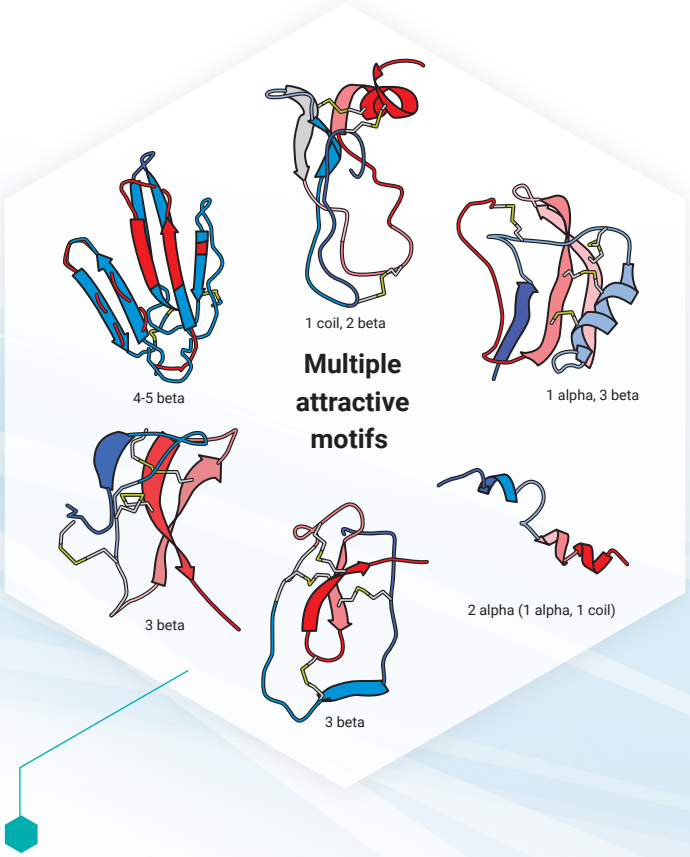
Peptide discovery
Discovery

GlyTech, Inc.
Glycoscience for Better Health

Peptide drug screening

Scaffold-based in vitro evolution

Combining natural scaffold peptide backbones and patented cDNA display technology, our platform increases the screenable peptide library size, shortens the selection period, assures the stability and solubility of discovered hits, and enables flexible optimization.



Highlights

- **Evolutionarily-optimized backbones**
  Natural, bioactive and rigid structures ensure that discovered hits have suitable drug-like properties.

- **Wide target applicability**
  Screening can be carried out against extracellular targets, intracellular targets, secreted targets, and non-antigenic targets.

- **Large screening space**
  Taking advantage of the benefits of cDNA display, our practical screening space reaches 10^{11} ~ 10^{13} compounds.

- **Diversified leads**
  Multiple functionalities can be obtained within the same screen, including both agonists and antagonists.

- **High-quality deliverables**
  In addition to hit sequence and validation data, we chemically synthesize selected candidates and deliver them to you for evaluation.

- **Lasting competitiveness**
  Highly original compounds with robust IP and lock-out policy.

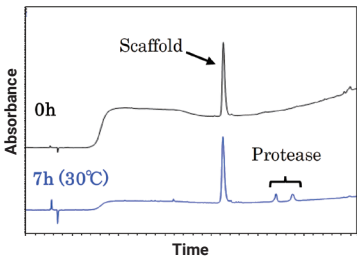
Scaffold features

Many scaffold peptides that are stable, soluble, protease resistant, and bioactive have been discovered in nature. Like antibodies, they share similar constant structures, but bind to different targets because the sequences of their binding regions vary.

Using such scaffold peptides as backbones in drug discovery increases the probability of finding promising leads that have a greater chance of having desirable drug properties.

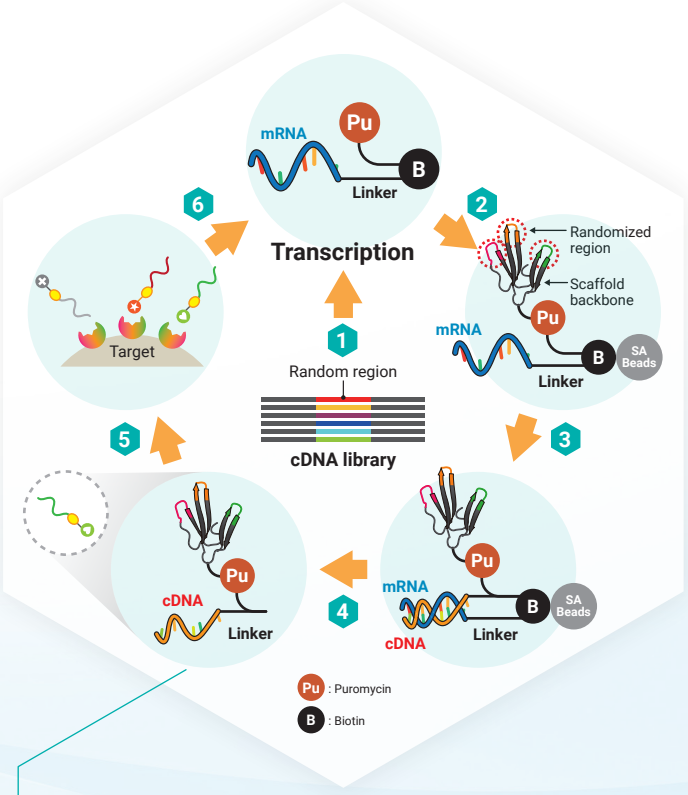
We have more than 6 types of highly effective, natural structure-derived 3D scaffold peptides that we use as starting points in our cDNA-based screening platform. The structure used is chosen to match the drug target and desired function.

