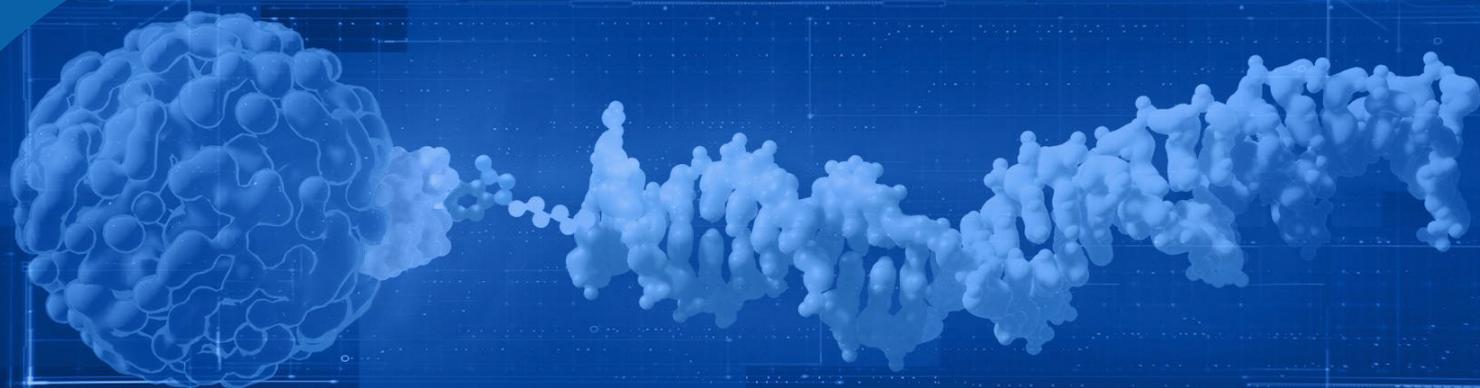




HitS Website



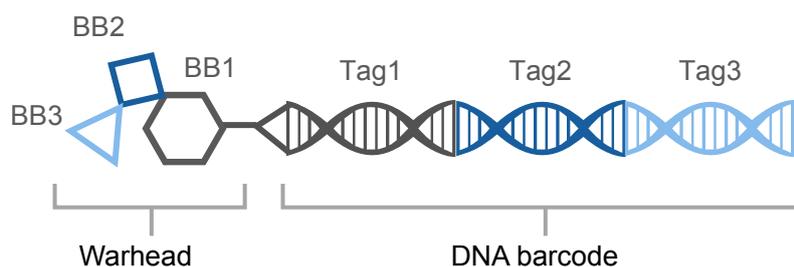
HANDBOOK



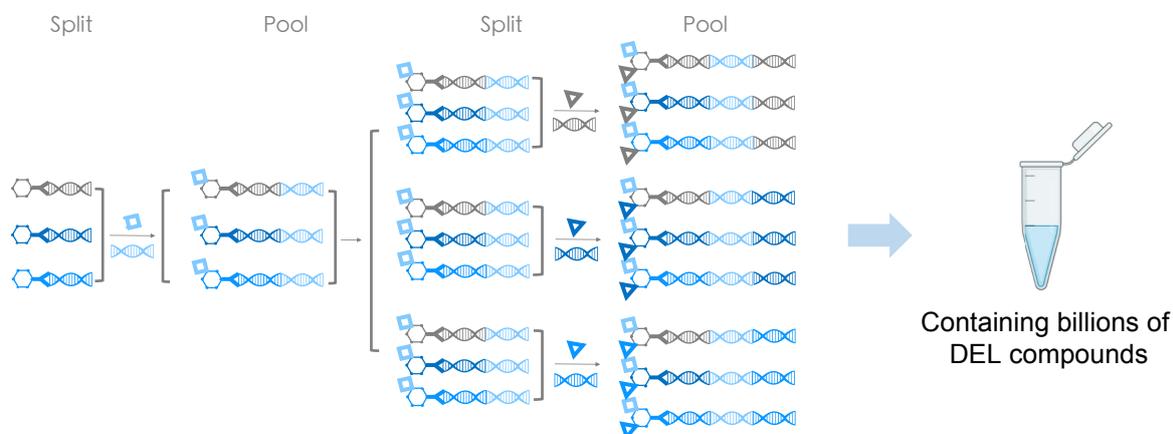
An elegant approach for drug discovery

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.

