

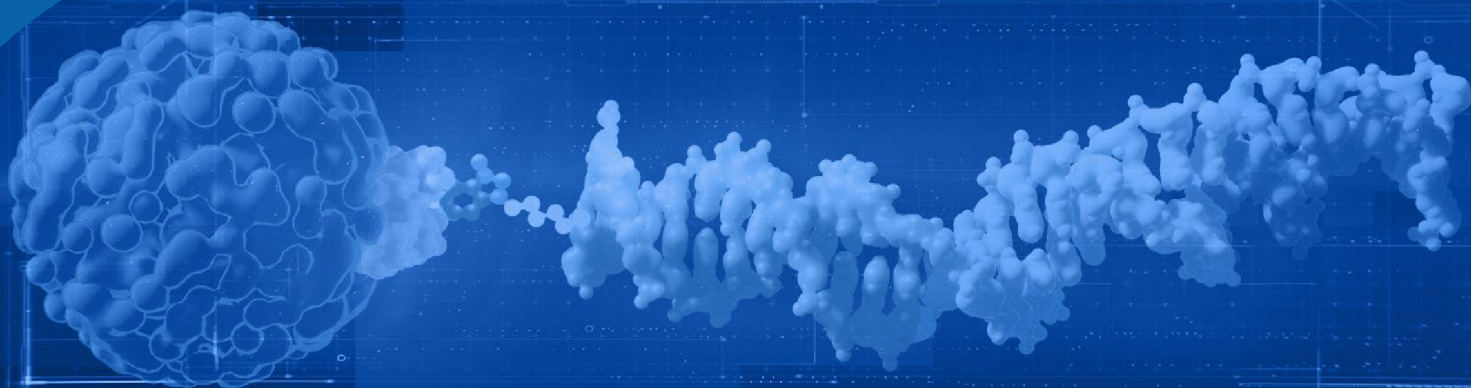


HitS Website



# HANDBOOK

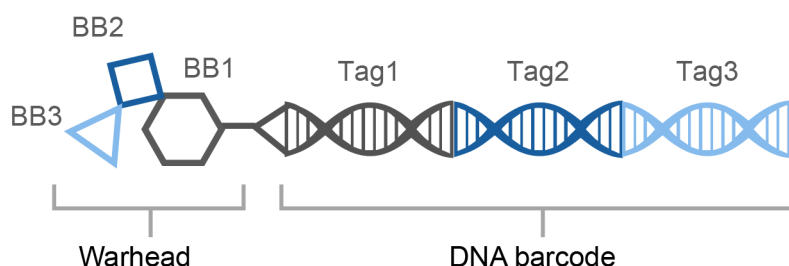
Contact Us: [DEL\\_service@wuxiapptec.com](mailto:DEL_service@wuxiapptec.com)



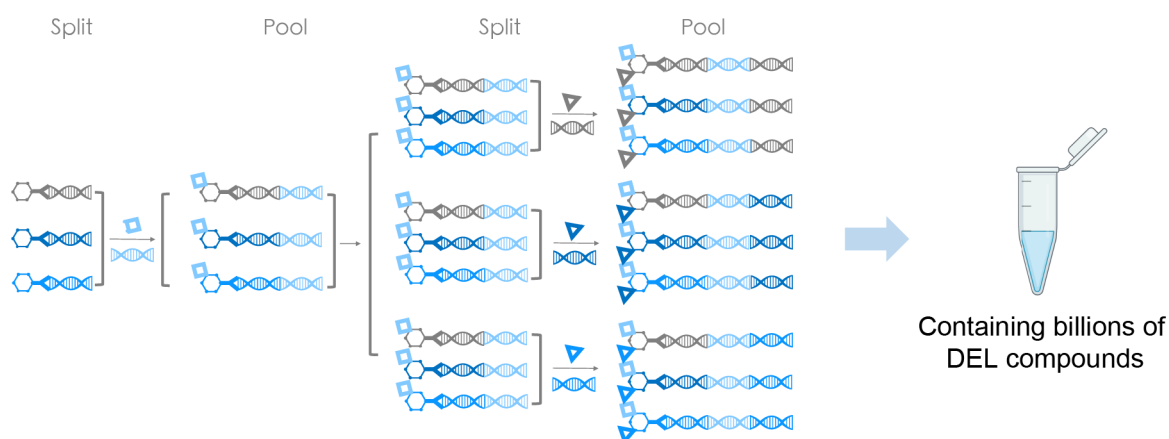
# An elegant approach for drug discovery

