AT-A-GLANCE

Protein Tags

Protein tags allow detection and purification without needing an antibody specific to your protein of interest. Small tags are unlikely to interfere with natural protein function and localization. Large tags can increase expression or solubility of your protein of interest. All of these tags can be used in bacteria, yeast, mammalian, or baculovirus transformed insect cells.

6xHis (0.84 kDa)

HHHHHH

- **Incorporate at:** N-terminus, internal sites, C-terminus
- **Binds to**: Ni^{2+}, Co^{2+}
- **Benefits:** Inexpensive purification, low immunogenicity allows in vivo injections
- **Limitations:** Purification of off-target proteins, does not work for metalloproteases or metal chelators
- **Recommended for:** Detection, purification, immobilization

FLAG (1.01 kDa)

DYKDDDK

- **Incorporate at:** N-terminus, C-terminus
- **Binds to:** anti-FLAG antibodies
- **Benefits:** Few effects on target protein, high specificity, easy tag cleavage
- **Limitations:** Antibody purification gives low protein yield
- **Recommended for:** Detection, purification

Glutathione S-Transferase (GST) (26 kDa)

MSPILGYWKIKGLVQPTRLLLEYLEEKYEEHLYERDEGDKWRNKKFEL-GLEFPNLPYYIDGDVKLTQSMAIIRYIADKHNMLGGCPKERAEISMLEGA-VLDIRYGVSRIAYSKDFETLKVDFLSKLPEMLKMFEDRLCHKTYLNGDH-VTHPDFMLYDALDVVLYMDPMCLDAFPKLVCFKKRIEAIPQIDKYLKSSKY-IAWPLQGWQATFGGGDHPPKSD

- **Incorporate at:** N-terminus, C-terminus
- **Binds to**: Glutathione
- **Benefits:** Highly expressed in *E. coli*, library of yeast GST-tagged ORFs
- **Limitations:** Large size, alters native state of protein, may require tag cleavage step after purification
- **Recommended for:** Increased expression, and increased solubility

Hemagglutinin A (1.0 kDa)

YPYDVPDYA

- **Incorporate at:** N-terminus, internal sites, C-terminus
- **Binds to:** anti-HA antibodies
- **Benefits:** Does not affect protein function or localization, particularly useful in mammalian expression systems
- **Limitations:** Antibody purification gives low protein yield
- **Recommended for:** Detection, purification

C-Myc (1.3 kDa)

EQKLISEEDL

- **Incorporate at:** N-terminus, internal sites, C-terminus
- **Binds to**: anti-Myc antibodies
- **Benefits:** Unlikely to affect protein function, high affinity antibody available
- **Limitations:** Can interfere with secretory protein translocation, low yield purification
- **Recommended for:** Detection, purification

Strep Tag II (1.06 kDa)

WSHPQFEK

- **Incorporate at:** N-terminus, C-terminus
- **Binds to**: Strep-Tactin
- **Benefits:** Strong and highly specific binding, high purity, elution under physiological conditions
- **Limitations:** Sensitive to high salt loading buffers, free strep-tactin can interfere with purification when only low levels of tagged protein are present
- **Recommended for:** Detection, purification, immobilization

S-tag (1.75 kDa)

KETAAAKFERQHMDS

- **Incorporate at:** N-terminus, internal sites, C-terminus
- **Binds to**: S-protein
- **Benefits:** Assays available for quantitation and detection without antibody
- **Limitations:** Not good for large scale purification
- **Recommended for:** Detection, purification

T7 (1.42 kDa)

MASMTGGQQMG

- **Incorporate at:** N-terminus, internal sites
- **Binds to**: anti-T7 antibody
- **Benefits:** May increase expression
- **Limitations:** Acidic elution conditions may affect protein
- **Recommended for:** Purification, increased expression

V5 (1.42 kDa)

GKPIPNPLLGLDST

- **Incorporate at:** C-terminus
- **Binds to**: anti-V5 antibody
- **Benefits:** Antibody highly specific in bacterial lysates
- **Limitations:** Some cross-reactivity in mammalian lysates
- **Recommended for:** Detection

Ready to get started?

