AXCELEAD
Drug Discovery Partners

Integrated phenotypic drug discovery solutions

We offer a “one-stop service” with full coverage from phenotypic screening to as well as target deconvolution

Phenotypic screening, which draws upon recent advances in screening tools and pathological cellular modeling systems, is increasingly being used to screen for small molecular compounds that affect specific phenotypes.

Phenotypic screening can be used to reveal new drug target pathways and identify compounds with unique mechanisms, such as protein degraders or RNA splicing modulators, which are beyond the scope of conventional target-based screening techniques.

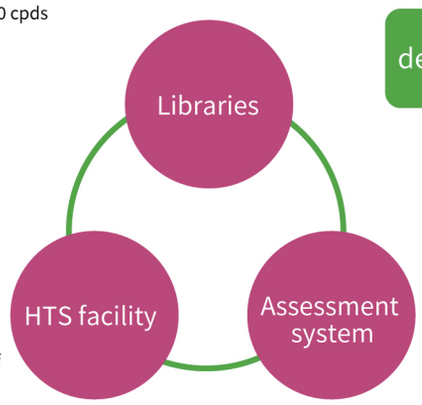
At the same time, target deconvolution, used to identify target proteins and mechanisms of action for hit compounds, is key to boosting the speed and success of subsequent lead optimization research. Axcelead offers a full range of integrated services, from phenotypic screening through to identification of target molecules/pathways using chemical proteomics with probes and fingerprinting approaches.

Drawing on extensive experience and expertise to offer the latest in phenotypic screening

- We offer an optimal compound library for phenotypic screening, including an extensive and high-quality diversity library, a focused library, and a biologically annotated library, while considering cost-effectiveness and throughput of assay systems.
- We have extensive industry experience in phenotypic screening using cell lines, iPSC-derived differentiated cells and primary cells (over 70 PJ).
- We utilize our comprehensive internal knowledge base together with public databases to accelerate your phenotypic drug discovery program.
- Axcelead brings together experts in Screening, Chemistry, Omics and Bioinformatics to perform seamless and efficient target deconvolution for HTS hit compounds, thus eliminating one of the major hurdles in the phenotypic drug discovery process.

Axcelead libraries > 1,500,000 cpds
- Diversity library
- Focused library
- Annotation library

Highly experienced researchers design optimized methodologies for exploration of hit compounds for target phenotypes.



Screening/Chemistry/Omics /Bioinformatics Groups
- Assay platform
- Cell line, iPSC, primary culture cells
- Material preparation, such as stable cell lines for HTS campaign
- CRISPR/CAS, Omics
- In-house legacy data, publicly available data

- BSL2 compatible
- Suitable for a wide range of assay systems
- Automation
- Compound management

Phenotypic Drug Discovery

>Identify hit compounds as the start point for optimization
>Identify hit compounds as the basis for new biology exploration

Assay development/optimization for HTS

Pilot screening

HTS

Hit compound
(target molecule: unknown)

	Pros	Cons
Phenotypic Drug Discovery	■Enables screening even when phenotype biology is unknown ■Identifies novel hit compounds for highly unique phenotypes ■Generates new biology insights	■Target molecule for hit molecule unknown

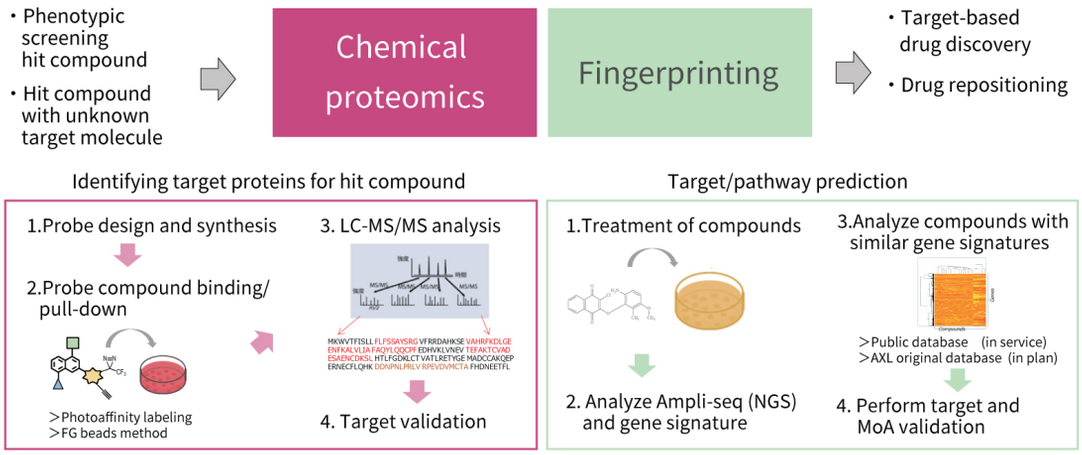
Hit compound optimization (drug discovery)