DNA-encoded library (DEL) is a technology that enables fast screening of billions of small molecule compounds in early phase of drug discovery. The aim of DEL technology is to discover novel chemical structures for validation and optimization.

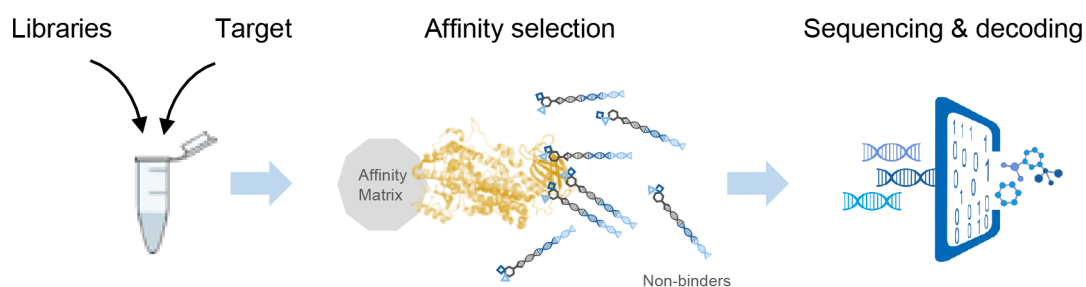
## A three-cycle DEL compound



DEL enables mass creation of chemical libraries by a combinatorial chemistry approach, namely Split & Pool.



DEL makes it possible to screen billions of compounds in a small tube. Thanks to high-throughput sequencing technology, compounds can be uniquely identified by their DNA barcodes.



# Introduction

DELlight provides a self-service platform for clients to explore enormous amount of DEL molecules without sharing target information.