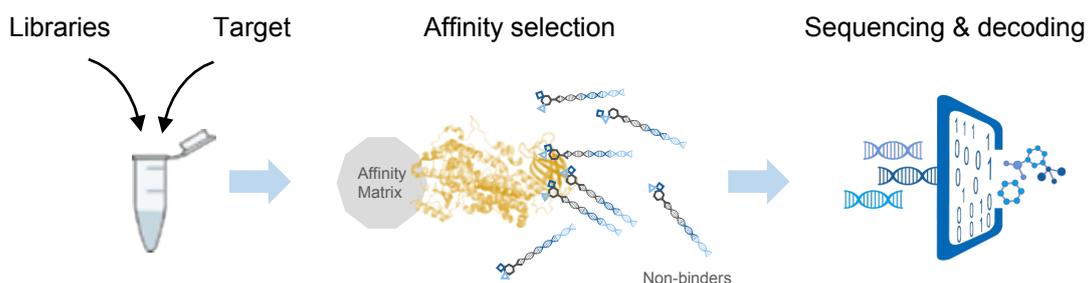
A three-cycle DEL compound



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

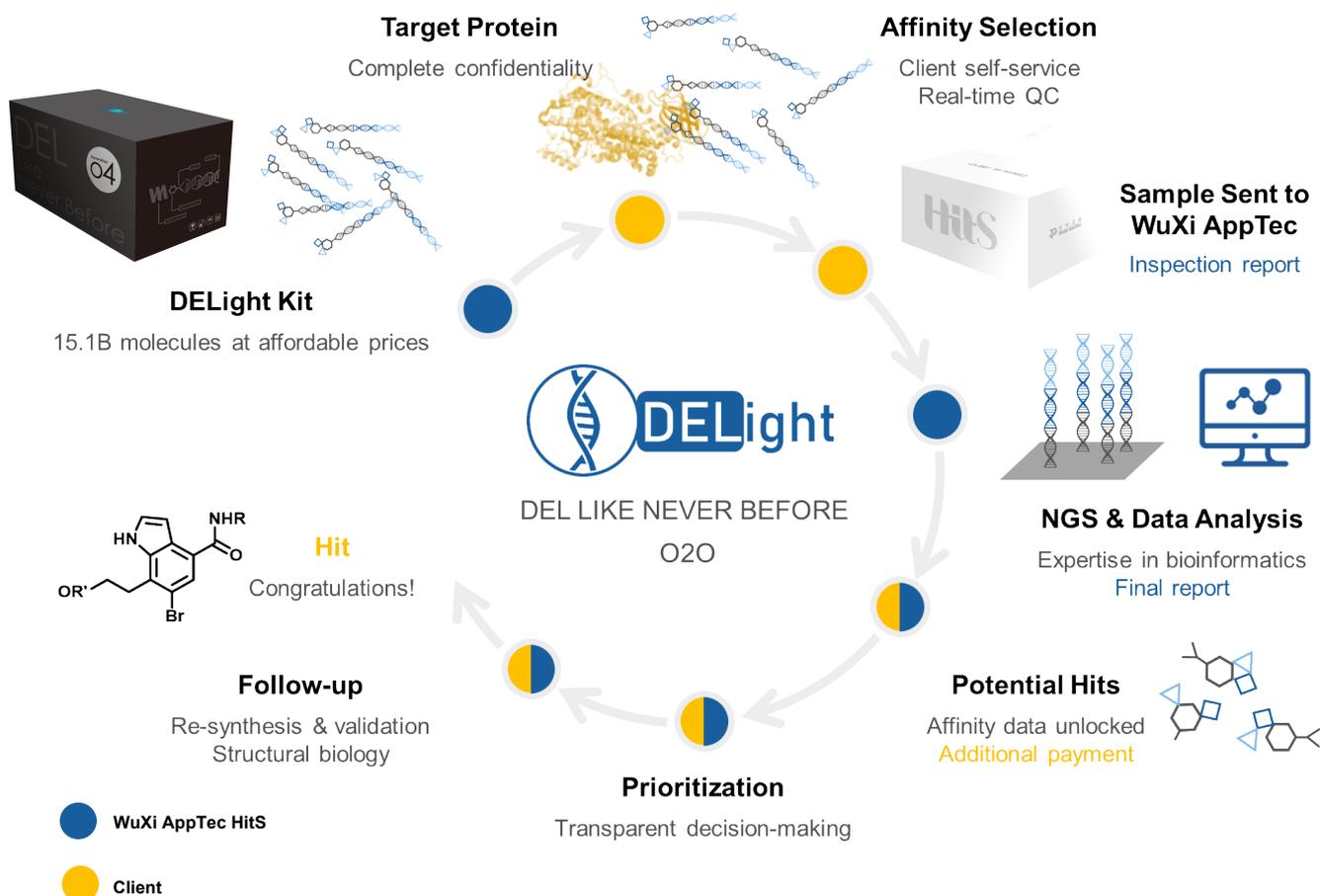


Well-balanced chemical space



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 (G1-G4)
- 58 libraries, 10.8 B of compounds

- Self-QC package
- *Buffer A
- *Buffer B
- *Dipsticks
- *Reaction tubes

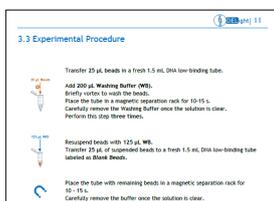


- Imidazole
- Sheared salmon sperm DNA

- Post selection sample collection vials * 8

Technical support

Instruction file
Examples of different screening setup logic.



User manual with step-by-step instructions



Tutorial videos on affinity selection



DELIGHT teaching lab in Boston (US) and Suzhou (China)

Service included

| | |
|---------------------------------|--|
| Post-processing | <ul style="list-style-type: none"> ▪ Sample quantitation by qPCR ▪ PCR amplification and purification |
| Sequencing | <ul style="list-style-type: none"> ▪ Selection Sequencing |
| Data analysis & online platform | <ul style="list-style-type: none"> ▪ DEL result Decoding ▪ Filtering For Noise ▪ Online data visualization ▪ Data performance assessment |

Data package

- DELight users can choose to purchase the data package of affinity data and associated chemical structures.
- Obtain a free online meeting for data analysis tutorial.
- Frequent Hitter Index: Frequent hitters producing often unknowingly false positive that could waste much effort in drug discovery research, such as PAINS.