Barriers to phenotypic drug discovery (Mechanism-of-action analysis and target deconvolution)
⇒Axcelead target deconvolution service

Two solutions for target deconvolution!

- Axcelead offers two solutions for identifying target molecules and mechanism-of-actions for HTS hit compounds.
- The first involves chemical proteomics. ADDP’ s highly experienced chemists support a probe synthesis for chemical proteomics by using Structure-activity-relationship (SAR) information to enable a comprehensive and highly sensitive LC/MS analysis process.
- The other solution utilizes the unique gene expression profile (fingerprint) associated with the hit compound. The unique fingerprint data of the compound can be used to identify potential target molecules and MoAs by comparing with the fingerprint data of well-annnotated reference compounds from internal and public databases.

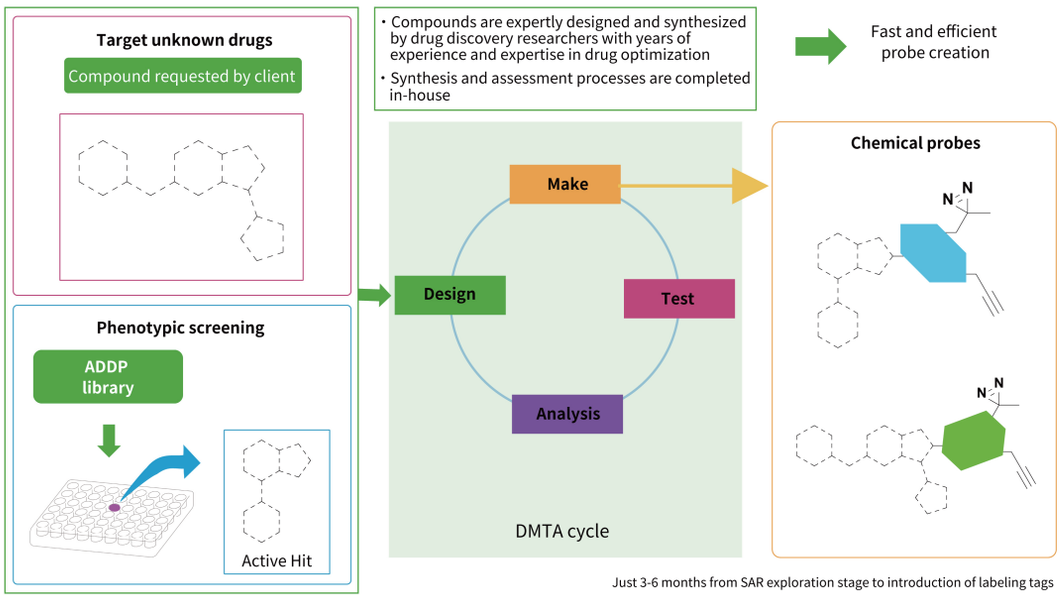
Target deconvolution



Axcelead harnesses the combined expertise of drug researchers in multiple fields to create seamlessly integrated solutions

