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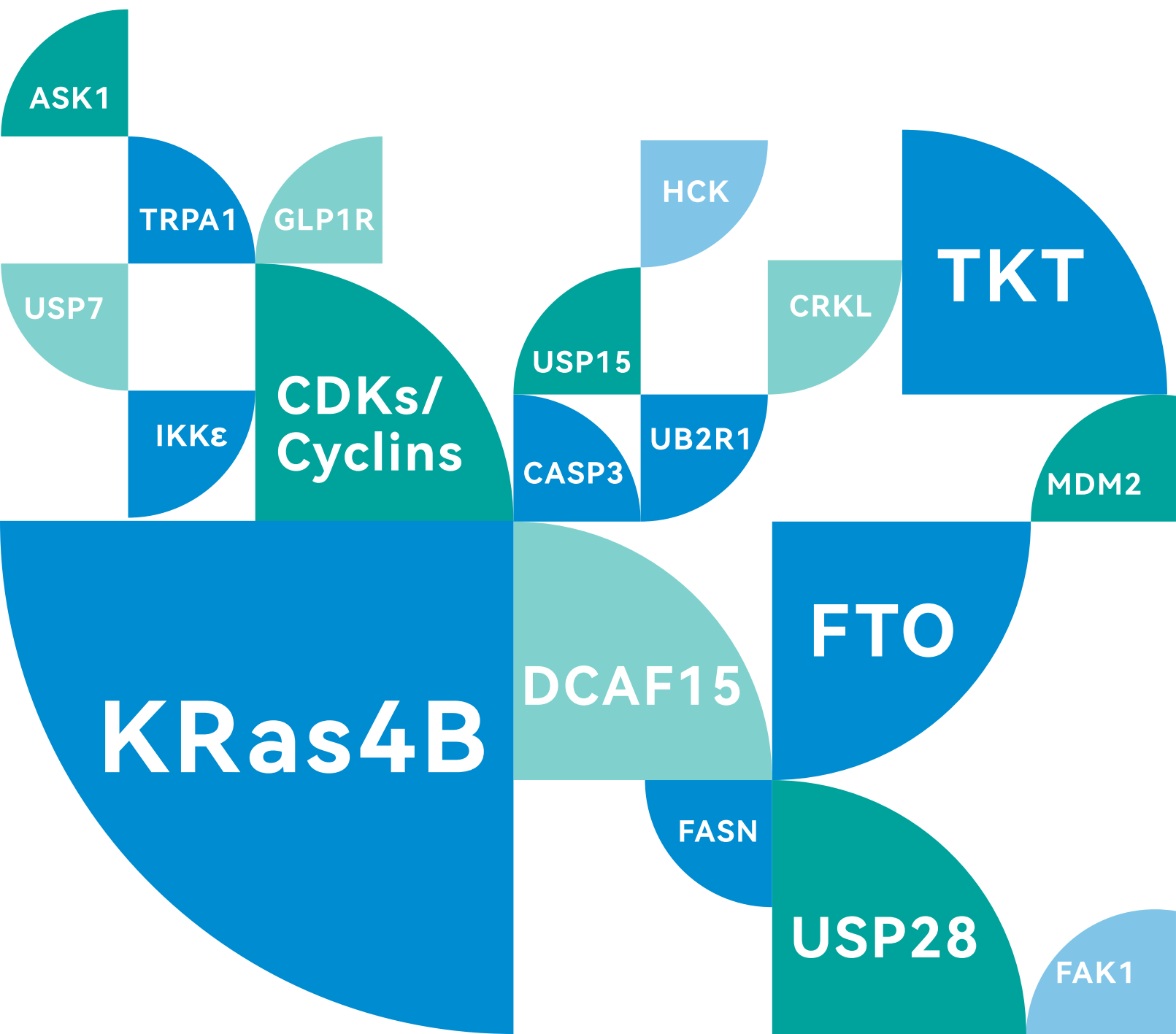
Protein Catalog



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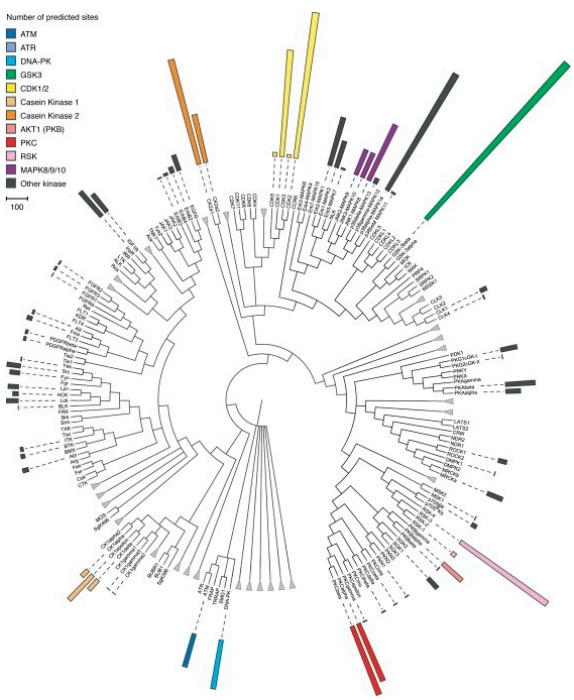
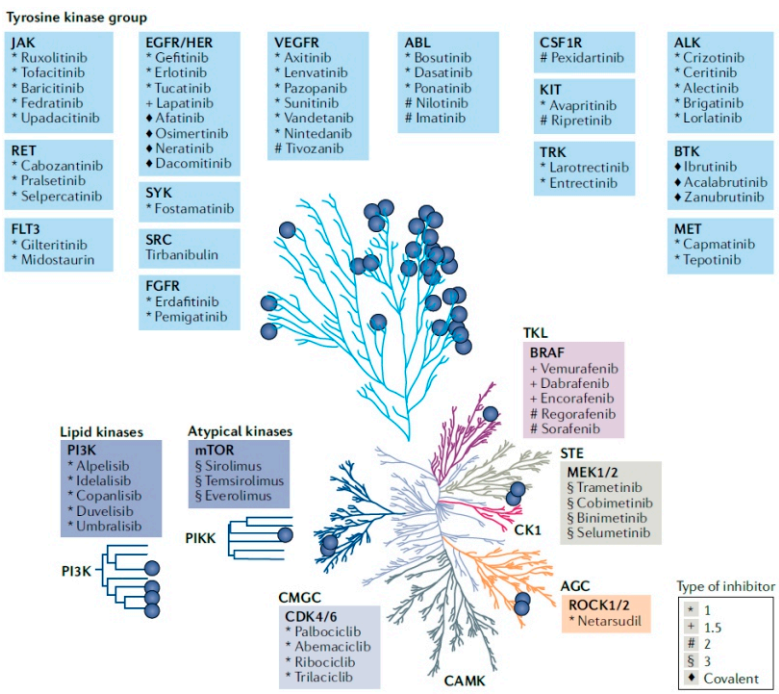
Protein Kinase is a protein that modifies other proteins by chemically adding phosphate groups to phosphorylate them. Protein kinases are involved in numerous physiological processes, including cell proliferation, survival, apoptosis, metabolism, transcription, and differentiation. Pharmacological and pathological studies have shown that protein kinases are ideal drug targets for many diseases, such as tumors, inflammatory, CNS diseases, cardiovascular diseases and diabetes. Kinases are now divided into 10 categories, AGC, CAMK, CK1, CMGC, TK, TKL, STE, RGC, Other, and Atypical. Among them, tyrosine (TK) kinases are the focus of current research.

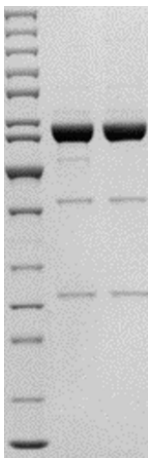


Number of Predictions in the Human Kinome
Cell. 2007 Jun 29;129(7):1415-26.

