCO
UniProt AC	P01089
Protein Name	2S albumin
Gene Name	
Organism	Ricinus communis (Castor bean).
Sequence Length	258
Subcellular Localization	
Protein Description	2S seed storage proteins..
Protein Sequence	MAKLIPTIALVSVLLFIANASFAVRTTITITIEIDESKGEREGSSSSQCRQEVQRKDLSSCERYLRQSSRRSPGEEVLRMPGDENQQQESQQLQCCNQVKQVRDECQCEAIKYIAEDQIQGQLHGEESEVAQRAGEIVSSCGVRCMRQTRTPSQGCRGQIQEQQLNRQCQEYIKQVSGQGPRRSNDQERSLRGCCDHLKQMQSQCRCEGLRQAIEQQSQGQLQGQDVFEAFRTAANLPSMCGVSPTECRF



Overview of Protein Modification Sites with Functional and Structural Information

Experimental PTM Sites

(*DZ-PTM) Disease-associated PTM Sites based on SAP

MAKLIPTIALVSVLLFIANASFAVRTTITITIEIDESKGEREGSSSSQCRQEVQRKDLSSCERYLRQSSRRSPGEEVLRMPGDENQQQESQQLQCCNQVKQVRDECQCEAIKYIAEDQIQGQLHGEESEVAQRAGEIVSSCGVRCMRQTRTPSQGCRGQIQEQQLNRQCQEYIKQVSGQGPRRSNDQERSLRGCCDHLKQMQSQCRCEGLRQAIEQQSQGQLQGQDVFEAFRTAANLPSMCGVSPTECRF

Protein Variants

Search by Protein/Gene Keyword

Select a Category

Protein Name Gene Name

Input the Keyword

albumin

(eg. Protein Name = Serine/threonine-protein kinase Chk2 / Gene Name = CHEK2)

Search

Clear

Example

Purification and sequencing of napin-like protein small and large chains from *Momordica charantia* and *Ricinus communis* seeds and determination of sites phosphorylated by plant Ca(2+)-dependent protein kinase

G M Neumann¹, R Condon, G M Polya

<https://awi.cuhk.edu.cn/dbPTM/index.php>

Posttranslační modifikace – „crosstalk“

The next level of complexity: Crosstalk of posttranslational modifications

A. Saskia Venne*, Laxmikanth Kollipara* and René P. Zahedi

Leibniz-Institut für Analytische Wissenschaften – ISAS – e.V., Dortmund, Germany

Beside gene expression and translational control, which are relatively slow, PTM of proteins represents the major level of regulation, from very fast and reversible to slow or irreversible processes. PTMs affect protein structure and act as molecular switches, which regulate the interaction of proteins with DNA, cofactors, lipids, and other proteins. In the past few years, evidence for extensive crosstalk between PTMs has accumulated. The combination of different PTMs on protein surfaces can create a “PTM code,” which can be recognized by specific effectors to initiate/inhibit downstream events, only inducing/retaining a signal once the complementary incoming signals are present at the same time and place. Although MS-based proteomics has substantially improved our knowledge about PTMs, currently sensitive and dedicated analytical strategies are available only for few different types of PTM. Several recent studies focused on the combinatorial analysis of PTMs, but preferentially utilized peptide-centric bottom-up strategies might be too restricted to decipher complex PTM codes. Here, we discuss the current state of PTM crosstalk research and how proteomics may contribute to understanding PTM codes, representing the next level of complexity and one of the biggest challenges for future proteomics research.

Keywords:

Cell biology / Crosstalk / Interplay / Phosphorylation / PTM code / Ubiquitination

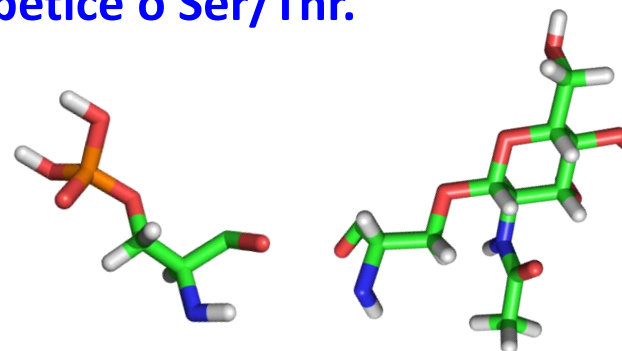
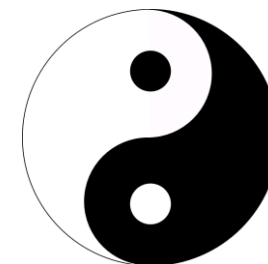
Pozitivní
Negativní

- **Pozitivní** – první PTM slouží jako signál pro připojení (odstranění) jiné PTM.
- **Negativní** – přímá kompetice dvou PTM o stejnou aminokyselinu, případně první PTM „maskuje“ místo pro druhou PTM a zabrání jejímu připojení/odstranění.

Hart *et al.* - “*yin-yang hypothesis*”

O-fosforylace/*O*-glykosylace (*O*-GlcNAc)

Kompetice o Ser/Thr.