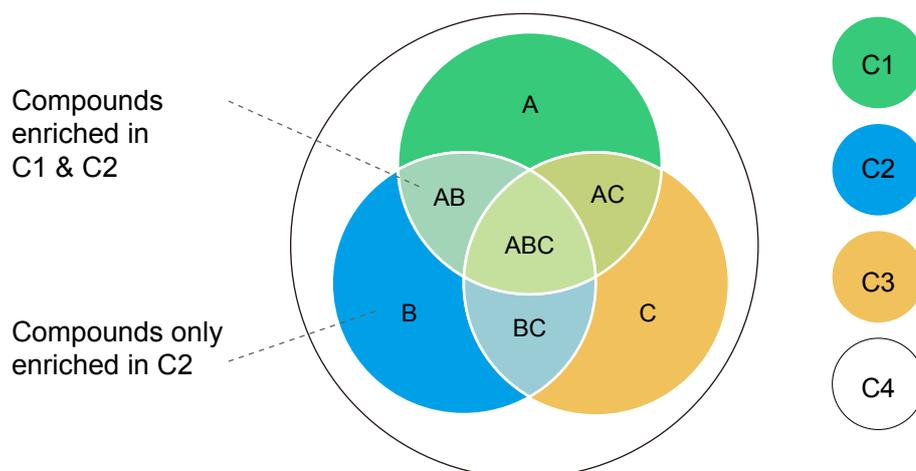
What to prepare for a DELIGHT screen

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 |



**Please refer to the instruction file for more information about the screening setup logic.*

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, Pierce™ streptavidin Magnetic Beads (Thermo 88816)
- Protein capture test is needed prior to affinity selection

Lab Equipments

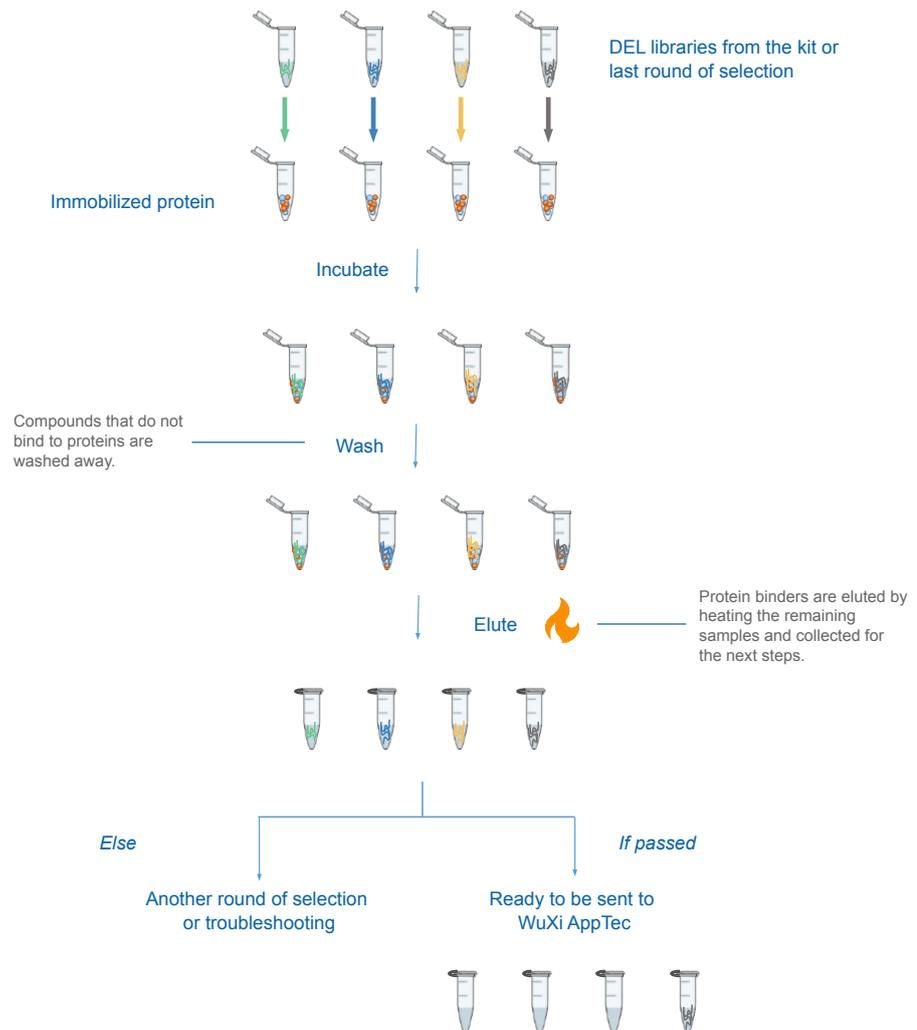
- PCR system
- Gel electrophoresis & imaging system