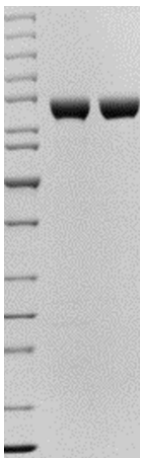


FDA-approved kinase inhibitors mapped onto the human kinome.
Nat Rev Drug Discov volume 20, Issue: 11, Pages : 839–861 (2021)

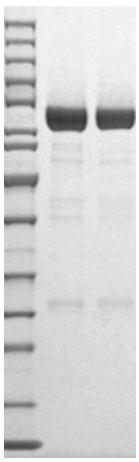
ACK



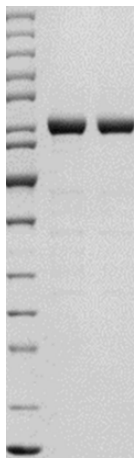
AKT1



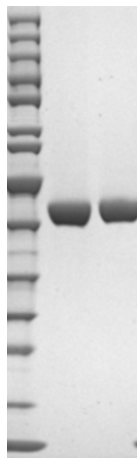
AKT3



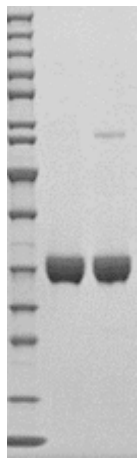
AURA



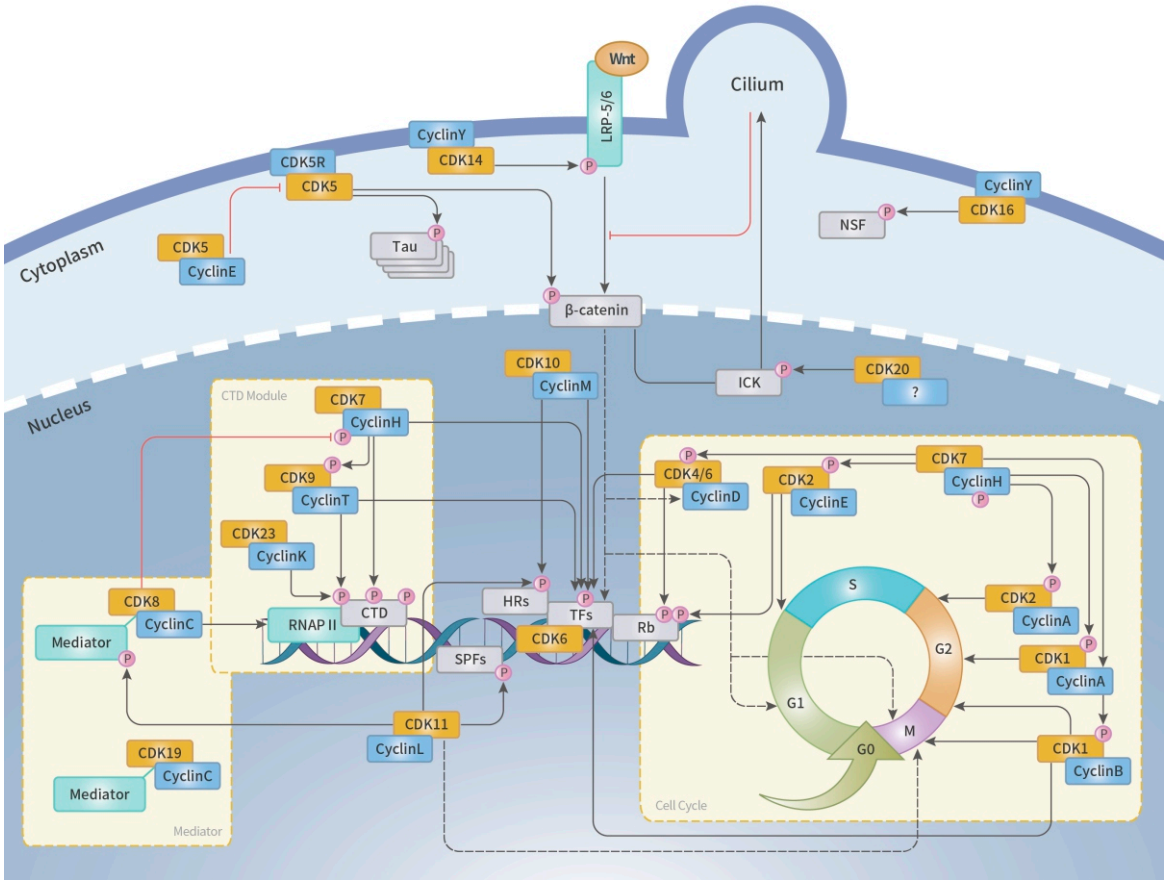
PGK1



PIM1



Hot Targets				
ABL	EPHB2	MAP2K6	p85/p110	PRKCG(PKCγ)
ABL1	EPHB3	MAP2K7	PAK2	PRKCH(PKCη)
AKT1	ERBB4	MAP3K21	PAK3	PRKCI(PKCι)
AKT3	ERK1	MAP3K4	PAK4	PRKCZ(PKCz)
ASK1	ERK2	MAP3K6	PAK5	PRKD1
AURB/INCENP	ERN2	MAP3K8	PAK6	PRKD2
AURC/INCENP	HCK	MAP4K3(GLK)	PDPK1	PRKD3(PKD3)
AURKA/INCENP	IKKε	MAP4K4(HGK)	PEAK1	RIPK1
BIKE	IRAK1	MAP4K6	PGK1	RIPK3
BRSK1	IRAK4	MAPK4	PIK3C2B	ROCK1
BRSK2	JAK1	MAPK7	PIK3C2G	RSK1
CaMK1α	JAK3	MAPKAPK2	PIK3CA	RSK2
CaMK1δ	JNK1	MAPKAPK3	PIK3CG	RSK3
CAMK2D	JNK2	MAPKAPK5	PIK3R3	RSK4
CAMK2α	JNK3	MELK	PIM1	SPHK1
CHUK	LIMK1	MK2	PIM2	STK38
cKIT	LRRK2	MKNK1	PIM3	STKLD1
CKS1	MAP2K1	MKNK2	PKLR	TAB1
CKS2	MAP2K3	P38α (MAPK14)	PRKCD(PKCδ)	TNIK
cRAF1	MAP2K4	P70S6K	PRKCE(PKCε)	TYK2

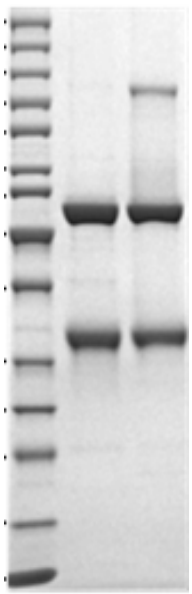


Cyclin-dependent kinases (CDKs) belong to the family of serine/threonine protein kinases and are key kinases involved in cell cycle regulation and regulation of transcription. Among them, cell cycle-related proteins are CDK1, CDK4/6, CDK5, and those related to transcriptional regulation are CDK7, CDK8, CDK9, CDK11, and CDK20.

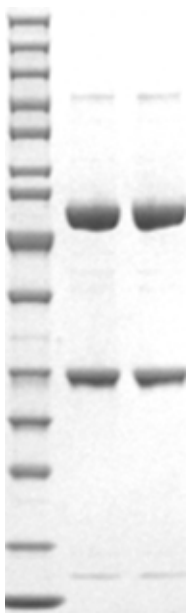
Hot Targets	
CDK1	CDK3
CDK1/Cyclin B1	CDK3/Cyclin C
CDK1/Cyclin E1	CDK3/Cyclin E1
CDK1/Cyclin E2	CDK3/Cyclin E2
CDK1/CyclinA2	CDK4
CDK2	CDK4/Cyclin D1
CDK2/Cyclin A2	CDK4/Cyclin D2
CDK2/Cyclin D1	CDK4/Cyclin D3
CDK2/Cyclin E1	CDK5
CDK2/Cyclin E2	CDK5/CyclinB1
CDK2/Cyclin O	CDK5/p25

Hot Targets	
CDK5/p35	CDK9/Cyclin T2
CDK6	CDK10/Cyclin M
CDK6/Cyclin D1	CDK12/Cyclin K
CDK6/Cyclin D2	CDK12/Cyclin T1
CDK6/Cyclin D3	CDK13/Cyclin K
CDK7	CDK13/Cyclin T1
CDK7/Cyclin H/MAT1	CDK15/Cyclin Y
CDK8/Cyclin C/MED12	CDK16/Cyclin Y
CDK9	CDK17/Cyclin Y
CDK9/Cyclin K	CDK18/Cyclin Y
CDK9/Cyclin T1	CDK19/Cyclin C/MED12

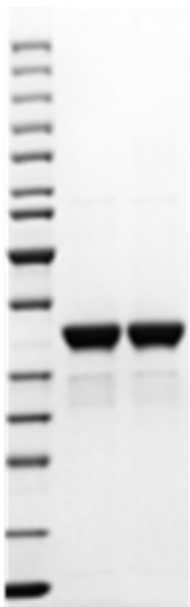
CDK4/Cyclin D3



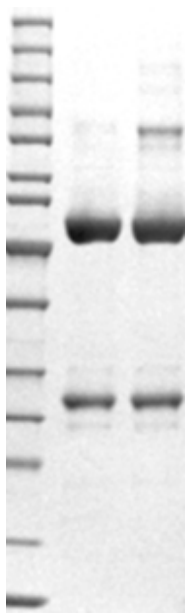
CDK1/Cyclin B1



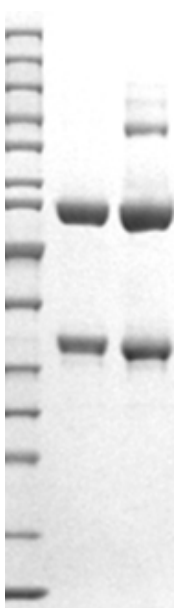
CDK4



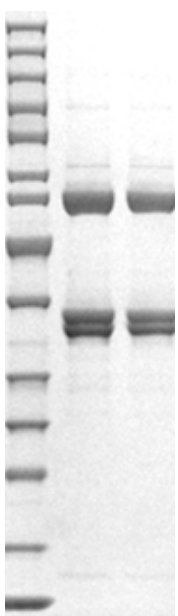
CDK5/p25



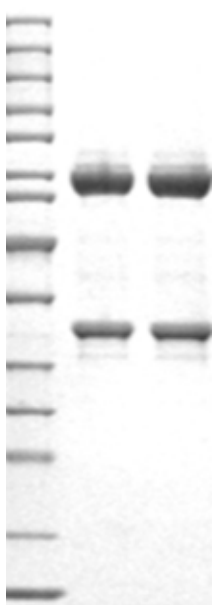
CDK6/Cyclin D2



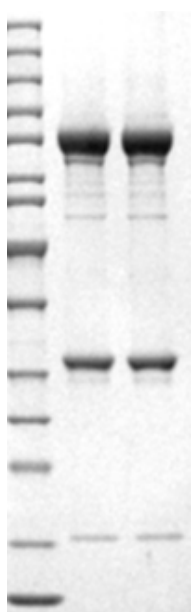
CDK7/Cyclin H/MAT1



CDK12/Cyclin K



CDK19/Cyclin C/MED12



Ub-Proteasome System(UPS)