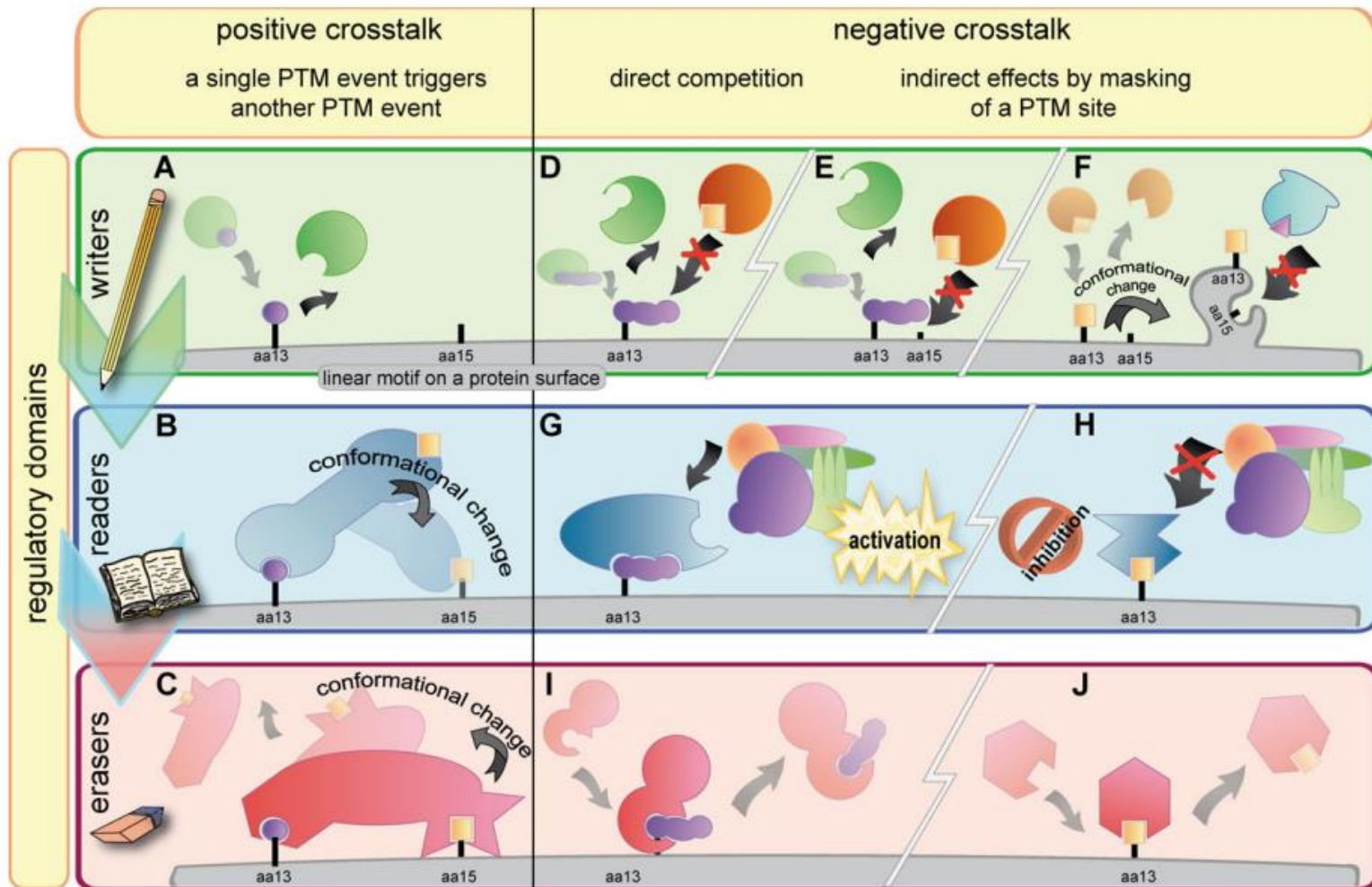


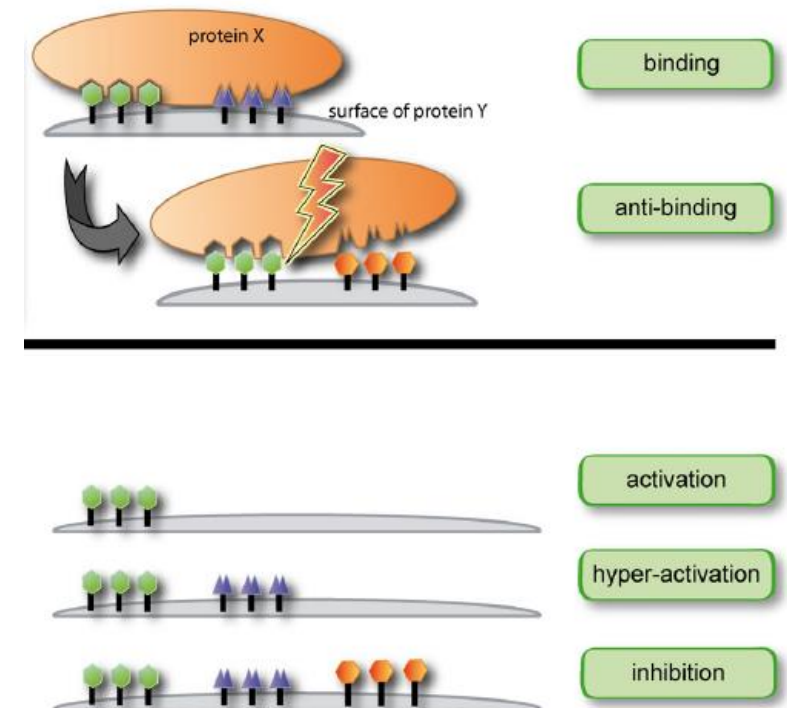
Figure 1. Classification of PTM crosstalk. Short linear motifs on protein surfaces enable protein–protein interaction and can be processed by different regulatory domains. Depending on their function they are classified as writers, readers, and erasers (green, blue, and red rows). In general, positive and negative crosstalk can be distinguished. (A) A writer attaches a PTM to an amino acid (aa) on a target protein. (B) This PTM can attract a reader and trigger the addition of a second PTM, e.g. by recruitment of another writer, or induced by a conformational change of the reader protein itself. (C) Vice versa, a PTM can be read and removed by an eraser protein. Negative crosstalk can be subdivided in direct competition and indirect effects. (D) Two different PTM compete for the same residue. (E) Two PTM have different binding sites but upon initial attachment of the first PTM, the second binding site is indirectly masked. (F) The first PTM leads to a conformational change, which conceals the second PTM binding site from its writer. (G) Depending on which PTM is bound to the respective site different downstream events are initiated: After PTM of the target protein, a protein complex is recruited and the corresponding pathway is triggered. (H) Another PTM can block the respective site such that the pathway is inhibited instead. (I, J) Attached PTM can be removed by an eraser.