Learn how with our helpful technical articles:

SigmaAldrich.com/protexpsys

SigmaAldrich.com/flagtagvectors

How to Choose your Protein Tag

What Size is Each Tag?

Smaller epitope tags are less likely to interfere with natural protein activity			
6xHis	**HA**	**FLAG**	**StrepTag II**
0.84 kDa	1.0 kDa	1.01 kDa	1.06 kDa
T7	**C-Myc**	**V5**	**S-Tag**
1.1 kDa	1.3 kDa	1.42 kDa	1.75 kDa

Larger protein tags can improve expression levels and solubility
GST
26 kDa

Where Can Tags Be Added?

N-Terminus Best location to increase protein expression		**Internal Sites** Best when both terminals are inside folded protein structure		**C-Terminus** Best for preserving N-terminus signal sequences	
6xHis HA FLAG StrepTag II	T7 c-Myc S-Tag GST	6xHis HA T7	c-Myc S-Tag	6xHis HA FLAG StrepTag II	c-Myc V5 S-Tag GST

What Other Characteristics Should I Consider?

Minimal Effects on Protein Localization and Function		**Low Immunogenicity: Great for Downstream *in vivo* Injections**
6xHis HA StrepTag II	FLAG c-Myc S-Tag	6xHis
Best for Increasing Expression and Solubility		**Easily Cleavable Tags**
T7	GST	**FLAG** – Enterokinase from bovine: **E5144** **GST** – Thrombin protease: **SAE0147**

How to Use your Protein Tag

Purify – Beads and Resins

Agarose Resin:
Porous, higher capacity, may have nonspecific binding

6xHis	Ni-NTA His•Bind® Superflow™ Resin	**70691**
FLAG	ANTI-FLAG® M2 Affinity Gel	**A2220**
HA	Monoclonal Anti-HA–Agarose	**A2095**
GST	Glutathione–Agarose	**G4510**
c-Myc	Anti-c-Myc Agarose Affinity Gel	**A7470**
V5	Anti-V5 Agarose Affinity Gel	**A7345**
T7	T7•Tag® Antibody Agarose	**69026**
S-tag	S-protein Agarose	**69704**

Elution:
Competitive peptides to elute protein from resin or beads

FLAG	3X FLAG® Peptide	**F4799**
Strep Tag II	D-Desthiobiotin	**71610**
V5	V5 Peptide	**V7754**

Magnetic Beads:
Non-porous, high specificity, easy handling

6xHis	PureProteome Nickel Magnetic Bead System	**LSKMAGH**
FLAG	Anti-FLAG® M2 Magnetic Beads	**M8823**
HA	Anti-HA Magnetic Beads	**SAE0197**
GST	Glutathione High-Capacity Magnetic Agarose Beads	**G0924**
c-Myc	Anti-C-Myc Magnetic Beads	**SAE0201**
V5	Anti-V5 Magnetic Beads	**SAE0203**

Kits and Spin Columns:
Easy all-in-one protocols

6xHis	HIS-Select® Spin Columns	**H7787**
FLAG	FLAG® M Purification Kit	**CELLMM2**
HA	Anti-HA Immuno-precipitation Kit	**IP0010**
GST	Glutathione–Agarose	**G3907**
c-Myc	T7•Tag® Affinity Purification Kit	**69025**
FLAG® HA	Tandem Affinity Purification Kit	**TP0010**

Detection - Antibodies

	Quantify	Visualize		Sort
Tag	**Western Blot**	**Immuno-fluorescence**	**Immuno-cytochemistry**	**Flow Cytometry**
6XHis	H1029	16-254 (direct)	05-949	SAB5600227
FLAG	F7425	F4049 (direct)	F2555	F3165
HA	04-902	H7411 (direct)	H3663	SAB4600119
GST	G1160	Not Available	MAC111	Not Available
c-Myc	M4439	F2047 (direct)	M4439	SAB4700447
Strep Tag II	71590	SAB2702216	SAB2702215	Not Available
V5	V8012	SAB2702199	V8012	Not Available
T7	AB3790	AB3790	AB3790	Not Available
S-tag	71549	71549	MAC112	Not Available