**Complete confidentiality of target information**



**Compatible with computational tools**

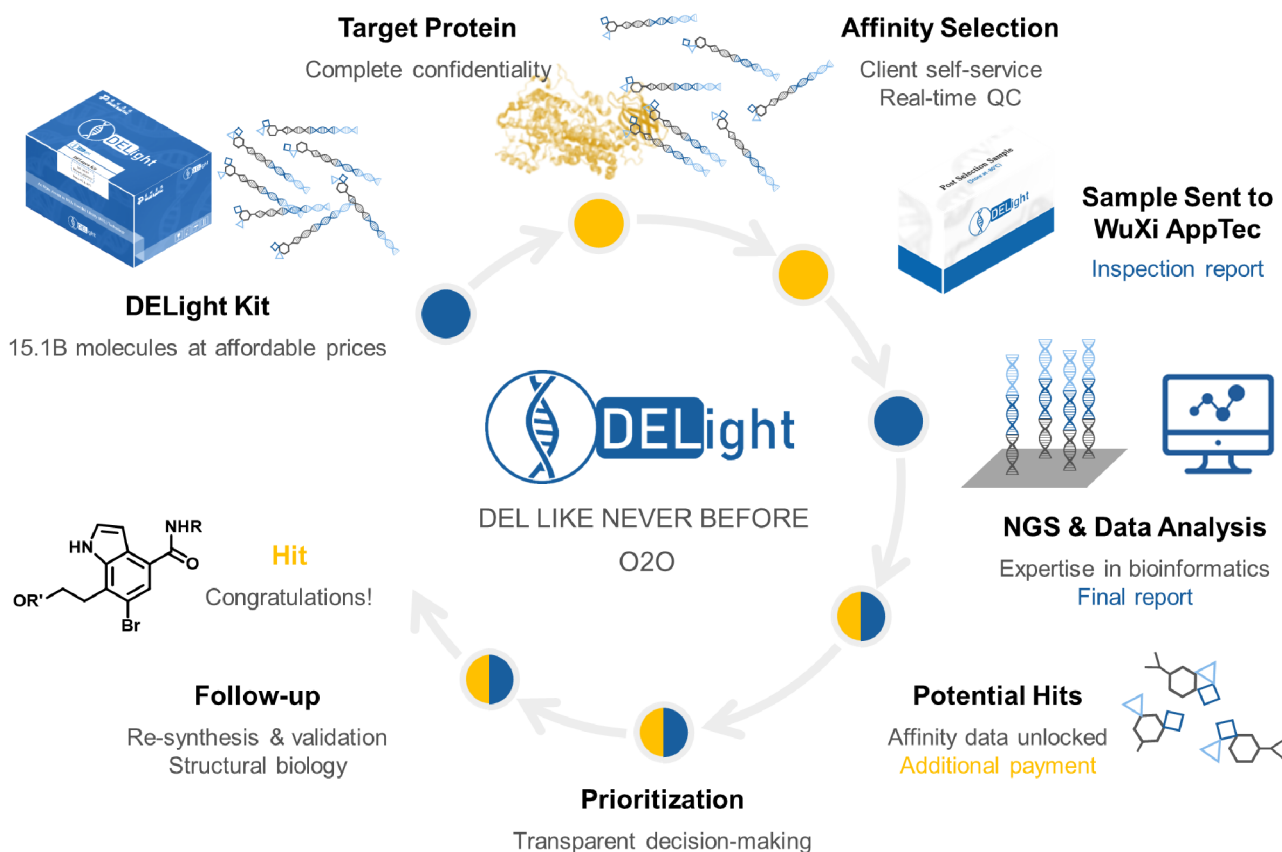


**Well-balanced chemical space**




**Fast turn-around**

DELlight users are able to conduct affinity selection experiments in their own labs, and WuXi AppTec HitS is responsible for post-selection processing, sequencing and data analysis.




# What is included in DELight service


## DELight kit




- DELight libraries for 4 experimental conditions
- 58 libraries, 15.1B of compounds



- Materials for real-time quality control (QC) test
- Comprising of reference samples, PCR supermix and primers

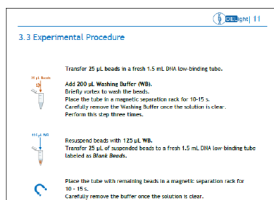



- Sheared salmon sperm DNA, 10x PBS buffer containing 0.5% Tween 20
- For preparing washing buffer & selection buffer

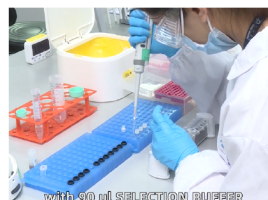


- Post-selection sample tubes
- To be sent to WuXi AppTec

## Technical support



User manual with step-by-step instructions



Tutorial videos on affinity selection



DELight teaching lab in Boston and Munich

## Service included

Post-selection processing	<ul style="list-style-type: none"> <li>▪ Sample quantitation by qPCR</li> <li>▪ PCR amplification</li> </ul>
Sequencing	<ul style="list-style-type: none"> <li>▪ Next generation sequencing (NGS)</li> </ul>
Data analysis & online platform	<ul style="list-style-type: none"> <li>▪ Decoding</li> <li>▪ Filter setting</li> <li>▪ Online data visualization platform</li> </ul>

## Data package

DELight users can choose to purchase the data package of affinity data and associated chemical structures.