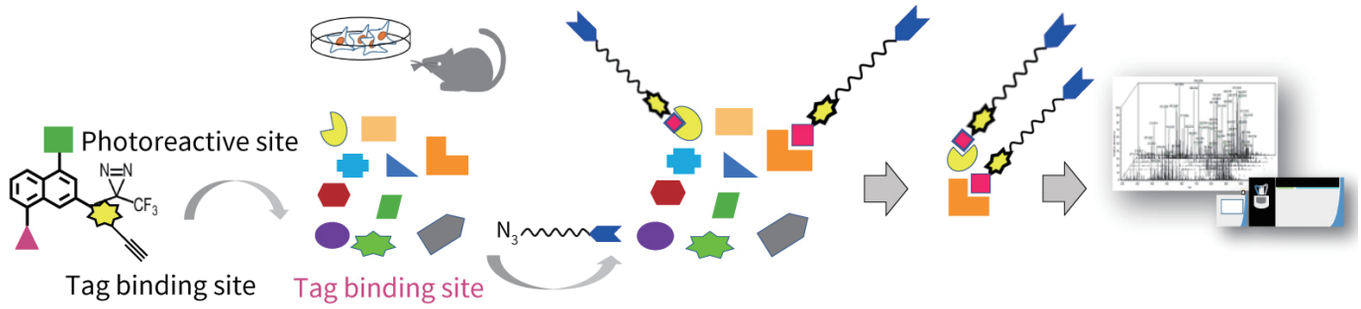
Drug researchers working together to develop new probes

- Medicinal chemists optimize the probe design based on in-depth analysis of structure-activity relationships.
- Drawing on extensive experience and expertise in synthetic chemistry, they design highly efficient probe synthesis processes.
- New probes are subject to a rigorous assessment regime at the hands of experienced researchers.
- The assessment findings are analyzed to identify potential design improvements as part of the DMTA (design-make-test-analyze) cycle.
- The in-house researchers work together to develop new probes quickly and efficiently — even those with a high degree of complexity.



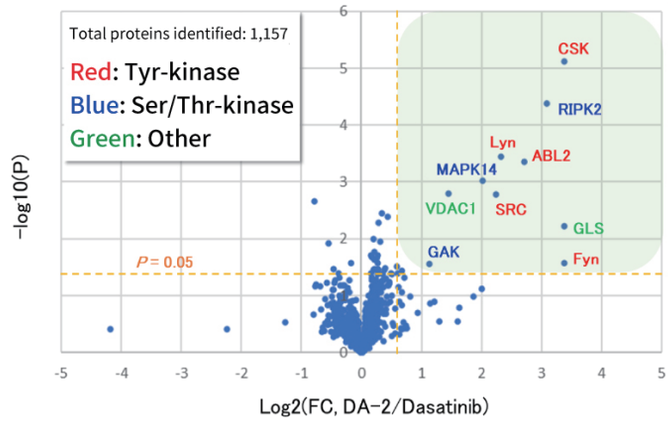
Identification of target molecules using chemical proteomics to perform comprehensive, high-sensitivity binding protein analysis

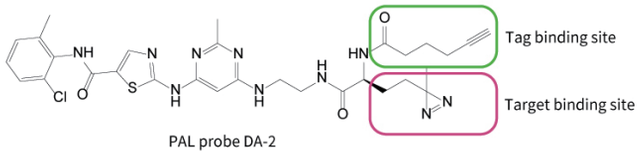
- We perform target exploration on endogenous proteins.
- Targets can be captured via covalent bonding of proteins that interact with the compound when the binding affinity of the compound is low.
- We use the comprehensive and high-sensitivity technique of proteomics to select target candidates from the captured protein groups.
- We have successfully identified a number of new targets that were either low-affinity or not reported in the literature.



① Synthesis of exploration probes ② Interactive proteins labeled via covalent bonding ③ Tag labels for chromatography ④ Affinity chromatography using tags ⑤ Comprehensive and highly sensitive LC/MS analysis

Identifying targets in crude compounds from proteins that provide drug efficacy





Global Kinase panel assay

Gene	FC_DA-2/Dasatinib	Kinase inhibitor IC50 (nM)_Dasatinib	Literature
CSK	10.4	1.1	○[1)2)]
LYN	5.02	ND	○[2)]
SRC	4.75	0.10	○[1)2)]
FYN	>10.4	0.23	○[2)]
RIPK2	8.53	1.0	○[3)]
ABL2	6.58	0.10	
MAPK14	4.06	184	○[3)]
GAK	2.19	8.0	

1) Int J Mol Sci., 21, 9276, 2020 2) J Am Chem Soc., 134, 3001, 2012, 3) J Am Chem Soc., 138, 14609, 2016

Identifying Dasatinib target Kinase with low affinity or that are not found in the literature

Axcelead is your first choice for target deconvolution

With a wealth of experience and expertise in drug design and development, Axcelead guarantees you the very best experimental designs.

