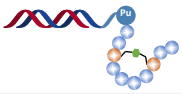
WuXi AppTec

WuXi Biology

Peptide Early Discovery Service

Peptide Hit Discovery

WuXi AppTec provides multiple approaches to discover peptide hits, including DNA-Encoded Library (DEL) and display technologies. Peptide DELs are synthesized through chemical reactions, while display technologies utilize biological synthesis. The combination of DEL and display technologies allows clients to explore vast chemical space.

	Peptide DEL	mRNA Display	Phage Display
			
Library Diversity	10^11	>10^12	10^9
Features	• **High throughput decoding** and affinity-based screening • **Computational simulation** techniques enhanced • **Various cyclization strategies** • Highly **customizable** • High **backbone and side chain diversity** • Incorporation of **abundant unnatural AAs** • '**Permeable** peptide' properties	• **Flexible choice in peptide length** • Incorporation of **limited unnatural AAs**	• **Natural amino acids** dominate • Compatible with **cellular selection** and ***in vivo* selection**

Bicyclic peptides constrained on a molecular scaffold not provided

Off-The-Shelf & Highly Customizable Peptide Libraries

Peptide DEL

Off-the-shelf collection (420+ Billion):

Linear Libraries

Small Cyclic Libraries

Cyclic Libraries

RDC Warhead Cyclic Peptide Libraries

Well-validated tools for peptide DEL customization:

- **1,400+** validated natural and unnatural AAs
- **1000+** α-AAs with diverse side chains (D/L ratio **3:4**)
- **300+** non-alpha AAs with diverse backbones
- **10%** AAs with α*N*-alkylation
- **10+ types** of cyclization strategies established
- Peptide fragment **(2~5 AAs)** condensation

Phage Display

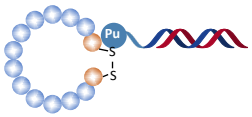
Linear peptide:

- X7, X12 (commercial)
- X9, X30 (customized)

Mono-cyclic peptide:

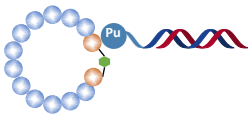
- CX7C, CX13C (customized)
- CX4CX9 (customized)

mRNA Display



Cyclized by disulfide bond

MCX_nC, n=6-15



Cyclized by chemical linker

MCX_nC, n=6-15

WuXi AppTec

WuXi Biology

Peptide Hit-to-Lead Optimization

Bioassay Platform for Peptide Profiling

	Binding/PPI	Permeability*	Stability*	Functionality	Specificity/toxicity
Biophysics	☑				
Biochemistry	☑	☑	☑	☑	☑
Structural biology	☑				
Cell biology		☑	☑	☑	☑
ADME		☑	☑		☑
DMPK		☑	☑	☑	☑

*Specific assessments required for peptides in the early stage, e.g.: Aggregation, GI digestion, Circulating stability, Formulation stability

Peptide Modeling:

- Virtual screening
- Virtual residue / alanine scan
- Binding mode and hotspot prediction
- Data-driven model
- Molecular dynamics

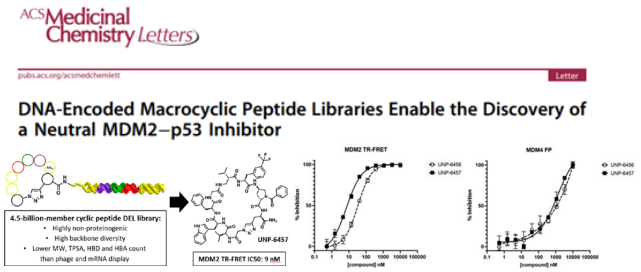
Peptide Conjugation: Linker synthesis & payload modification

Unnatural AA Availability: 3000+ Fmoc-AAs catalog products & customized synthesis

Peptide Synthesis: Linear, cyclic peptides and peptidomimetics

Showcases of Integrated Peptide Discovery

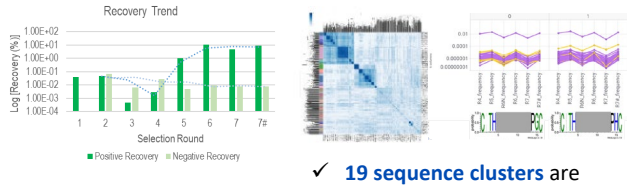
Cyclic Peptide for Protein-Protein Interaction Disruption



✓ UNP-6457, a neutral nonapeptide discovered in **cyclic peptide DEL**, inhibits MDM2–p53 interaction with an IC_{50} of **8.9 nM**

Peptide Discovery Using mRNA Display

➢ **mRNA Display Screening with CXnC, n=8-15**



✓ Selection performance of target shows a **good** enrichment trend

✓ **19 sequence clusters** are observed with count number >= 10

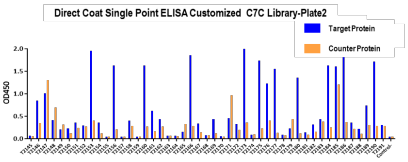
Peptide Name	KD (nM) with Target in SPR	KD (nM) with Target/Ligand in SPR
Peptide 1	17	/
Peptide 8	8.6	62.5

✓ Both **orthosteric** and **allosteric** binders were discovered

✓ 21 peptides were selected with hit rate close to **62% (KD <20 μM)**

Peptide Discovery Using Phage Display

➢ **Antigen X panning against C7C cyclic phagemid library**



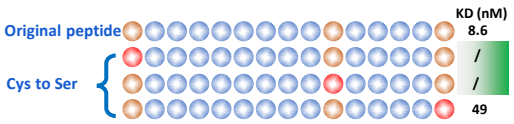
- **Abundant positive clones** were discovered from the output pool of **library panning**

Peptide Name	EC50 (nM) in ELISA	KD (nM) in SPR
P13	55.45	85.6
P25	87.37	68.5

✓ The affinities of P13 and P25 peptides in further **SPR** data are consistent with **ELISA**, both less than **100nM**

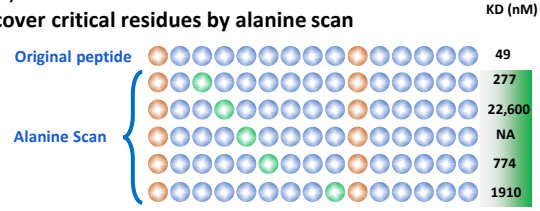
Peptide Optimization Services

➢ **Discover critical cyclization site by Cys to Ser mutation**



✓ SPR results show that the first two cysteine residues are important for cyclization

➢ **Discover critical residues by alanine scan**



✓ Residues at positions 3-6 and 9 are essential for binding

USA: mahnaz_arjomand@wuxiapptec.com
EU/UK/Israel: dave_madge@wuxiapptec.com
China/Singapore/Australia: xu_longji@wuxiapptec.com
Japan: fumio_itoh@wuxiapptec.com
Korea: sycho@wuxiapptec.com