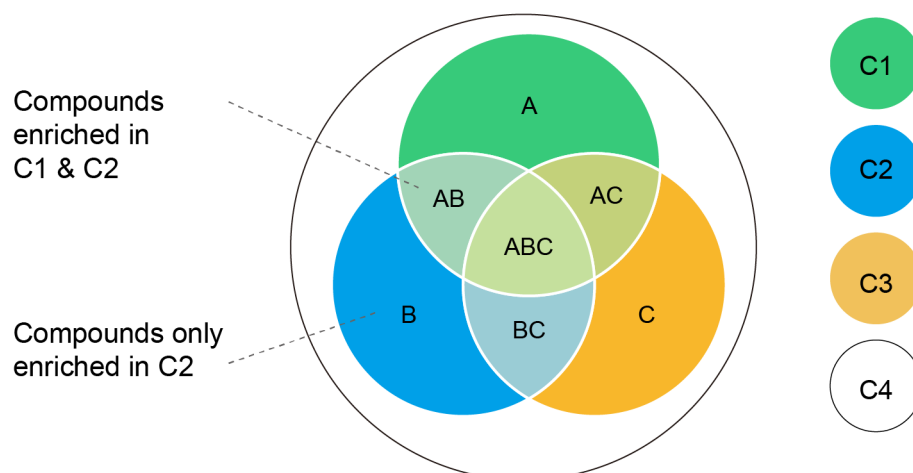
# What to prepare for a DELight screen

## Experimental design

Experimental designs that are commonly used for DELight:

- Different types of proteins
- Domains or mutations of interest
- Protein samples plus additional reagents, such as inhibitors

#	1	2	3	4
Condition	Protein 1	Protein 1 + Inhibitor	Protein 1_D1	NTC
Purpose	Main target	To block a pocket	Domain of interest	To remove background noise



## Protein & affinity matrix

Requirements for protein:

- Having certain tags for immobilization
- Pure, homogenous, and properly folded

Requirements for affinity matrix:

- Compatible with protein tags
- Magnetic beads are recommended, such as HisPur™ Ni-NTA Magnetic Beads
- Protein capture test is needed prior to affinity selection

## Lab Equipments

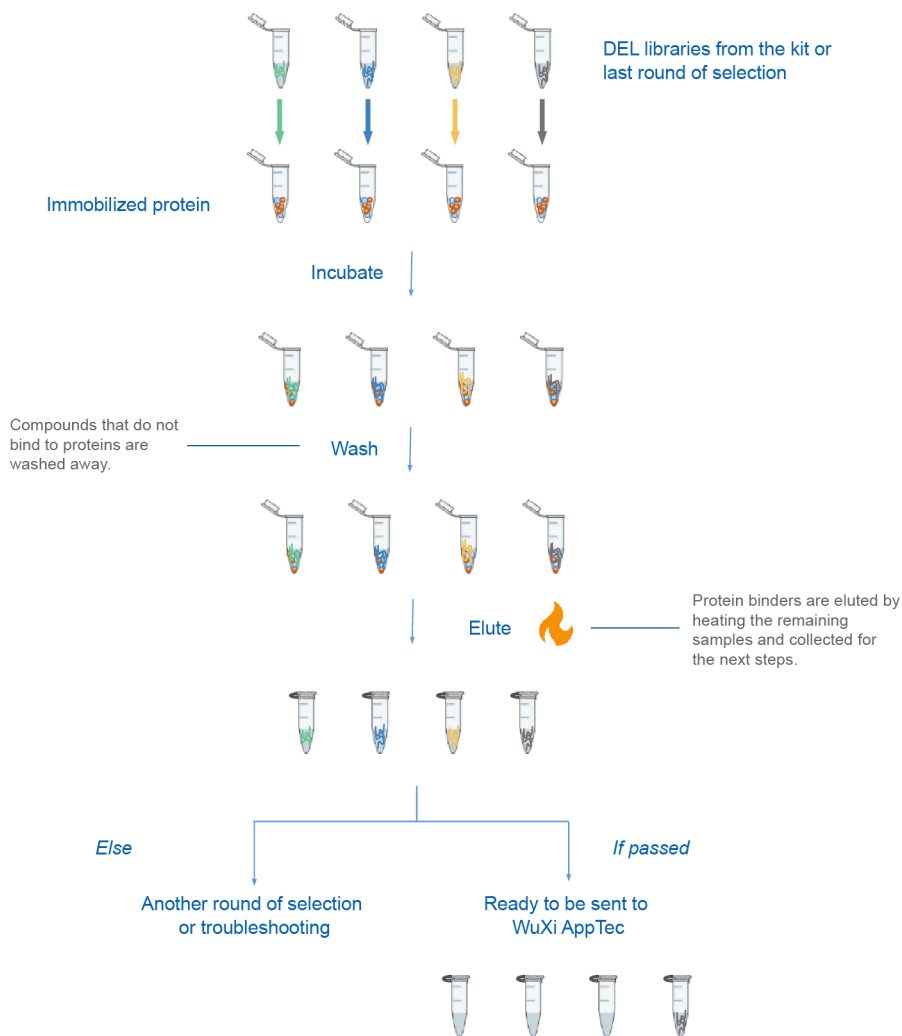
- PCR system
- Gel electrophoresis & imaging system