- **Pozitivní** – první PTM slouží jako signál pro připojení (odstranění) jiné PTM.
- **Negativní** – přímá kompetice dvou PTM o stejnou aminokyselinu, případně první PTM „maskuje“ místo pro druhou PTM a zabrání jejímu připojení/odstranění.

The next level of complexity: Crosstalk of posttranslational modifications

Posttranslační modifikace – „crosstalk“

- „Crosstalks“ – vyšší úroveň regulace aktivity proteinů, prevence „chybných“ aktivací/inaktivací. Složitější regulace při zachování stejného množství PTM – různé kombinace, různé efekty, případně různé úrovně odezvy.
- Různé proteiny s různou funkcí – mohou podléhat stejným „crosstalk“ mechanismům.
- Histon H3 a protein p53 – specifická methylace konkrétního lysinu vyvolá acetylaci druhého lysinu, ve vzdálenosti deset aminokyselin od prvního.
- Existuje obecný „PTM kód“ sloužící k lepší regulaci aktivity proteinů???



Posttranslační modifikace – „crosstalk“

PTMcode: a database of known and predicted functional associations between post-translational modifications in proteins

Pablo Minguez¹, Ivica Letunic², Luca Parca³ and Peer Bork^{1,4,*}

¹European Molecular Biology Laboratory, Meyerhofstrasse 1, 69117 Heidelberg, ²Biobyte solutions GmbH, Bothestr. 142, 69126 Heidelberg, Germany, ³Department of Biology, Centre for Molecular Bioinformatics, University of Rome 'Tor Vergata', Via della Ricerca Scientifica snc, 00133 Rome, Italy and ⁴Max-Delbrück-Centre for Molecular Medicine, Berlin-Buch, Germany

Received September 15, 2012; Revised October 16, 2012; Accepted October 31, 2012

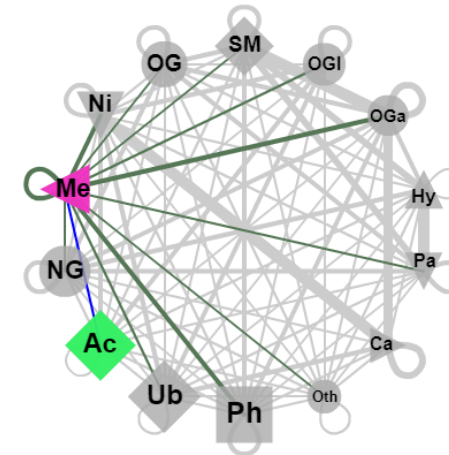
PTMcode v2: a resource for functional associations of post-translational modifications within and between proteins

Pablo Minguez¹, Ivica Letunic², Luca Parca¹, Luz Garcia-Alonso³, Joaquin Dopazo³, Jaime Huerta-Cepas¹ and Peer Bork^{1,4,*}

¹European Molecular Biology Laboratory (EMBL), Meyerhofstrasse 1, 69117 Heidelberg, Germany, ²Biobyte solutions GmbH, Bothestr. 142, 69117 Heidelberg, Germany, ³Computational Genomics Department, Centro de Investigación Príncipe Felipe (CIPF), Valencia, Spain and ⁴Max-Delbrück-Centre for Molecular Medicine, Berlin-Buch, Germany

Received September 15, 2014; Revised October 13, 2014; Accepted October 16, 2014

PTMcode 2



<http://ptmcode.embl.de/>

Known and predicted PTM functional associations

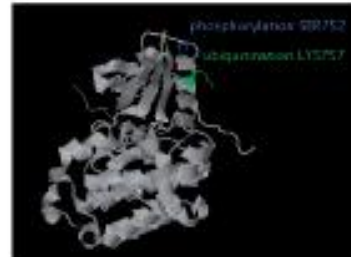
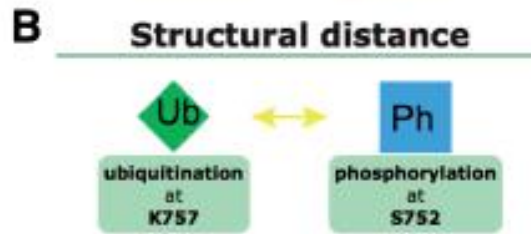
PTMCode is a resource of known and predicted functional associations between protein post-translational modifications (PTMs) within and between interacting proteins. It currently contains 316,546 modified sites from 69 different PTM types which are also propagated through orthologs between 19 different eukaryotic species. A total of 1.6 million sites and 17 million functional associations more than 100,000 proteins can currently be explored.

PTMcode 2

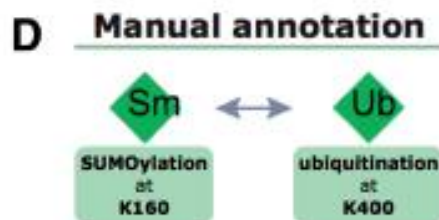
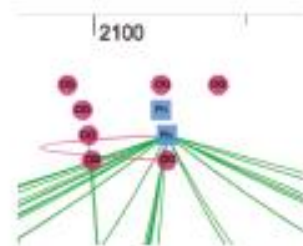
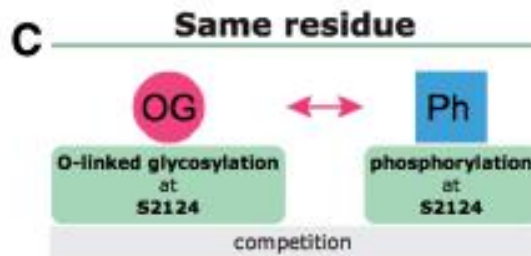


```

38611.AV081LP00000011804 XXXXXXXXXXXXXXXXXXXX
13616.AV081LP000000000159 SKPILL50KA1P...ITVMYFQDVC
42214.AV081LP0000000001392
812179.AV081LP000000011828 FQCFETFPFR...C...C...
5986.ENOC1P00000017087 FQCFETFPFR...C...C...
5371.ENOC7P00000001727
32093.AV081LP0000000004003 F...E...E...P...I...T...P...A...P...D...C...K...E...
30218.AV081LP0000000179197 T...E...E...P...I...T...P...A...P...D...C...E...
5256.ENOC3AP000000017911
35144.ENOC8AP0000000148613
5836.ENOP1N000000017208 FQCFETFPFR...C...C...
5686.ENOP0B00000004428 FQCFETFPFR...C...C...
8621.ENOCAP000000000524 FQCFETFPFR...C...C...CKYHWLVF
8621.ENOCAP00000001480 FQCFETFPFR...C...C...
  