Protease test

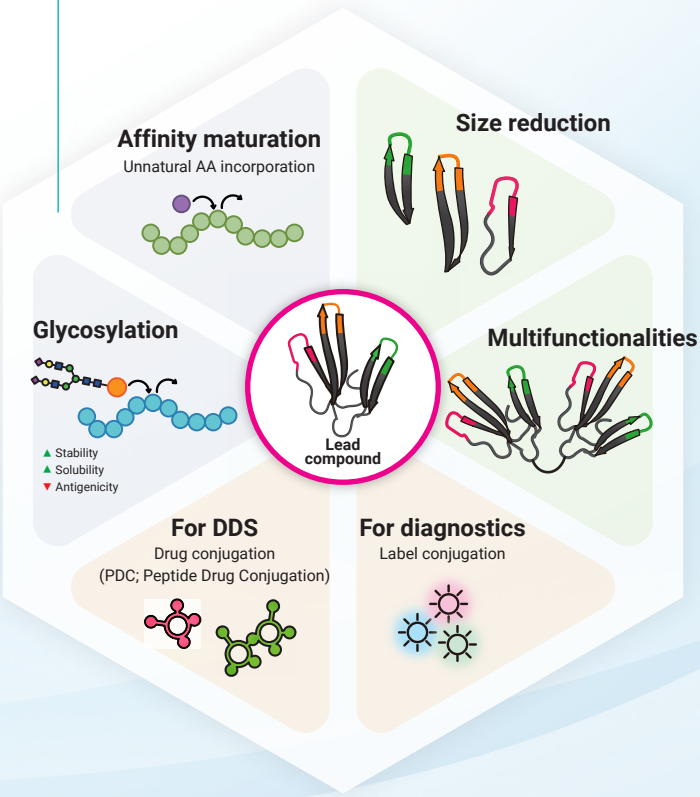


Expected properties

- Bioactivity
- High solubility
- High stability
- High protease resistance



Further modifiable



Highly efficient screening (cDNA display technology)

Owing to the stability of cDNA and our proprietary linker, our platform has the advantages of faster cDNA template preparation, lack of linker cleavage step, and simpler purification steps, allowing for more flexibility in selection criteria and a vast screening space (10^{11}-10^{13}) while also shortening the screening cycle time to less then 8 hours. This means a more efficient screening process and higher probability of discovering promising candidates compared with conventional display technologies.

Screening process

1. Preparation of cDNA library and transcription to mRNA ligated with puromycin linker.
2. Cell-free translation of the mRNA to obtain the corresponding peptides linked via puromycin.
3. Purification of the peptide-mRNA conjugate by affinity and reverse transcription to obtain peptide-cDNAs.
4. Purification of the peptide-cDNA conjugate using preinstalled C-terminal His tag.
5. Selection of molecules binding for the desired target.
6. Recovery of binding molecules and then PCR amplification to generate binder-concentrated library ready to proceed to further selection cycle(s).

Case studies

1. Expected affinity (against VEGF): ~nM

Hits with strong affinities as low as several nM can be obtained, with pM affinity possible after affinity maturation.

Loop1	Loop2	Loop3	Kd (nM)
PLTRVV	HGDHHTLSEW	EEPTAHV	2.1±0.5

Ref.: Tai Kubo et. al., *ACS Comb. Sci*. 2016, 18, 117−129

2. Diverse functionality (against IL-6R)

Depending on the sequences of the variable regions, various functions can be obtained within the same screen, such as non-competitive, competitive, and agonist activity.

Loop1	Loop2	Loop3	Function
SRPRLN	GLAPRAIRAQ	TPRARTG	Non-competitive
QLLACR	ATRHTLGHNL	ACETPAS	Competitive and non-inhibitory
QLLACR	ATRHTLGHNL	ELTHPVD	Competitive and inhibitory
APLPYT	ATRHTLGHNL	TGPGAER	Competitive and agonist

*Loop = binding site

Ref.: Tai Kubo et. al., *Mol. Brain*. 2011, doi:10.1186/1756-6606-4-2

www.glytech-inc.com
glytech-info@glytech-inc.com
@GlyTech @GlyTech
GlyTech, Inc.
Glycoscience for Better Health