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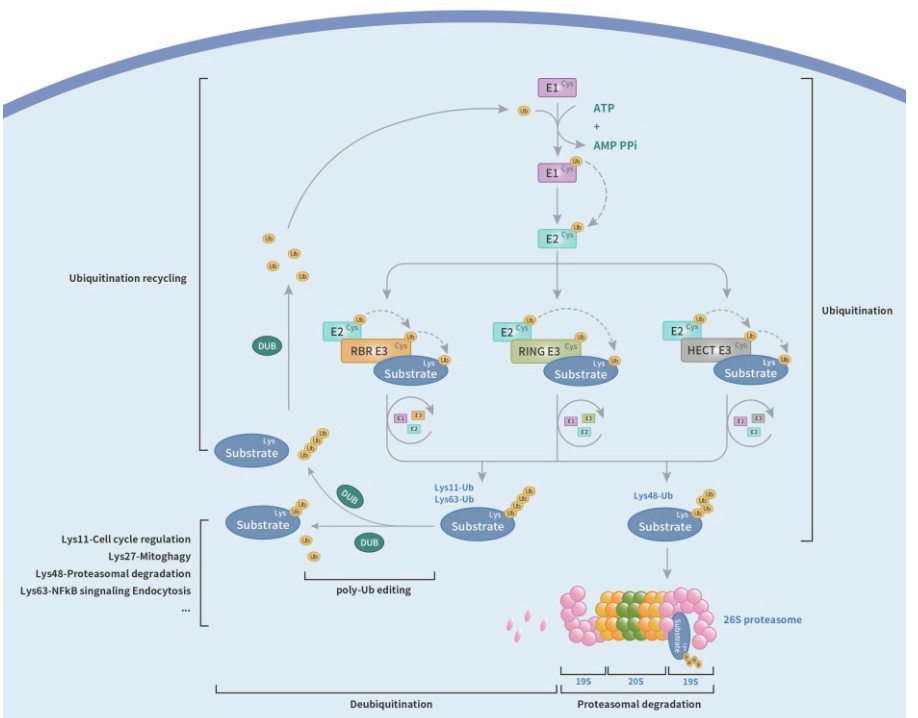
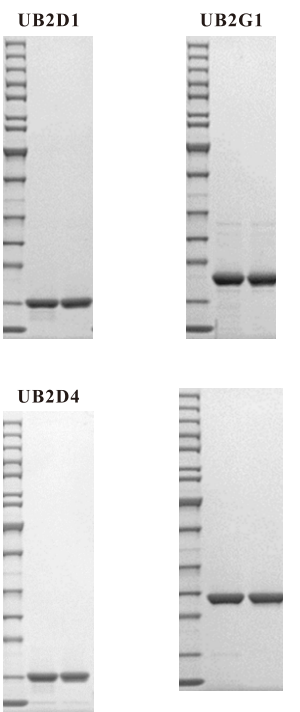
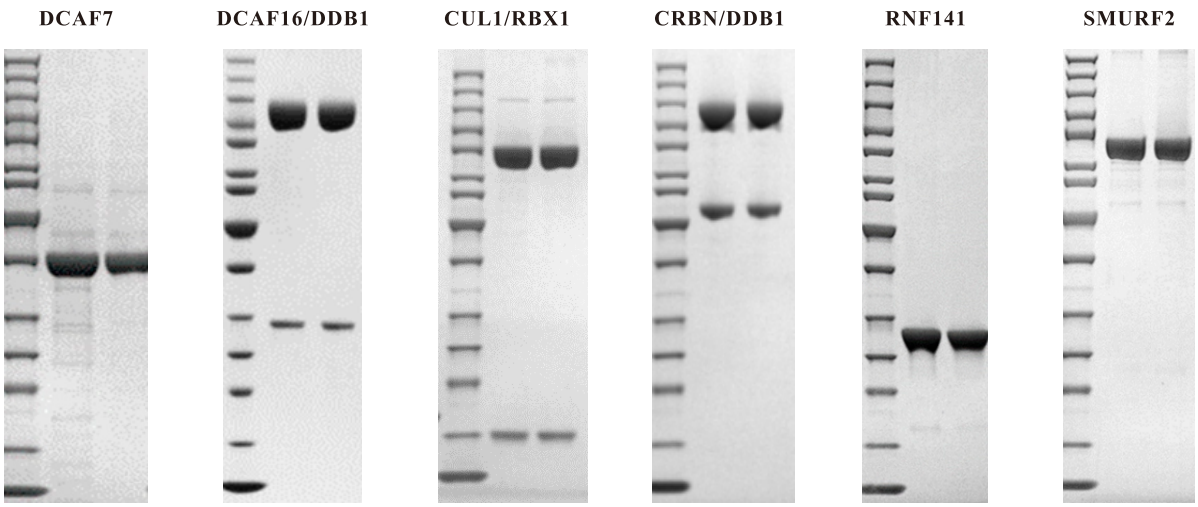
Protein degradation is a regulated, multistep process. Ubiquitin is loaded onto E1-activating enzymes in an ATP-dependent manner and then transferred to E2-binding enzymes. The same E2 can bind to many E3 ligases, which in turn can ubiquitinate multiple target substrate proteins. E3 ligases bind specific substrate proteins based on substrate degron motifs. Sorting, lysosomal disruption, or proteolytic cleavage and degradation by the 26S ubiquitin proteasome by different labeling of K48 residues on substrate-bound Ubs. DUBs deubiquitinases catalyze the removal of Ub and regulate Ub-mediated pathways.

Hot Targets	
UBA5	UB2R1
UBA6	UB2Q2
UBA7	UBE2B
UBE2W	UB2E2
UB2E3	UE2NL
UB2D3	UEVLD
UB2Q1	UB2V1
UB2V2	UB2E1
UFC1	UB2L6
UBE2A	UB2R2
UBE2Z	UBC9
UB2D4	UB2L5
UBE2S	UBE2C
UB2G1	UBE2F
UBE2H	UB2G2
UB2D1	UB2L3
UBE2N	UBE2K
UBE2O	UBE2T



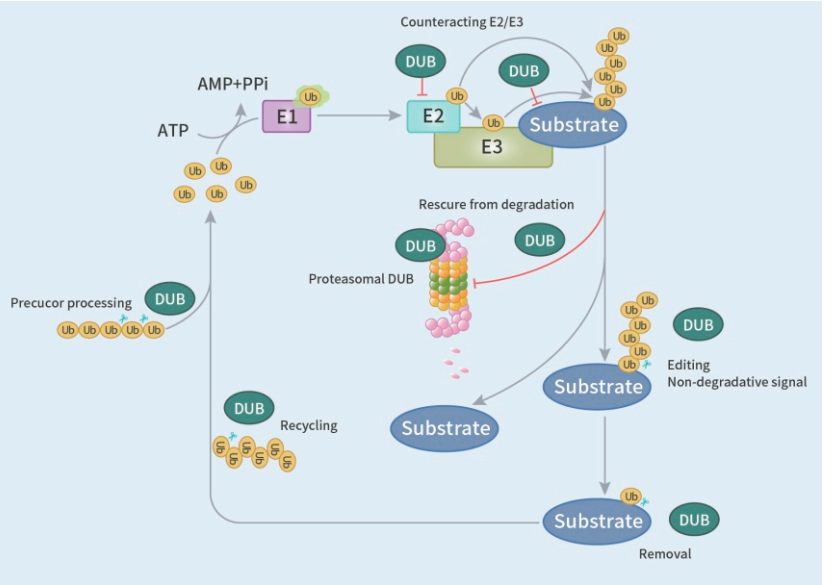


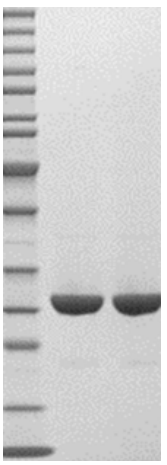
Ubiquitination of E3 ligases regulates cellular trafficking, DNA repair, and signal transduction, and has profound implications in cell biology. E3 ligases are also key players in cell cycle control, mediating the degradation of cyclins, and cyclin-dependent kinase inhibitor proteins. The human genome encodes more than 600 E3 ligases.