```

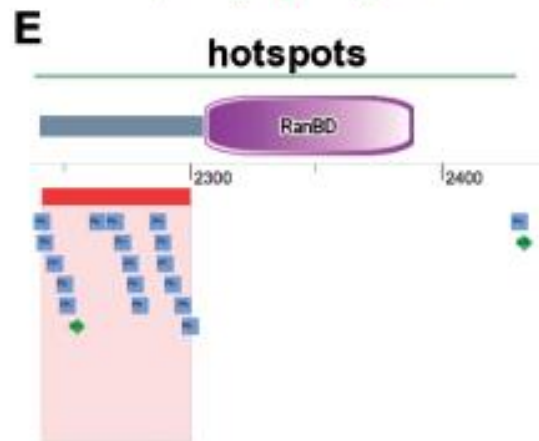


These PTMs are located 4.47 Å apart on the protein structure.



This association was annotated based on the following information from PubMed publication [18408734](#):

SUMOylation enhances ubiquitination that leads to proteins degradation



PTMcode: a database of **known** and **predicted** functional associations between post-translational modifications in proteins

A: Dvě modifikovaná rezidua jsou evolučně konzervovaná.

B: Dvě modifikovaná rezidua jsou blíže, než je pro PTM typické.

C: Dvě PTM probíhají ve stejném místě.

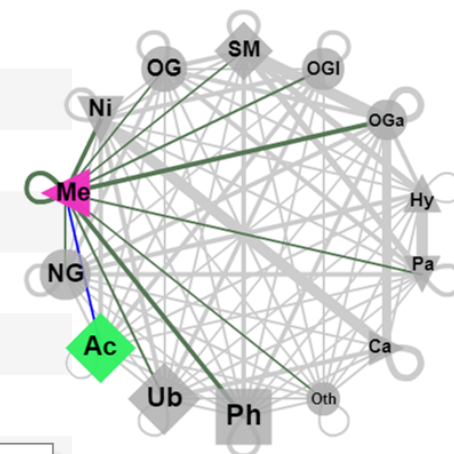
D: Manuální anotace (publikace). Známé experimentální „crosstalks“.

E: „Hotspots“ – oblasti proteinu s vysokým výskytem modifikací.

Functional associations between acetylation and methylation

The table below lists all proteins in our database where a functional association between acetylation (Ac) and methylation (Me) was predicted. The evidence supporting the prediction is listed in the last column. Click on any evidence type box to display more details about it. To explore any protein in detail, click on it to pre-fill the input form above.

Akap8	Mus musculus	Ac	K301	87	Me	R188	86	■
AKAP8L	Homo sapiens	Ac	K257	55	Me	R237	86	■
ALB	Homo sapiens	Ac	K198	88	Me	K75	86	■
ALB	Homo sapiens	Ac	K183	41	Me	K75	86	■
ALB	Homo sapiens	Ac	K558	93	Me	K558	93	■
ALB	Homo sapiens	Ac	K75	86	Me	K75	86	■
ALB	Homo sapiens	Ac	K569	92	Me	K558	93	■
ALB	Homo sapiens	Ac	K524	81	Me	K558	93	■ Structural distance
ALDH1A1	Homo sapiens	Ac	K367	59	Me	R68	79	■
ALDH1A1	Homo sapiens	Ac	K128	64	Me	R68	79	■
ALDH1A1	Homo sapiens	Ac	K419	37	Me	R68	79	■
ALDH1A1	Homo sapiens	Ac	K412	54	Me	R68	79	■
Aldoa	Mus musculus	Ac	K200	68	Me	K322	77	■
ALS2	Homo sapiens	Ac	K1281	84	Me	R481	89	■
ANKRD12	Homo sapiens	Ac	K1036	67	Me	K1036	67	■
ANKRD12	Homo sapiens	Ac	K1034	75	Me	K1034	75	■
ANKZF1	Homo sapiens	Ac	K310	77	Me	K599	97	■