- Microcentrifuges
- Rotators
- Heaters

# Affinity selection & Quality control

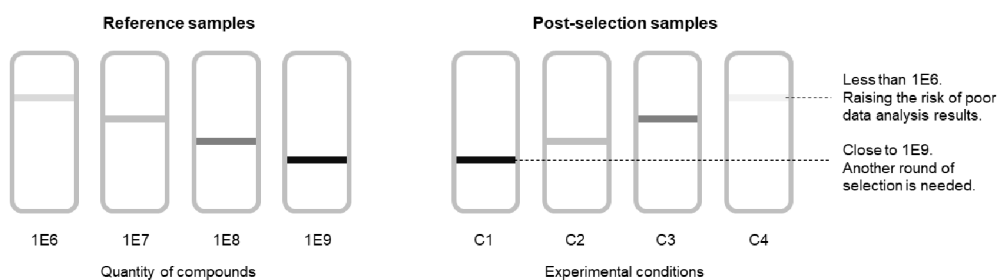
## Affinity selection

Usually 2-4 rounds of affinity selection is needed to reach the desired quality of selection samples.



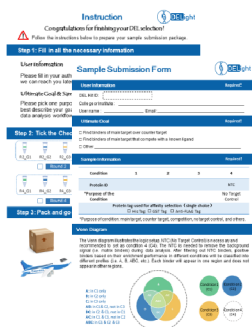
## Monitoring selection quality

Real-time QC test, powered by PCR and gel electrophoresis systems, helps to determine the quality of affinity selection.



# When affinity selection is completed

## Shipping samples



Fill in the sample submission form.

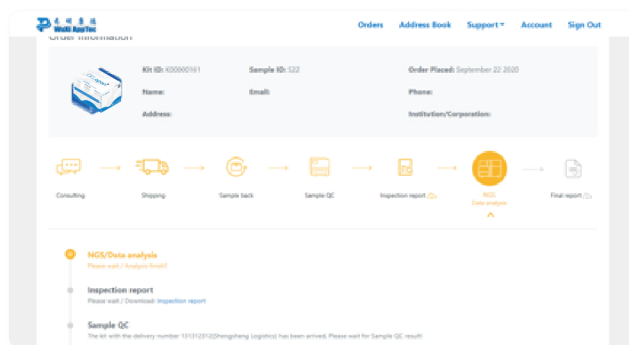
Store samples at  $-80^{\circ}\text{C}$  or on dry ice until shipment.

Ship with dry ice to WuXi AppTec at Shanghai, Boston or Munich.

## Online tracking

DELight users can track the progress of their samples through an online portal.

Website: <https://hits.wuxiaptec.com>



## Inspection report

Inspection report is provided for users based on post-selection processing results.