Our services include chemistry for fast and efficient probe design and synthesis using SAR; proteomics for comprehensive, high-sensitivity pull-down assay of bonded proteins; bioinformatics to identify target molecules via phenotype correlation analysis; and high-speed phenotype verification biology using KD and KO/KI processes.

Chemistry ← Fast and efficient design and synthesis of covalent bonded probes using SAR

Proteomics ← Comprehensive, high-sensitivity pull-down analysis of binding proteins

BI ← Locating molecules with potential connection to phenotype

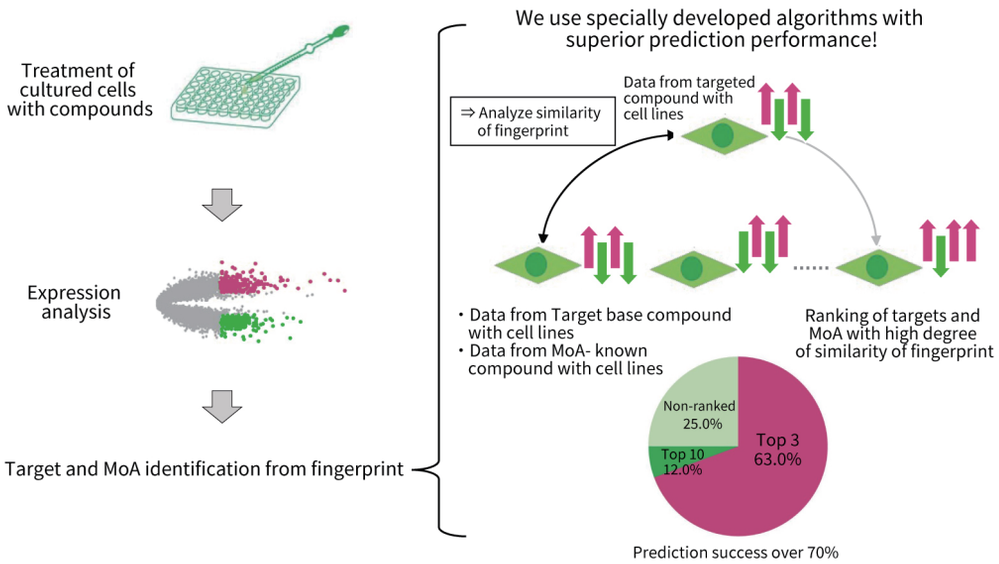
Molecular biology ← Rapid target molecule verification and validation using KD and KO/KI techniques

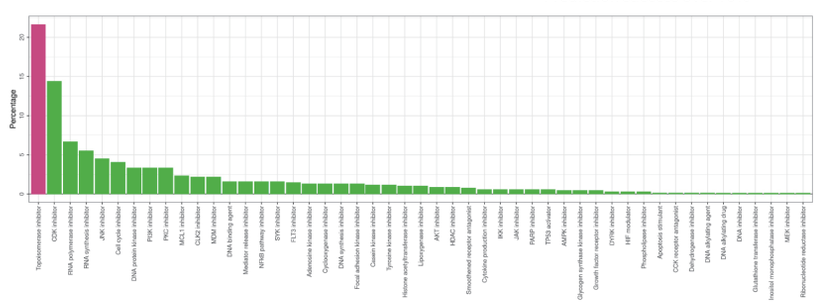
Axcelead boasts a wealth of experience and expertise in drug discovery

Target deconvolution via fingerprinting

We supply the MoA and target for any compound based on the unique gene expression data (fingerprint) associated with the changes that occur when the compound is added to the cell line, as well as information held in public databases. Our specially developed analysis algorithms deliver enhanced prediction accuracy.

- Ttranscriptome data is generated from the compound through phenotypic screening.
- Candidate target molecules and MoA are identified via fingerprinting cross-referenced against public databases.
- Coordinating the findings with the dedicated ADDP database ensures a higher likelihood of success.





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