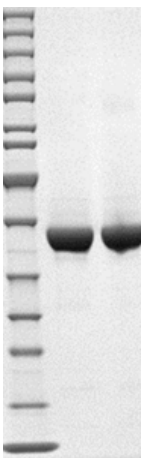


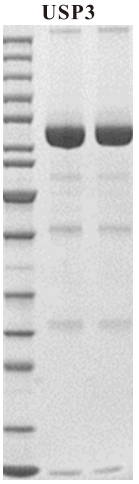
Hot Targets			
CRBN/DDB1	DCAF12/DDB1	KMT2D	TRIM38
CRBN/DDB1/CUL4A/RBX1	DCAF13	LIVIN	TRIM54
CUL1/RBX1	DCAF15/DDB1	LONRF2	TRIM69
CUL2/RBX1	DCAF16/DDB1	MDM2	UHRF1
CUL3/RBX1	DCAF16/DDB1/CUL4A/RBX1	MDM4	UHRF2
Cul4a/RBX1	KBTBD11	NEDD4L	VHL/EloB/EloC
CUL5/RBX1	KBTBD2	NOSIP	WHSC1
CBLB	KBTBD6	NSMCE1	WWP1
CBLC	KBTBD7	PELI1	WWP2
DCAF1	KBTBD8	PELI2	XIAP
DCAF4	KCTD1	SH3RF3	ZBTB7B
DCAF7	KLHL14	SMURF2	ZFAND3
DCAF8/DDB1	KLHL21	RNF4	ZFAND5
DCAF9/DDB1	KLHL3	RNF8	ZNRF2
DCAF10/DDB1	KLHL42	TRIM2	SKP1/SKP2
DCAF11/DDB1	KMT2C	TRIM3	

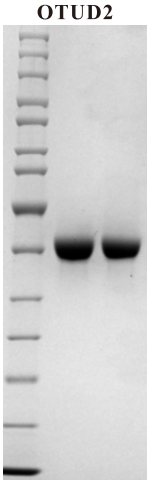
Reverse modification to add ubiquitin to targeted proteins relies on deubiquitinases (DUBs), which catalyze the cleavage of single Ub or polyubiquitin chains. The human genome encodes about 100 potential DUBs, which can be divided into 6 families: ubiquitin-specific proteases (USPs), ubiquitin COOH terminal hydrolases (UCHs), ovarian cancer proteases (OTUs), Josephins, JAB1/MPN/MOV34 family (JAMMs), novel ub-containing DUB family interacting motifs (MINDYs), and removing ubiquitin-like SUMOylases (SENPs).











Hot Targets		
USP1	USP27	OTUD2
USP2	USP28	OTUD6A
USP3	USP29	ZRANB1
USP4	USP30	VCPIP1
USP5	USP37	Cezanne1
USP6	USP40	JOSD2
USP7	USP46	ATXN3L
USP8	USP47	ATXN3
USP9X	USP48	AMSH-LP
USP10	USP51	SENP2
USP12	UCHL1	SENP3
USP15	UCHL3	SENP5
USP16	UCHL5	SENP6
USP20	BAP1	SENP7
USP21	OTUD1	SENP8
USP25		

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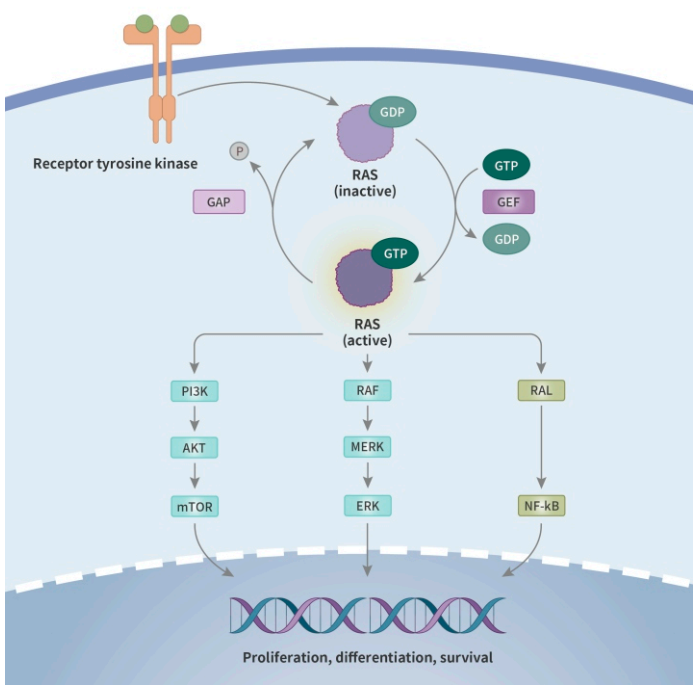
Biortus Protein		Uniprot ID	Modification
Kras	WT	P01116	Biotinylated/ GDP loaded/ GMPPNP loaded
	G12A		
	G12C		
	G12S		
	G12V		
	G12R		
	G12D		
	G13D		
	Q61K		
	Q61R		
	Q61H		
	Y64F		
	H95L		
	H95R		
	Q61K, H95L		
	G12C, H95R		
Nras	WT	P01111	
	G12C		
	G12D		
	G12A		
	G13D		
	Q61L		
	Q61H		
	Q61R		
	Q61K		
	S39W, Q61K		
	Q61K, R68S		
	Q61K, Q99L		
	Q61K, Y96C		
	Q61K, R68S		
	L95H		
Hras	WT	P01112	
	G12D		
	G12V		
	G13R		
	Q61R		
	Q61L		

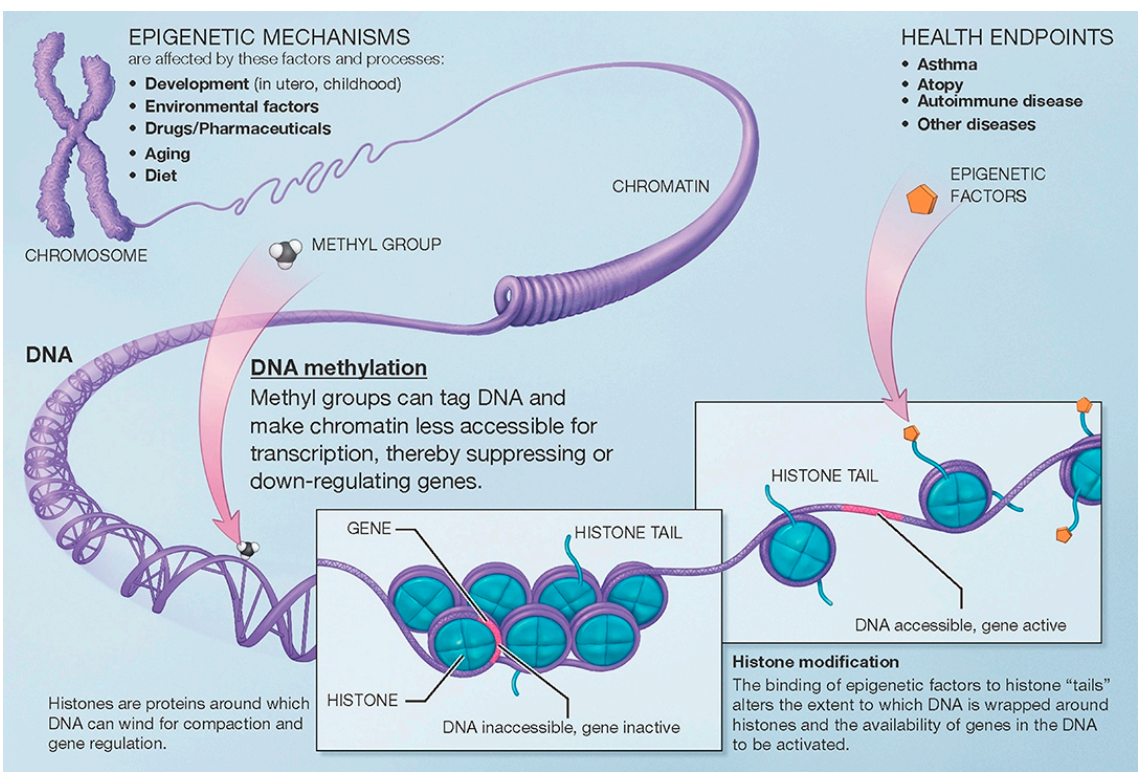
Ras protein family is a group of small GTP-binding proteins that play a critical role in signal transduction pathways. This family of GTPases includes several members, including H-Ras, K-Ras, N-Ras, and other less-studied isoforms like R-Ras, M-Ras, and Rap proteins.

Ras proteins act as molecular switches, cycling between an inactive GDP-bound state and an active GTP-bound state. Upon activation, Ras proteins bind to downstream effector proteins, such as RAF, PI3K, and RalGDS, initiating a signaling cascade that ultimately leads to changes in gene expression and cellular behavior.



At the base of epigenetics is the diverse covalent modifications of histones and nucleic acids that together regulate chromatin structure and gene expression. Epigenetic modifications are closely related to the occurrence and development of tumors. They mainly regulate gene function and expression levels through DNA methylation, histone modification, non-coding RNA regulation, and chromatin structural remodeling, thereby affecting tumor progression.