### qPCR Result

Sample ID	Purified Sample Volume( $\mu\text{L}$ )	Molecule Count*	Sample Assessment Based on MC	$\Delta\text{Ct}^{**}$	Sample Assessment Based on $\Delta\text{Ct}$
DELopen DEMO_1	90	$7.34\text{E}+07$	Good	4.58	Good
DELopen DEMO_2	90	$7.87\text{E}+07$	Good	5.19	Good
DELopen DEMO_3	90	$6.35\text{E}+07$	Good	4.33	Good
DELopen DEMO_4	90	$3.78\text{E}+07$	Good	5.00	Good

\*Molecule Count (MC): The total number of DEL molecules after affinity selection  
 $**\Delta\text{Ct} = \text{Ct}_{\text{specific}} - \text{Ct}_{\text{universal}}$

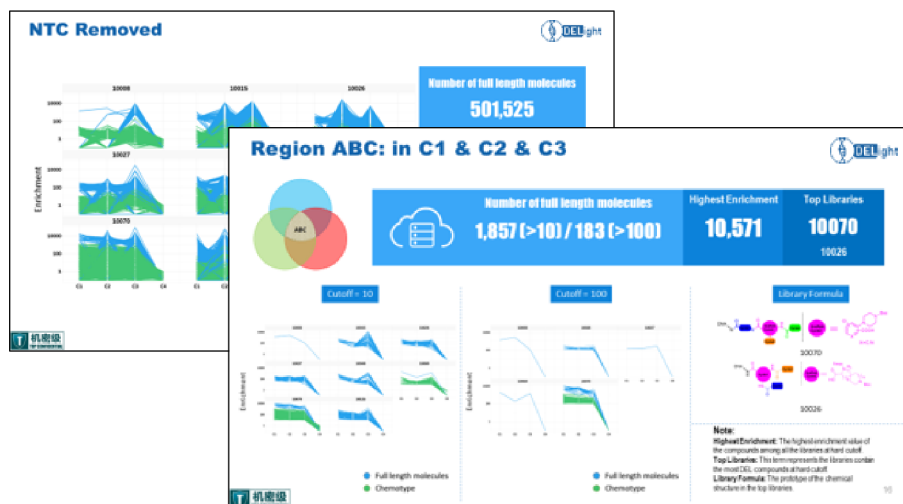


- The amount of DEL compounds
- Evaluation of contamination

# Understanding DELight screening data

## Final report

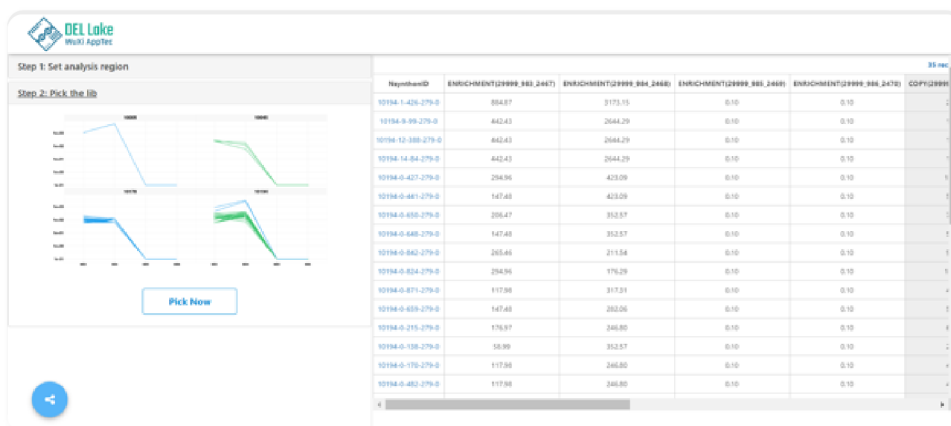
- Motif analysis to detect possible DNA binding sites of the target protein
- Enrichment of compounds and chemotypes across different conditions