- Microcentrifuges
- Rotators
- Heaters

Affinity selection & Quality control

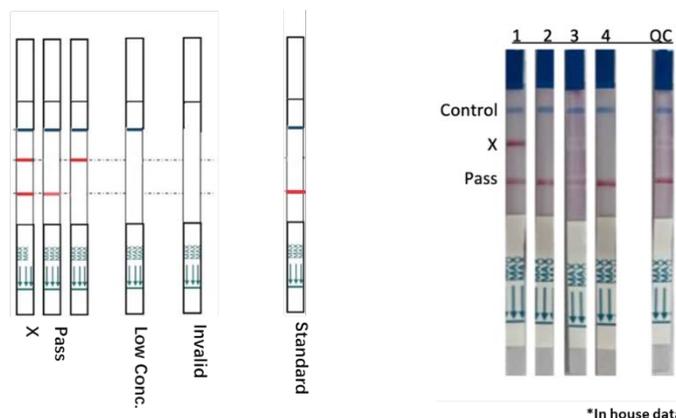
Affinity selection

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



Monitoring selection quality

Fast semi-quantification QC test helps to estimate molecule counts of each selection sample.



When affinity selection is completed

Shipping samples

Client Information

Sample Information

Protein Tag (Single choice)

His Tag Avi Tag FLAG Tag GST Tag

For samples using His tag, is imidazole applied to the selection?

Yes No

Customer Name: _____

User Name: _____

Phone: _____

Address: _____

City: _____

Country: _____

Zip: _____

Order No: _____

Order Date: _____

Order Status: _____

QR Code

Track your sample and other information. <http://www.hitsapp.com>



Fill in the sample submission form.

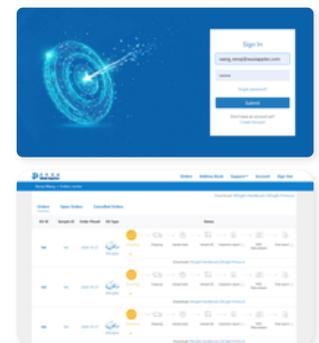
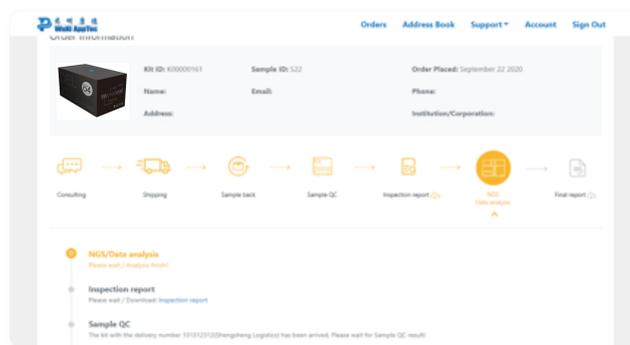
Store samples at -80°C or on dry ice until shipment.

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

Online tracking

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

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



Inspection report

Inspection report is to check if the submitted samples meet predetermined NGS sequencing requirement.

qPCR Result

| Sample ID | Purified Sample Volume(μL) | Molecule Count* | Sample Assessment Based on MC | ΔCt ** | Sample Assessment Based on ΔCt |
|----------------|---|-------------------|-------------------------------|----------------------|--|
| 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 | $3.76\text{E}+07$ | Good | 5.00 | Good |