Browse PTMs

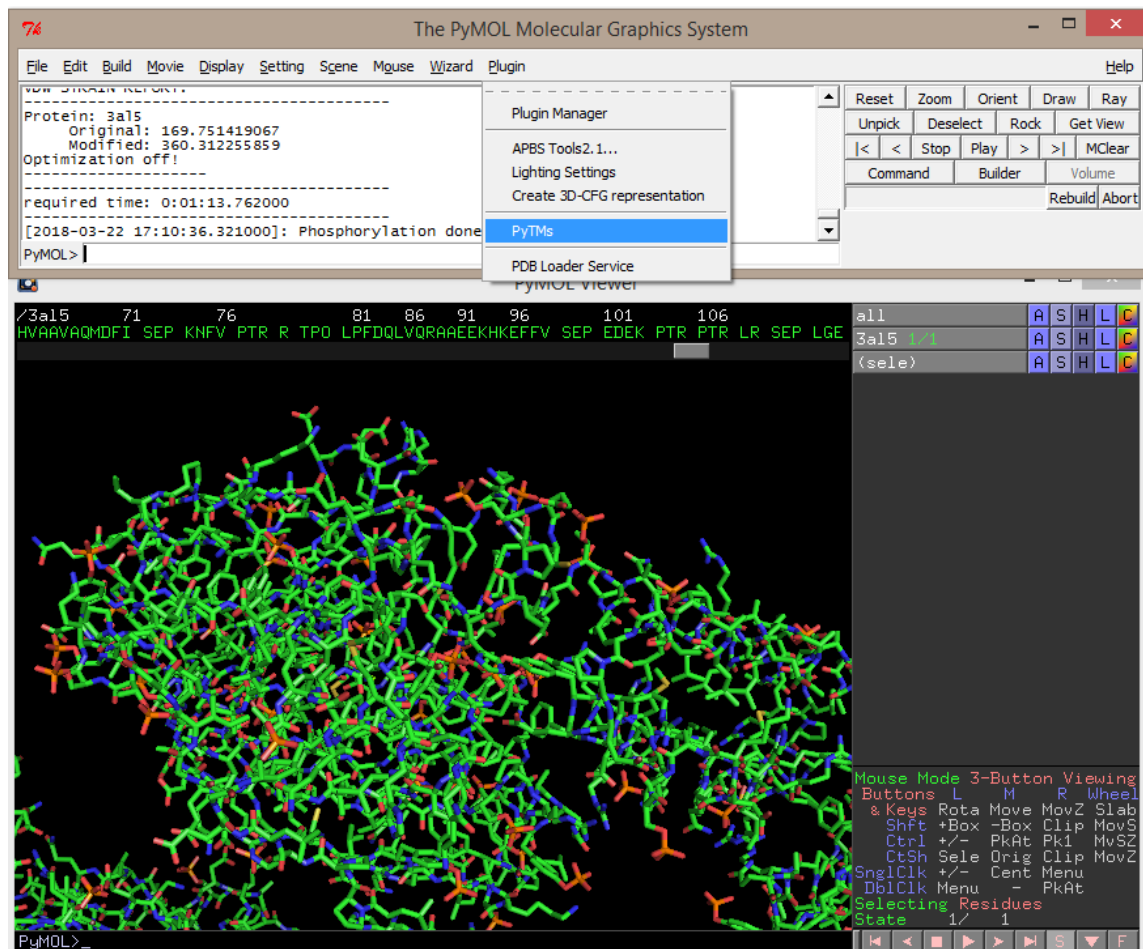
PTMcode requires Adobe Flash Player version 11.1.0 or greater. Since 2021, Flash is no longer supported by Adobe. You can still access PTMcode using an older plugin version (e.g. v 11.9.900), and possibly an older browser version (Firefox 58 works fine with this plugin).

Posttranslační modifikace - vizualizace

The image shows the PyMOL interface. The top menu bar includes File, Edit, Build, Movie, Display, Setting, Scene, Mouse, Wizard, Plugin, and Help. The 'Builder' menu item is circled in green. Below the menu bar, a text area displays system information and a warning: 'This Executable Build integrates and extends Open-Source PyMOL. invalid syntax (Lenka M/pymolpluginsrc.py, line 9)'. The main window shows a command prompt with 'PyMOL>' and a message: 'No License File - For Evaluation Only (0 days remaining)'. The 'Builder' dialog box is open, showing tabs for Chemical, Protein, and Nucleic Acid. It contains buttons for atoms (H, C, N, O, P, S, F, Cl, Br, I, -CF3, -OMe), bonds (GH4, C=C, C#C, C#N, C=O, C=OO, C=ON, NC=O, S=O2, P=O3, N=O2), and other options like El-stat, Bumps, Undo, and Redo. A mouse control panel is visible at the bottom right.

The image shows the PyMOL interface with a 3D molecular model. The top menu bar includes File, Edit, Build, Movie, Display, Setting, Scene, Mouse, Wizard, Plugin, and Help. The 'Plugin' menu item is circled in green. The 'Plugin Manager' dialog box is open, showing a list of plugins: APBS Tools2.1..., Lighting Settings, Create 3D-CFG representation, PyTMs (highlighted), and PDB Loader Service. The main window shows a command prompt with 'PyMOL>' and a message: 'No License File - For Evaluation Only (0 days remaining)'. The 3D model is a protein structure with atoms colored by element (carbon in green, oxygen in red, nitrogen in blue). The command line shows: '/3a15 71 76 81 86 91 96 101 106 all A S H L C'. The mouse control panel is visible at the bottom right.

Posttranslační modifikace - vizualizace



PyTMs

Main About

SELECT PTM:

- Display vdW strain
- Acetylation
- Carbamylation
- Citrullination
- Cysteine oxidation
- Malondialdehyde adducts
- Methionine oxidation
- Methylation
- Nitration
- Phosphorylation**
- Proline hydroxylation
- S-Nitrosylation

SOFTWARE

Open Access

PyTMs: a useful PyMOL plugin for modeling common post-translational modifications

Andreas Warnecke^{1*}, Tatyana Sandalova², Adnane Achour² and Robert A Harris^{1*}

Abstract

Background: Post-translational modifications (PTMs) constitute a major aspect of protein biology, particularly signaling events. Conversely, several different pathophysiological PTMs are hallmarks of oxidative imbalance or inflammatory states and are strongly associated with pathogenesis of autoimmune diseases or cancers. Accordingly, it is of interest to assess both the biological and structural effects of modification. For the latter, computer-based modeling offers an attractive option. We thus identified the need for easily applicable modeling options for PTMs.