## Interacting with data

Online platform for users to interact with copy numbers and enrichment scores

Website: <https://hits.wuxiapptec.com>



Set the cutoff for enrichment

condition	Func	enrichment
983_2467	>=	50
984_2468	>=	50
985_2469	<=	10

Close Save changes

Please select a lib

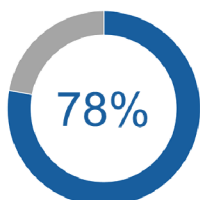
10178	Rank 1
10178	Rank 1
10194	Rank 2

- Customizing data analysis

- Looking into specific DEL libraries



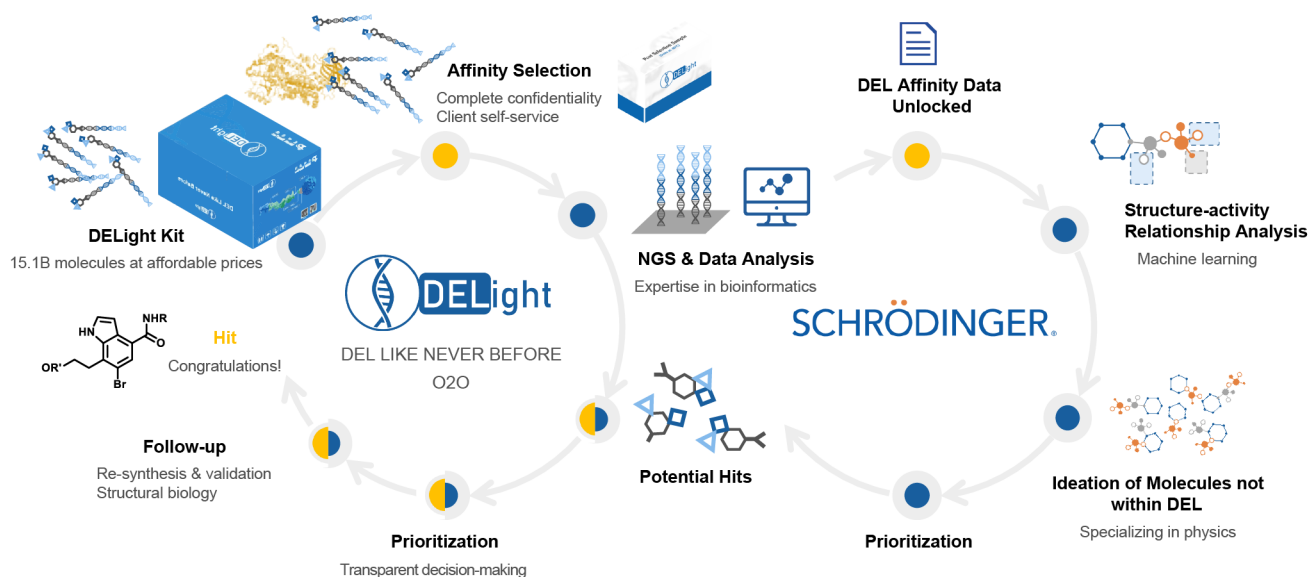
# Data package & Machine learning



DELlight data package discloses a large amount of data and is compatible with computational tools, such as machine learning and artificial intelligence (AI). Around 78% of past users have chosen to unlock their data packages.

## What's in the package

- Copy numbers and enrichment scores of compounds
- Chemical structures of enriched compounds
- Pre-calculated molecular properties such as molecular weight