Hot Targets	
AR	HDAC2
BPTF	HDAC4
CECR2	JMJD2A
EHMT1	JMJD2C
EIF1AX	JMJD2D
EIF4A1	KDM1A
EIF4E	KDM2A
EIF5A	KDM5A
ESR1	KDM6B
ESR2	KDM8
EXOSC2	MYST1
Histone-H2A	NR5A1
Histone-H2B	NR6A1
Histone-H3	PHF8
Histone-H3.3	PRMT5/MEP50
Histone-H3.3	SIRT3
Histone-H3K4C	Sirt6
Histone-H4	WDHD1

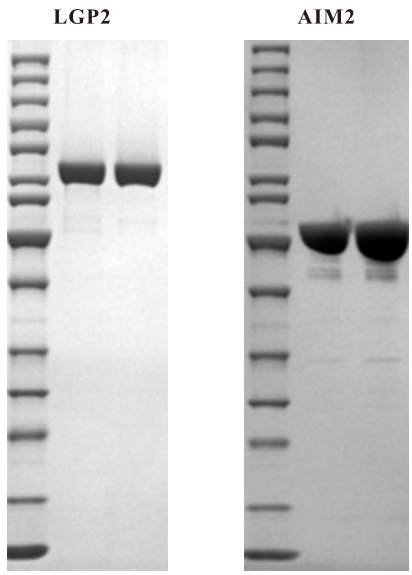


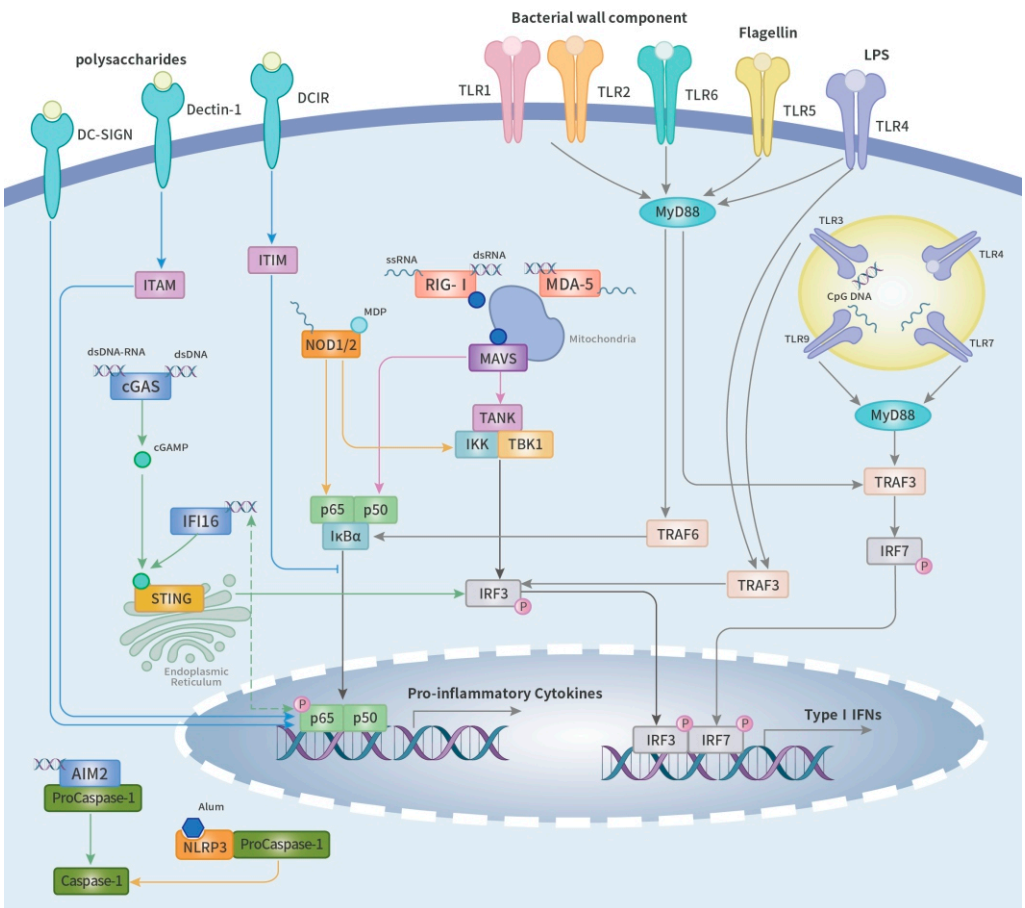
Overview of mechanisms involved in epigenetic regulation of gene expression.
Front Pediatr. 2019 Apr 2;7:115.

BIORTUS USA

Pattern recognition receptors (PRRs) are cell-encoded host sensors that detect two classes of molecules: pathogen-associated molecular patterns (PAMPs) associated with microbial pathogens, and host-released upon cell injury or death Damage-associated molecular patterns (DAMPs) associated with cellular components. PPRs can be divided into the following categories: membrane-bound PPRs include Toll-like receptors (TLRs) and C-type lectin receptors (CLRs); cytoplasmic PPRs include NOD-like receptors (NOD-like receptors (NLRs), RIG-I-like receptors (RLRs), and Cytosolic DNA sensors (CDSs).

Hot Targets
XRCC6
DDX41
AIM2
Sox2
MRE11A
IFI16
LRRFIP1
Dectin-1
ZBP1
MB21D1
Mincle
LGP2
NLRP6
NLRP5
NLRP1
PYHIN1