*Molecule Count (MC): The total number of DEL molecules after affinity selection

** $\Delta\text{Ct} = \text{Ct}_{\text{Target}} - \text{Ct}_{\text{Internal}}$

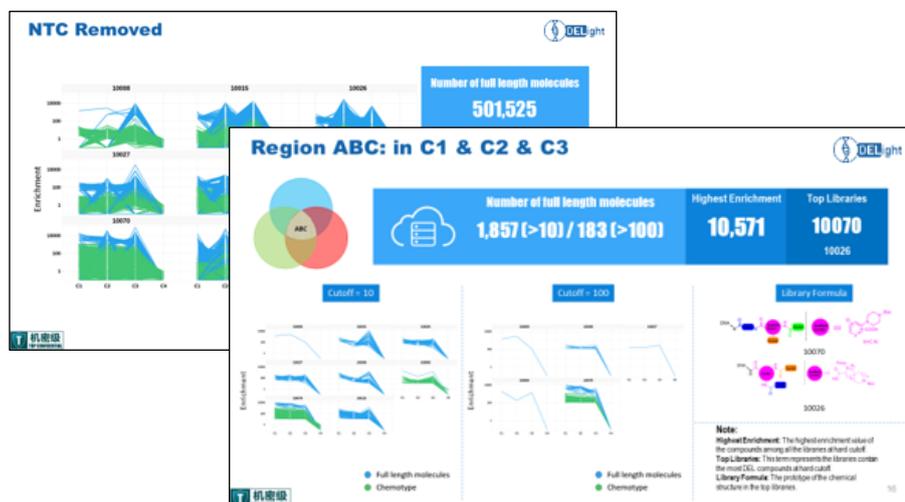


▪ The amount of DEL compounds

Understanding DELight screening data

Final report

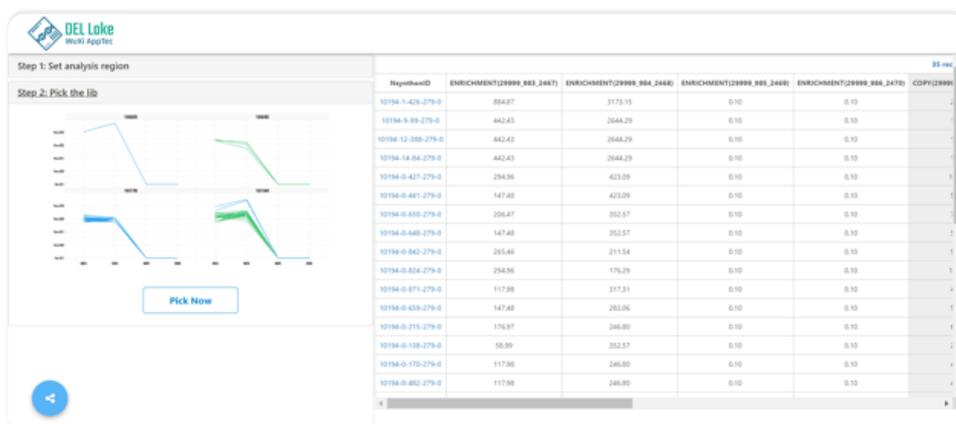
- Motif analysis to detect possible DNA binding sites of the target protein
- Enrichment of compounds and chemotypes across different conditions