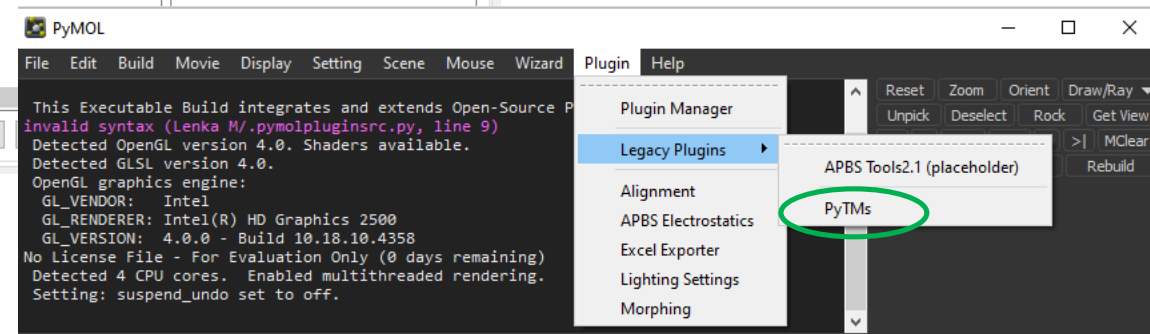
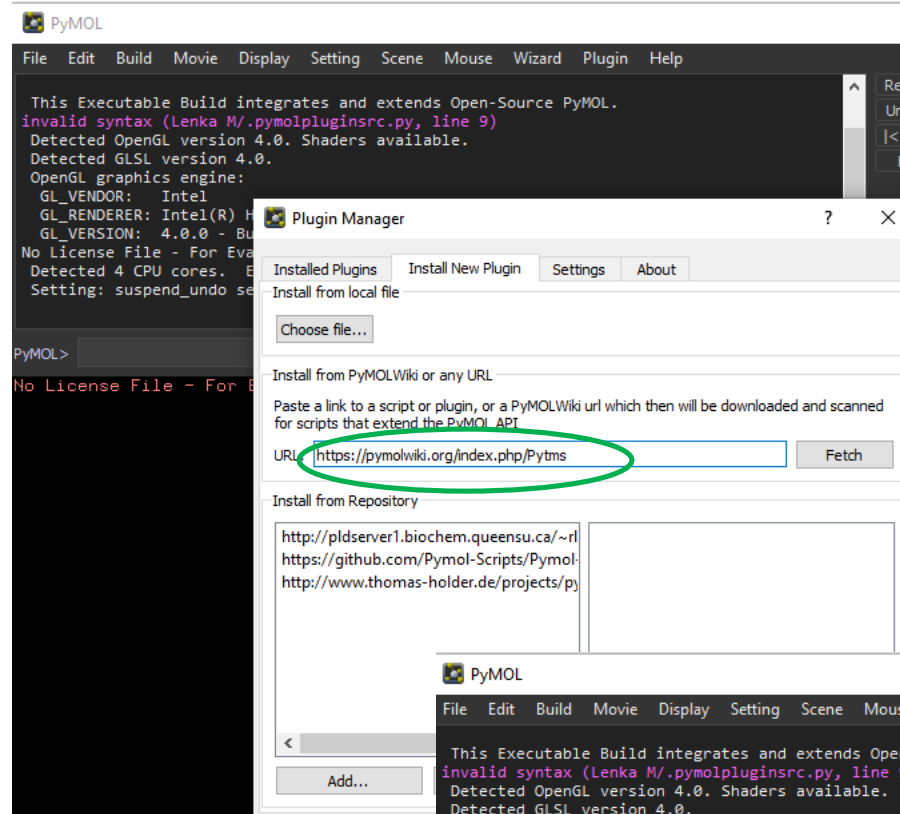
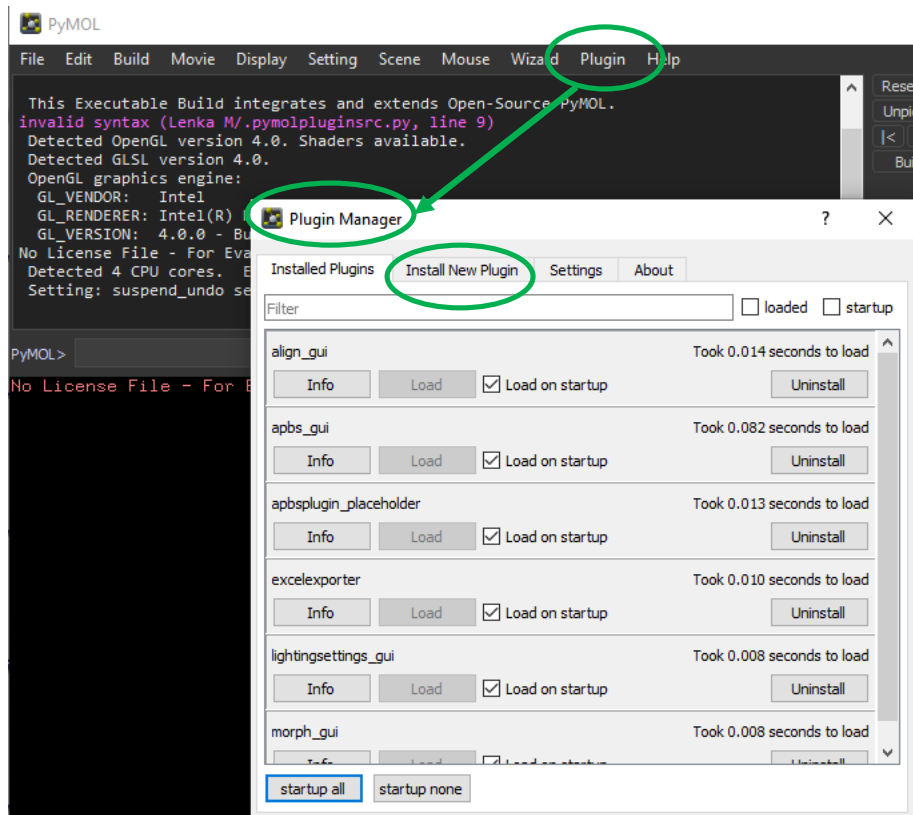
Results: We developed PyTMs, a plugin implemented with the commonly used visualization software PyMOL. PyTMs enables users to introduce a set of common PTMs into protein/peptide models and can be used to address research questions related to PTMs. Ten types of modification are currently supported, including acetylation, carbamylation, citrullination, cysteine oxidation, malondialdehyde adducts, methionine oxidation, methylation, nitration, proline hydroxylation and phosphorylation. Furthermore, advanced settings integrate the pre-selection of surface-exposed atoms, define stereochemical alternatives and allow for basic structure optimization of the newly modified residues.

Conclusion: PyTMs is a useful, user-friendly modelling plugin for PyMOL. Advantages of PyTMs include standardized generation of PTMs, rapid time-to-result and facilitated user control. Although modeling cannot substitute for conventional structure determination it constitutes a convenient tool that allows uncomplicated exploration of potential implications prior to experimental investments and basic explanation of experimental data. PyTMs is freely available as part of the PyMOL script repository project on GitHub and will further evolve.