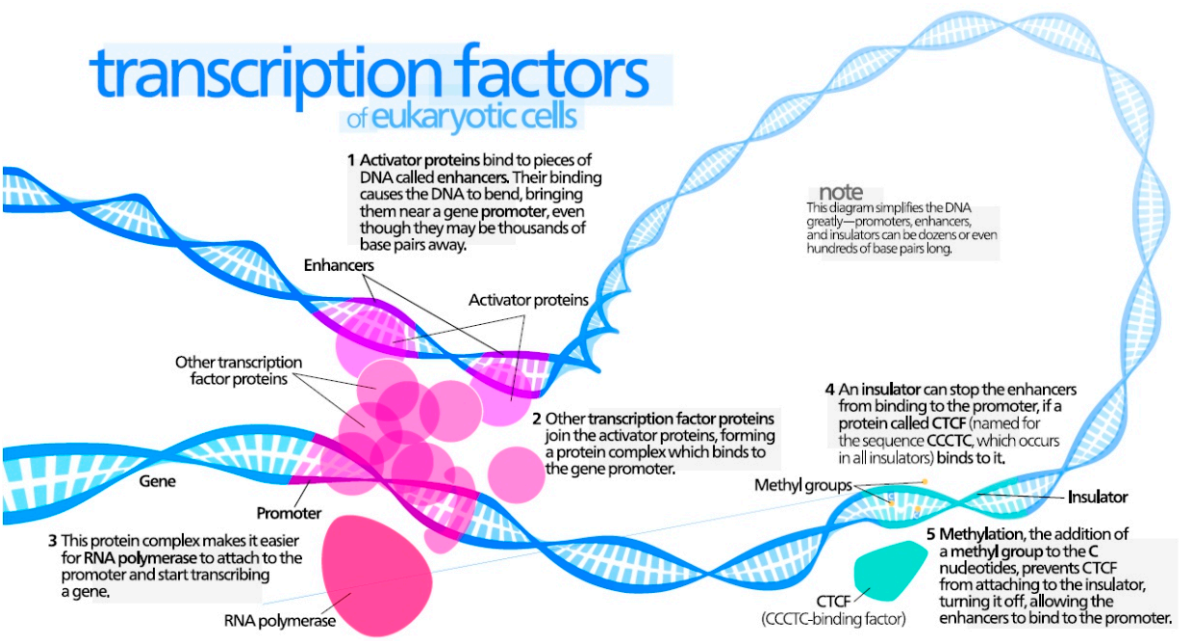




BIORTUS USA

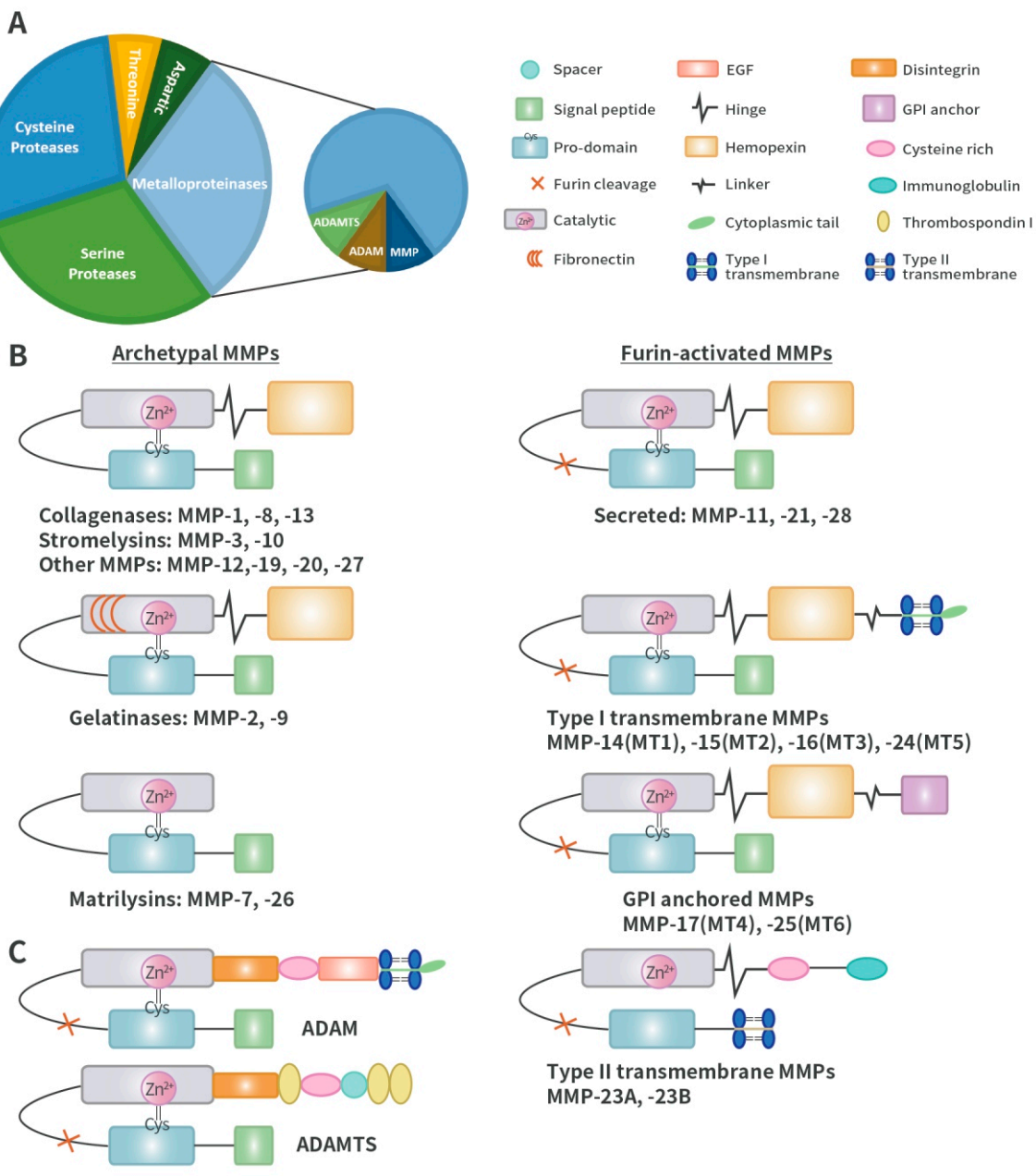
Transcription factors (TFs) are a class of protein molecules that specifically bind to specific sequences of genes, thereby controlling the expression of target genes with specific intensity at specific time and space. As an important part of gene expression regulation, TFs are widely involved in physiological and pathological processes in vivo. It is estimated that there are at least 1600 transcription factors in the human genome, of which about 19% are closely related to various diseases, including cancer, autoimmune diseases, diabetes, cardiovascular diseases, etc. In view of the direct regulation effect of TFs on target genes, they have higher specific disease regulation ability than upstream signaling proteins such as kinases and GPCRs, and can avoid the side effects caused by crosstalk of signaling pathways.

Hot Targets
HMGB1
CBFB
BRPF1
BRPF3
HIF1α
ERG
FOXP3
FOXR2
MAX
MYC
E2F1
PIR
SNAI1



Transcription Factors
Book: General Biology (Boundless) 16.5C: Cancer and Transcriptional Control

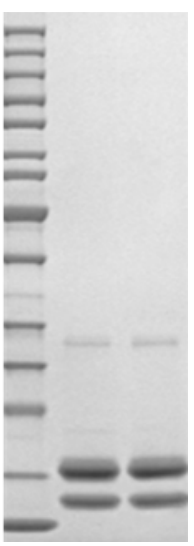
In the human genome, there are at least 569 proteases and their homologues, which can be divided into 5 categories: 21 aspartic proteases, 28 threonine proteases, 150 cysteine proteases, 176 serine proteases, and 194 metalloproteases, including members of the MMP, ADAM, and ADAMTS families. These proteases are involved in protein catabolism and digestion and are also involved in cell signaling. Some proteases are extremely important signaling molecules involved in many life processes. Protease signaling pathways are tightly regulated, and dysregulation of protease activity can lead to diseases such as cardiovascular disease, inflammation, cancer, osteoporosis, and neurological diseases.



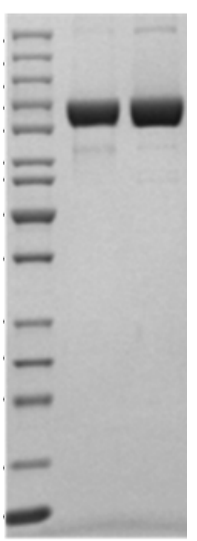
Protease classification and structure

Hot Targets				
CA7	D-psicose 3-epimerase	Galactokinase	Lipoxygenase	Lysine decarboxylase
Carbonyl reductase	EDC20	GALNS	Hmp	maiA
Carboxylesterase	eltD	GCY1	HPGDS	malQ
Cas9	ENO1	Gdh	HpGT	Maltooligosyl trehalose synthase
CASP3	Epoxide hydrolases	gdh2	HPRT1	MDO
Cephalosporin C	Esterase	GGPS1	hydA	metK
cgt	estZF172	glucan phosphorylase	hydB	MGLL
CHAC1	EXOSC5	GLUD1	hydD	MGMT
ClpC1	EXOSC8	Glycosyltransferase	hydG	MMP-13
CMPK	EXOSC9	GNPDA2	Hyoscyamine 6 beta-hydroxylase	monomeric sarcosine oxidase
COLAER	FASN	GOX2015	IDH1	Mtg
colE7	fbaA-5R	GSCOC	Ido	Multi-copper polyphenol oxidoreductase
Cyclopentanone monooxygenase	FDH1	GSTP1	inuB	NADH dehydrogenase
dai	FEN1	gucD	KLK	NADPH-dependent aldose reductase
DDC AADC	FH	gyaR	L-arabinose isomerase	Nap
DHFR	FHIT	gyrA	L-asparaginase	N-Carbamoylase
D-hydantoinase	FNTA	gyrB	LC-cutinase	NIT2
Dit	FTO	Hdhb	leucyl aminopeptidase	nitA
DPP8	fum	hflC	Lipase	Nitrilase

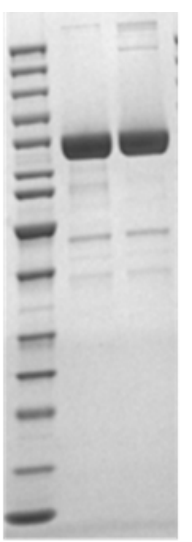
CASP3



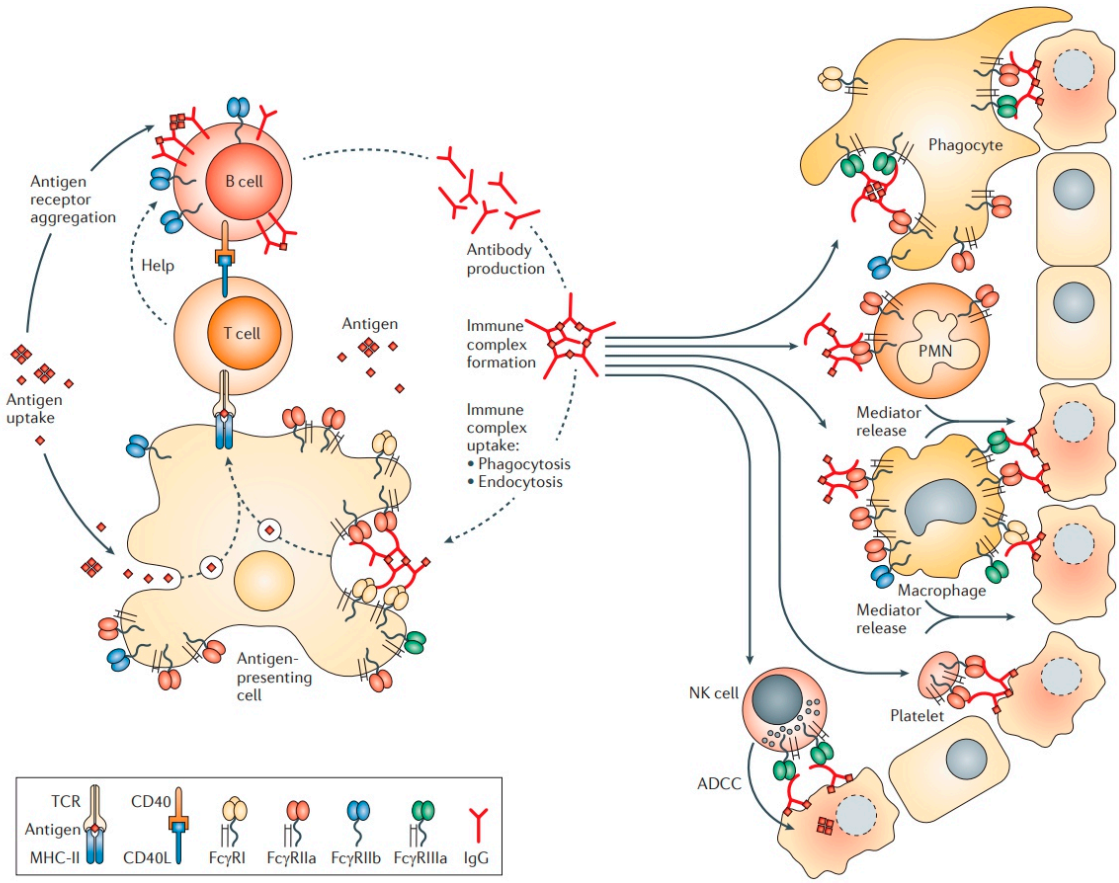
DPP 8



FTO



FASN



The role of Fc receptors in normal antibody-based activation of cell responses
Nat Rev Drug Discov volume 11, Pages 311-331 (2012)

Clusters of differentiation (CDs) usually act as receptors or ligands and play a very important role in cells. Some CD proteins are not involved in cell signaling, but have other functions, such as cell adhesion. There are currently 371 human CD proteins. Immunoglobulin receptors (IgRs), also known as Fc receptors (FcRs), are a class of cell surface receptors that bind to specific Ig Fc segments to trigger cellular activity.