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

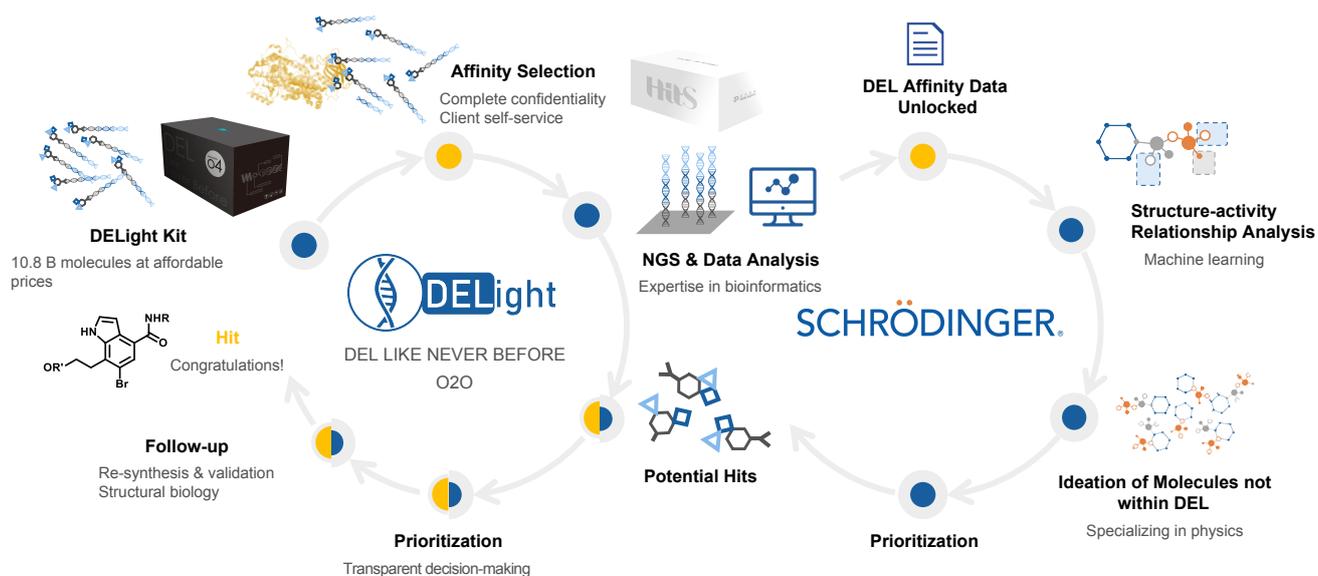
- Looking into specific DEL libraries

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. Most 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

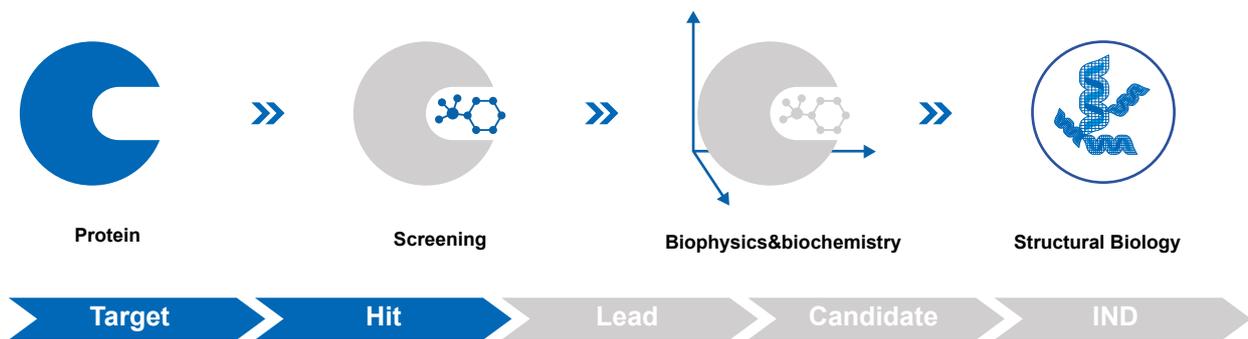


WuXi AppTec HitS offers the option of machine learning to explore chemical compounds that are not in DELlight libraries through our partnership with Schrodinger.

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.

| | | |
|---|---|--|
|  <p>One-stop solution customizable</p> <p>46+ Billion</p> <p>Target exclusivity For all drug developers Access to unique scaffolds</p> |  <p>Unprecedented data release</p> <p>10.8 Billion</p> <p>Target confidentiality For all drug developers Easy access with reduced risk</p> | <p>DELOpen</p> <p>Freraccess to DEL, data sharing</p> <p>4.4 Billion</p> <p>Target confidentiality For academic users Open source</p> |
|---|---|--|

HitS Website: <https://hits.wuxiapptec.com>
Contact Us: DEL_service@wuxiapptec.com
North America: Declan Ryan declan.ryan@wuxiapptec.com
Europe: Dave Madge dave_madge@wuxiapptec.com





Wechat

Contact Us: DEL_service@wuxiapptec.com