Keywords: Post-translational modifications, PyMOL plugin, Structural bioinformatics, Modeling, Acetylation, Carbamylation, Citrullination, Oxidations, Malondialdehyde adducts, Nitration

<https://pymolwiki.org/index.php/Pytms>

Posttranslační modifikace - vizualizace



```

TITLE 2 BACTERIUM
COMPND MOL_ID: 1;
COMPND 2 MOLECULE: HALOHYDRIN DEHALOGENASE;
COMPND 3 CHAIN: A, B, C, D;
COMPND 4 ENGINEERED: YES
ObjectMolecule: Read secondary structure assignments.
ObjectMolecule: Read crystal symmetry information.
CmdLoad: PDB-string loaded into object "7wkq", state 1.
Setting: seq_view set to on.
You clicked /7wkq//A/LEU`47/CB
Selector: selection "sele" defined with 32 atoms.
Executive: Colored 6560 atoms and 1 object.

```

PyMOL>

```

/7wkq 26 31 36 41 46 51 56 61 66 71 76 81 86 91 96 101 106 111 116 121 126 131 136 141 146 151 156 161 166 171 176 181 186 191 196 201 206 211 216 221
SFYVGPLARELARREHNLVLDPAEGLVDELTA LGVEVEAVLGVNRLADPEAQLVAAQERFGRIDSAAAFSGRVVTGKFLDSTLEDLHSVVGQGLEAPYHFLKAVVPVMVEQGQGVLMVTSATAARPSRGASLYSSARAGATMMKNVAEVARNGVQVNAVGTNFMDFPEFLRASGANDPEIRARIEAAVPLGRLGTVEEFASFCM

```

No License File - For Evaluation Only (0 days remaining)

Reset Zoom Orient Draw/Ray
 Unpick Deselect Rock Get View
 < < Stop Play > > | MClear
 Builder Properties Rebuild

PyTMs

Main About

PyTMs: modeling post-translational modifications using PyMOL

SELECT PTM:

- Display vdW strain
- Acetylation
- Carbamylation
- Citrullination
- Cysteine oxidation
- Malondialdehyde adducts
- Methionine oxidation
- Methylation
- Nitration
- Phosphorylation
- Proline hydroxylation
- S-Nitrosylation

Selection: (sele

define above or choose: sele

surface selection cutoff (Å²): 0

Position: Lysines only N-termini only Both

Visualize clashes?: Yes No

Coloring (optional)
 Base / PTM

Hydrogens: remove hydrogens as is (detect) add hydrogens

Verbosity: quiet (no output on progress etc.)

Help Reset defaults

Selected: Acetylation

State 1/ 1


```

COMPND 3 CHAIN: A, B, C, D;
COMPND 4 ENGINEERED: YES
ObjectMolecule: Read secondary structure assignments.
ObjectMolecule: Read crystal symmetry information.
CmdLoad: PDB-string loaded into object "7wkq", state 1.
Setting: seq_view set to on.
You clicked /7wkq//A/LEU`47/CB
Selector: selection "sele" defined with 32 atoms.
Executive: Colored 6560 atoms and 1 object.
[2022-04-18 16:25:40.984316]: Initialized acetylation!
[2022-04-18 16:25:41.136728]: Modified: /7wkq//A/ALY`71/ | 100.00% [1 of 1]
[2022-04-18 16:25:41.196093]: Acetylation complete!

```

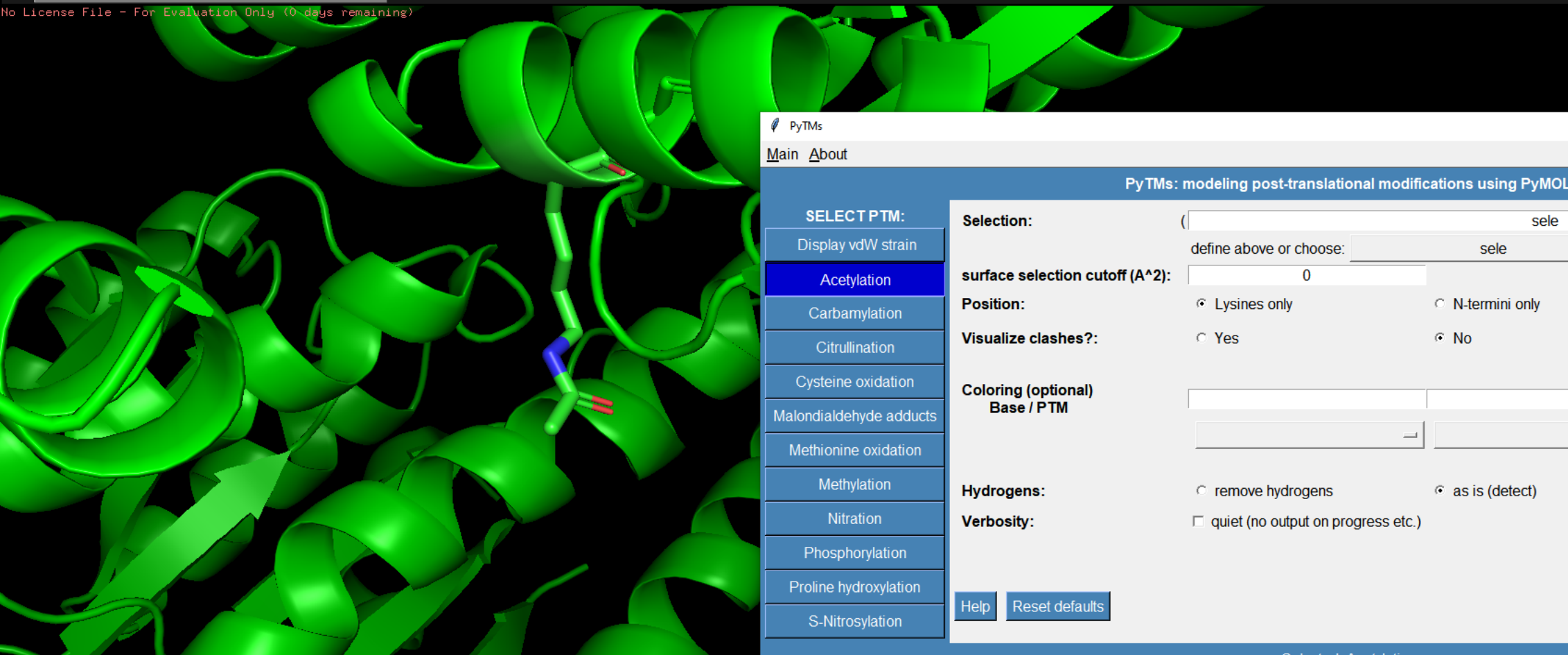
PyMOL>

```

/7wkq 26 31 36 41 46 51 56 61 66 71 76 81 86 91 96 101 106 111 116 121 126 131 136 141 146 151 156 161 166 171 176 181 186 191 196 201 206 211 216 221 all A S H L C
SFYVGP SLARELARREHNLV LGGP AEG LVD ELTALGVEVEAVL GVRNLADPES AQ ALY LVA A A QER FGRIDS A A A F SGRV V T G K F L D S T L E D L H S V V Q G C L E A P Y H F L K A V P V M V E G D G Q V L V M T S A T A A R P S R G A S L Y S S A R A G A T M M V K N V A E V A R N G V Q V N A V G T N F M D F P E F L R A S G A N D P E I R A R I E A A V P L G R L G T V E E F A 7wkq 1/1 A S H L C