Hot Targets
SIGN
PD-1
PD-L1
CD47
CD70
TIGIT
CD276
CD73
FCGR3A
Ig kappa chain

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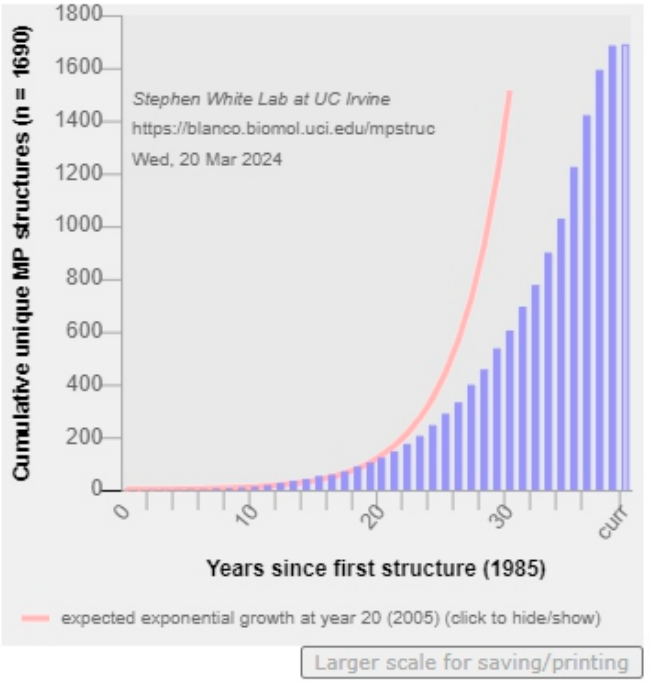
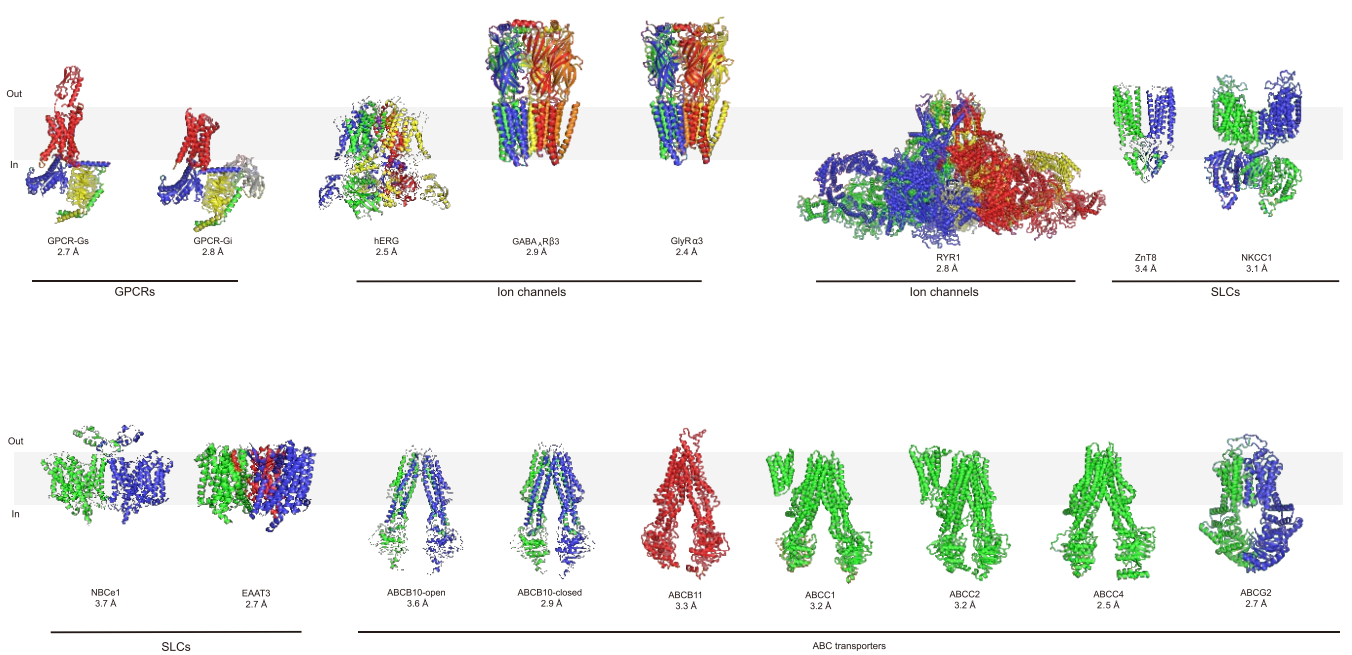


Membrane proteins play an important role in cells, they are involved in cell-to-cell, cell-to-matrix interactions, cell formation, and transmembrane transport of various ions, metabolites and proteins. Based on the importance of membrane proteins in various cellular functions, more and more membrane proteins have become drug targets for various diseases, and the study of membrane proteins has gradually become a research hotspot in recent years.

We have 2609 membrane protein plasmids, which include those important targets and known structure proteins.

- https://blanco.biomol.uci.edu/mpstruc/
- Last database update: 20/03/2024

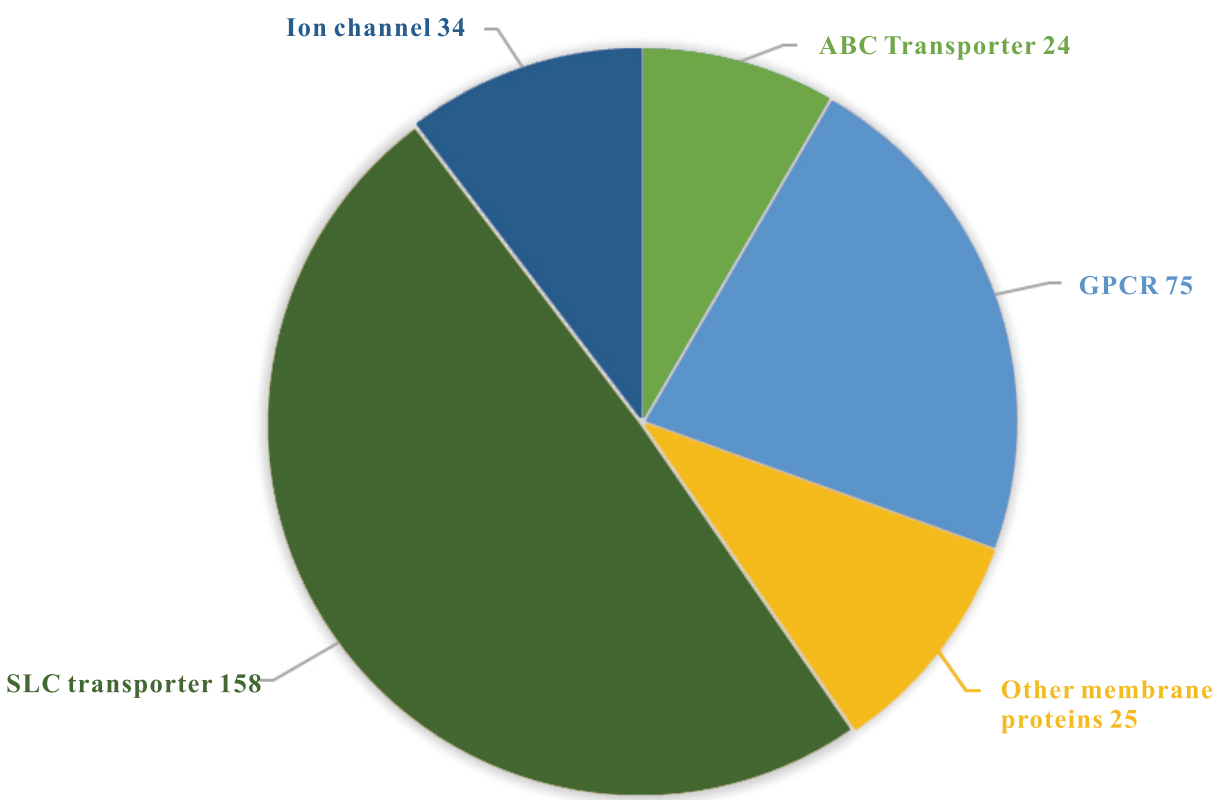
• Cryo-EM structures of membrane proteins



Membrane proteins are challenging targets: hard to expression recombinantly; difficult to keep them stable, homogenous, and active; and structural biology unfriendly;

Biortus USA has developed several proprietary methodologies to overcome the challenges, and the membrane protein collection in Biortus USA included in GPCRSuite®, ABCSuite®, SLCSuite® and IonChannelSuite®.