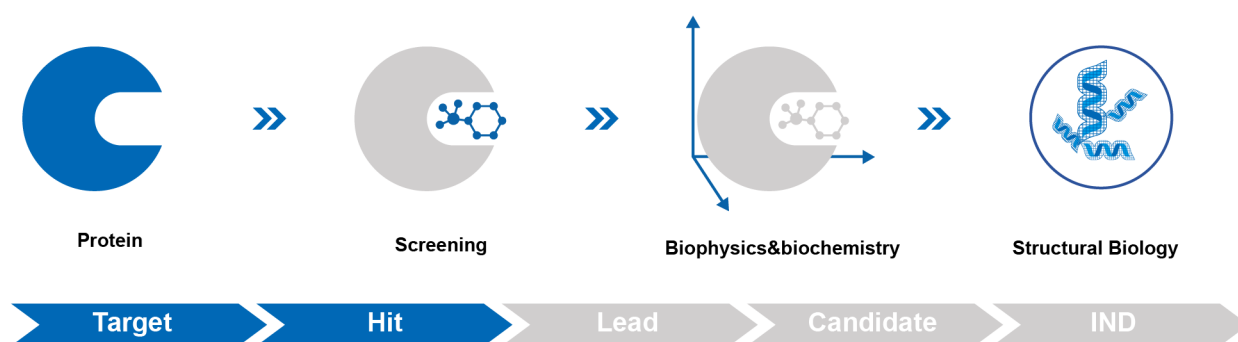


WuXi AppTec HitS offers the option of machine learning to explore chemical compounds that are not in DELight libraries through our partnership with Schrodinger.

## WuXi AppTec HitS

The industry-leading Target-to-Hit platform at WuXi AppTec HitS unit facilitates protein production, hit identification, biophysics and structural biology to accelerate drug discovery.

With operations and expert team located in China, Europe and North America, we proudly support pharmaceutical companies, biotech firms and academic researchers from all around the world.



HitS has an integrated team of experts in DEL screening, who specialize in chemistry, biology, bioinformatics and data analytics.

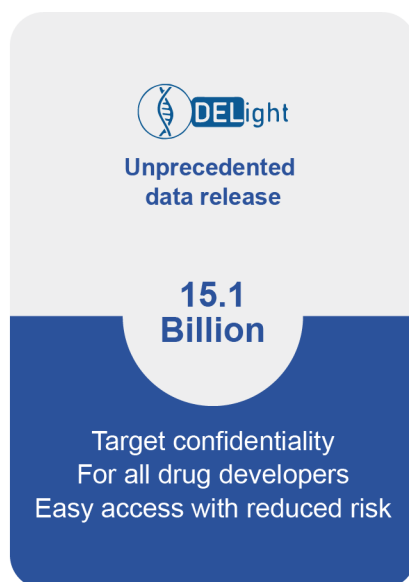
Our mission is to bring DEL service of high quality to drug developers by providing flexible business models and customized screening strategies.



**DEL<sup>pro</sup>**  
One-stop solution customizable

**46+ Billion**

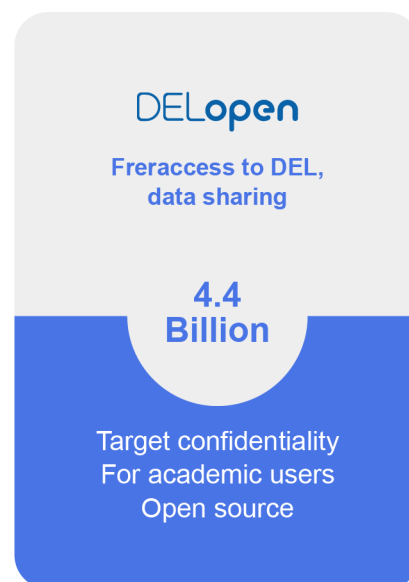
Target exclusivity  
For all drug developers  
Access to unique scaffolds



**DEL<sup>light</sup>**  
Unprecedented data release

**15.1 Billion**

Target confidentiality  
For all drug developers  
Easy access with reduced risk



**DELOpen**  
Freraccess to DEL, data sharing

**4.4 Billion**

Target confidentiality  
For academic users  
Open source

**HitS Website:** <https://hits.wuxiapptec.com>  
**Contact Us:** [DEL\\_service@wuxiapptec.com](mailto:DEL_service@wuxiapptec.com)  
**North America:** Declan Ryan [declan.ryan@wuxiapptec.com](mailto:declan.ryan@wuxiapptec.com)  
**Europe:** Dave Madge [dave\\_madge@wuxiapptec.com](mailto:dave_madge@wuxiapptec.com)





HitS Website

Email: [DEL\\_service@wuxiapptec.com](mailto:DEL_service@wuxiapptec.com)  
Website: <http://hits.wuxiapptec.com>