```

No License File - For Evaluation Only (0 days remaining)



PyTMs

Main About

PyTMs: modeling post-translational modifications using PyMOL

SELECT PTM:

Display vdW strain

Acetylation

Carbamylation

Citrullination

Cysteine oxidation

Malondialdehyde adducts

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Phosphorylation

Proline hydroxylation

S-Nitrosylation

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(sele

define above or choose: sele

surface selection cutoff (A²):

0

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 Lysines only N-termini only Both

Visualize clashes?:

 Yes NoColoring (optional)
Base / PTM

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Verbosity:

 quiet (no output on progress etc.)

Help

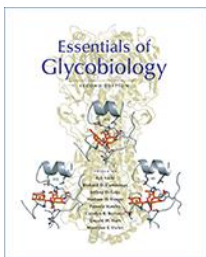
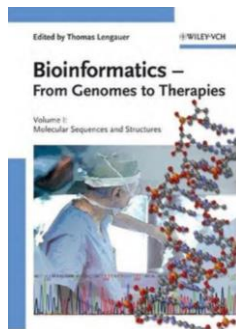
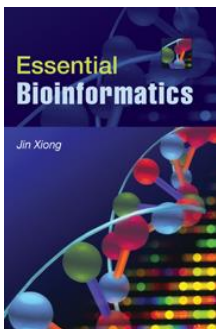
Reset defaults

Selected: Acetylation

Použitá a doporučená literatura

Bioinformatics-From Genomes to Therapies.
Editors(s): Prof. Dr. Thomas Lengauer.

Jin Xiong. Essential Bioinformatics.



Essentials of Glycobiology, 2nd edition
Chapter 42 Genetic Disorders of Glycosylation

Protein Posttranslational Modifications: The Chemistry of Proteome Diversifications

Christopher T. Walsh,* Sylvie Garneau-Tsodikova, and Gregory J. Gatto, Jr.

Post-translational Modifications and Their Biological Functions: Proteomic Analysis and Systematic Approaches

Jawon Seo and Kong-Joo Lee*

Golgi post-translational modifications and associated diseases

Sven Potelle¹ • André Klein² • François Foulquier¹

The next level of complexity: Crosstalk of posttranslational modifications

A. Saskia Venne*, Laxmikanth Kollipara* and René P. Zahedi

Leibniz-Institut für Analytische Wissenschaften – ISAS – e.V., Dortmund, Germany

Prediction of Posttranslational Modification of Proteins from Their Amino Acid Sequence

Birgit Eisenhaber and Frank Eisenhaber

PTMcode v2: a resource for functional associations of post-translational modifications within and between proteins

Pablo Minguéz¹, Ivica Letunic², Luca Parca¹, Luz Garcia-Alonso³, Joaquin Dopazo³, Jaime Huerta-Cepas¹ and Peer Bork^{1,4*}

¹European Molecular Biology Laboratory (EMBL), Meyerhofstrasse 1, 69117 Heidelberg, Germany, ²Biobyte solutions GmbH, Bothestr. 142, 69126 Heidelberg, Germany, ³Computational Genomics Department, Centro de Investigación Principe Felipe (CIPF), Valencia, Spain and ⁴Max-Delbrück-Centre for Molecular Medicine, Berlin-Buch, Germany

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PTMcode: a database of known and predicted functional associations between post-translational modifications in proteins

Pablo Minguéz¹, Ivica Letunic², Luca Parca³ and Peer Bork^{1,4*}

¹European Molecular Biology Laboratory, Meyerhofstrasse 1, 69117 Heidelberg, ²Biobyte solutions GmbH, Bothestrasse 142, 69126 Heidelberg, Germany, ³Department of Biology, Centre for Molecular Bioinformatics, University of Rome 'Tor Vergata', Via della Ricerca Scientifica snc, 00133 Rome, Italy and ⁴Max-Delbrück-Centre for Molecular Medicine, Berlin-Buch, Germany

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Andreas Warnecke^{1*}, Tatyana Sandalova², Adnane Achour³ and Robert A Harris^{1*}

dbPTM: an information repository of protein post-translational modification

Tzong-Yi Lee¹, Hsien-Da Huang^{1,2,*}, Jui-Hung Hung¹, Hsi-Yuan Huang¹, Yuh-Shyong Yang^{2,3} and Tzu-Hao Wang⁴

Protein post-translational modifications: *In silico* prediction tools and molecular modeling

Martina Audagnotto*, Matteo Dal Peraro*

Institute of Bioengineering, School of Life Sciences, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland
Swiss Institute of Bioinformatics (SIB), Lausanne, Switzerland