MEMBRANE PROTEINS IN BIORTUS



ABC Transporters

BIORTUS USA

ATP-binding cassette transporters (ABC-transporters) catalyze the vectorial transport of a great variety of substrates across biological membranes. They are intricate molecular systems that have representatives in all extant phyla from prokaryotes to humans. They are one of the largest and ancient protein superfamilies and are able to power the translocation of substrates (including sugars, amino acids, metal ions, peptides/proteins, and a large number of hydrophobic compounds) across biological membranes, often against a concentration gradient, by the hydrolysis of ATP.

Hot Targets				
ABCA1	ABCB1	ABCC2	ABCE1	bABCC1
ABCA2	ABCB10	ABCC4	ABCF3	CFTR
ABCA6	ABCB11	ABCC5	ABCG2	

Solute carriers (SLC)

Solute carriers (SLC) are a group of membrane transport proteins, comprising over 300 members, most of which are located in cell membranes. Their main function is to facilitate the transport of a wide variety of substrates across biological membranes, including the uptake of small molecules into cells.

Hot Targets					
ASCT2	SGLT1con	SLC19A3	SLC25A13	SLC30A10	SLC4A1
CHT	SGLT2	SLC1A1	SLC25A15	SLC30A2	SLC4A10
CNT3	SLC10A4	SLC1A2	SLC25A20	SLC30A3	SLC4A4
EAAT1	SLC11A1	SLC1A3	SLC25A22	SLC30A4	SLC4A7
ENT1	SLC11A2	SLC1A4	SLC25A37	SLC30A8	SLC51B
FPN	SLC12A1	SLC1A5	SLC25A39	SLC33A1	SLC52A1
GAT1	SLC12A2	SLC1A6	SLC25A45	SLC34A1	SLC52A3
GLUT1	SLC12A3	SLC20A2	SLC25A46	SLC34A3	SLC5A1
GLUT3	SLC12A4	SLC21A3	SLC25A5	SLC35A1	SLC5A8
GlyT1	SLC12A7	SLC22A12	SLC26A4	SLC35A2	SLC6A14
hMCT1	SLC14A1	SLC22A18	SLC26A5	SLC35F2	SLC6A17
hMCT4	SLC15A1	SLC22A2	SLC26A9	SLC35F2	SLC7A11
KCC1	SLC15A2	SLC22A23	SLC27A4	SLC37A4	SLC7A3
KCC2	SLC15A4	SLC22A4	SLC29A2	SLC38A1	SLC7A5
KCC3	SLC16A2	SLC22A6	SLC2A10	SLC38A2	SLC7A7
KCC4	SLC16A4	SLC22A6	SLC2A2	SLC3A2	SLC7A7/SLC3A2
NaCT	SLC17A3	SLC23A2	SLC2A3	SLC3A2/SLC7A11	SLC7A9
NTCP	SLC17A5	SLC24A4	SLC2A4	SLC40A1	SLC8A2
RhCG	SLC19A1	SLC25A11	SLC2A5	SLC44A1	SLCO1B1
SERT	SLC19A2	SLC25A12	SLC2A9	SLC46A1	SLCO2A1

GPCR

The G protein-coupled receptor (GPCR) superfamily has more than 800 members in the human genome, detecting a variety of extracellular chemical, biological, or physical signals that are critical for human biology and disease. Understanding their three-dimensional (3D) structures will help understanding their function and will enable the development of new therapeutic molecules.

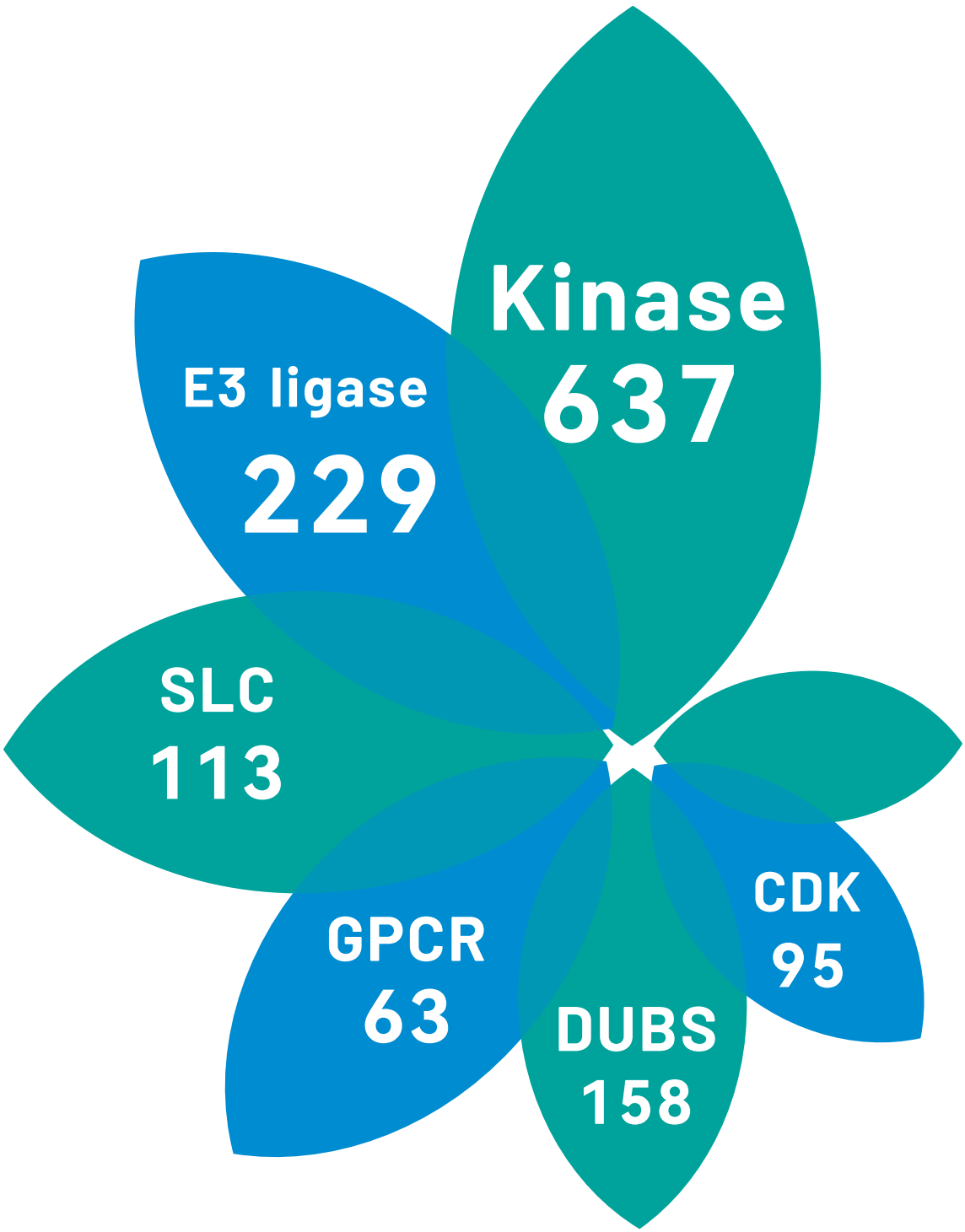
Hot Targets					
5HT1B	CCR2	EDNRA	GPR183	LT4R1	OXYR
5HT2A	CCR5	FFAR1	GPR52	M1R	P2ER3
A2AR	CCR7	GIPR	GPR75	M2R	P2Y1
AA2AR	CCR8	GLP1R	GPR88	MC4R	PAR1
ADRB2B	CCR9	GLP1R/Gas/Gaβ/Gaγ	GPRC5D	NPY1R	PAR2
AGTR2,AT2R	CNR1	GLR	GRM1	NPY2R	PE2R4
APJ	CXCR4	GNAI1/GNB1/GNG2	GRM5	OPRD1	SMO
AVPR2	DRD2	GPR155	HRH3	OX1R	TACR1
CaSR	DRD3	GPR158	HTR2B	OX2R	

Ion Channels

Ion channels are pores that open and close in an all-or-nothing fashion on time scales of 0.1 to 10 ms to provide aqueous channels through the plasma membrane that ions can traverse. There are a number of drugs which act by modulating the ion channels.

Ion channels that are normally modulated by membrane potential are known as voltage-sensitive ion channels. Voltage-sensitive ion channels mediate the conductance of sodium, calcium, and potassium. They provide rapid changes in ion permeability. These channels exhibit high ion selectivities, voltage sensitivities, and single-channel conductance.

Hot Targets				
GABRA1/GABRB2/GABRG2	GlyRα3	P2X3	TRPC1	TRPM7
GABRA1/GABRB3/GABRG2	HCN2	PANX1	TRPC3	TRPML1
GABRA5/GABRB3	hERG	TASK-1	TRPC5	TRPV1
GABRB3	KCNJ2	TEME175	TRPC6	TRPV3
GABRR1	Nav1.8	TRPA1	TRPM4	TRPV4



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