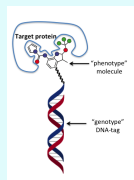


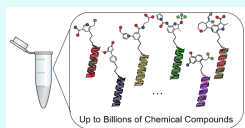


# Next Generation DNA-Encoded Library Technologies for Smarter Drug Discovery

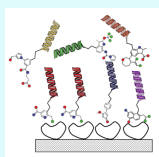
## DNA-Encoded Library Discovery Finding the Needle in the Haystack



DNA-Encoded Library solves the 'needle in a haystack' problem of drug discovery. A large collection of chemicals, each tagged with a unique DNA barcode, can be probed simultaneously against a protein target. DNA sequencing reveals the identities of bound compounds.



1) Library synthesis

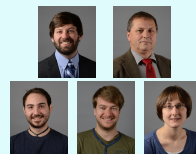


2) Selection on the target

Ranking	Counts	Code	Structure
#1	115	WVVVV	
#2	105	WVVVV	
#3	80	WVVVV	

3) Sequencing and analysis

## About DyNAbind



DyNAbind GmbH is a team of chemists, biologists and biotechnologists dedicated to leveraging our combined experience in early stage drug discovery. After developing with prestigious EXIST-Forschungstransfer funding, we founded in 2017 to deploy our technologies.

## Partnering with DyNAbind

Whether you come from pharma, biotech or academia, our team at DyNAbind is motivated to work with you to design the perfect hit discovery and optimization program for any protein target. Results are available in just weeks at an unbeatable price point. Get in touch with us today to learn more!

[www.dynabind.com](http://www.dynabind.com)  
[info@dynabind.com](mailto:info@dynabind.com)

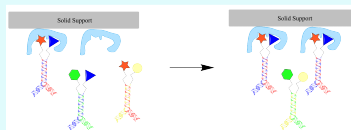
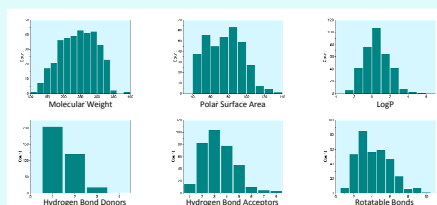
## A New Platform for DNA-Encoded Library Discovery The Highest-Quality Libraries and the World's Only Dynamic DEL Platform

DyNAbind's libraries stack the deck for drug discovery. Our collection is built from carefully-selected fragments and building blocks to ensure that every member of the library is a valid starting point for medicinal chemistry work. Our strict filtering ensures that all compounds remain in desirable physicochemical space, and an **average Tanimoto similarity of 0.195** ensures that these libraries are suited to any target class.

We further maximize your chances of successful discovery by building our libraries with our proprietary Dynamic Library architecture. Here, carefully engineered DNA interactions allow us to use two DNA strands, each presenting a molecular moiety. The DNA then reshuffles itself to automatically generate more copies of the most strongly binding molecular pairs.

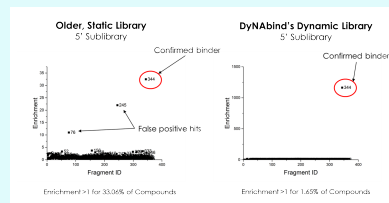
A head-to-head comparison against a non-dynamic library showed over 30-fold better enrichment of a positive control compound in a Carbonic Anhydrase II (CAII) selection.

### Physicochemical Properties of DyNAbind Library Fragments and Blocks



DyNAbind's Dynamic Library architecture is designed to allow dynamic DNA recombination in order to automatically generate additional copies of successfully binding pairs.

There are multiple advantages to this approach – not only does it offer dramatically improved signal-to-noise ratios and **reduced false positive hit occurrences**, but also allows us to individually purify and validate every library member, making DyNAbind's libraries the **most trustworthy on the market**.



DyNAbind's Dynamic Library architecture offers significant performance increases over earlier DEL technologies. Enrichment of a positive control compound is over 30X improved, with reduced false positive hits and more selective binder enrichment.

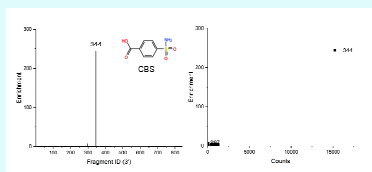
All together, DyNAbind currently has over 115 million compounds ready for selection against your target. Our collection takes advantage of both fragment and small molecule chemical space, and is constantly growing.

## From Initial Selection to Functional Assay Validation

### Hit Discovery and Optimization

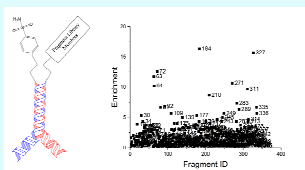
DyNAbind's technologies and chemistry expertise are ready to take your project through initial hit selection, affinity/specificity optimization, fully kinetic hit validation, fragment-linking and off-DNA resynthesis for follow-up functional analysis.

Here, a selection experiment using one of DyNAbind's fragment libraries on the enzyme Carbonic Anhydrase II yields a strongly enriched binder, fragment #344, 4-carboxy benzenesulfonamide.



Selection using a Dynamic Fragment library yielded strong enrichment and high count values for compound # 344, 4-carboxy benzenesulfonamide (CBS), a confirmed binder of the Carbonic Anhydrase II protein

To further optimize the identified binders, a maturation experiment can be performed. By fixing one DNA strand with the identified binder, the second strand can contain a fragment library to select for binders which further improve the affinity or specificity.



Affinity maturation selection against the protein combines a fragment library with a known binder to further improve the quality of hit compounds

### Hit Validation and Triage

After selecting for the most ideal binding pairs, DyNAbind's Binding Profiler system is used to rapidly obtain full kinetic profiles for the binders, without the need for time-consuming off-DNA resynthesis, by assembling the selected fragments on a DNA-functionalized biosensor surface.

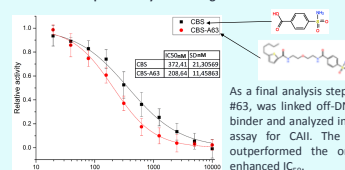
### Hit Validation for CBS-Fragment Pairs on CAII

Fragment ID	64	72	90	109	114
Structure					
$K_d$	980 ± 22.2 nM	603 ± 12.2 nM	580 ± 12.7 nM	278 ± 6.32 nM	209 ± 8.30 nM
$K_{on}$ (1/Ms)	1.104 ± 0.206	1.104 ± 0.167	8.769 ± 1.767	1.104 ± 0.288	1.064 ± 0.267
$K_{off}$ (1/s)	1.132 ± 0.226	7.26 ± 0.746	5.39 ± 0.816	4.24 ± 0.566	2.176 ± 0.736
Fragment ID	184	194	63	7	146 (N/C)
Structure					
$K_d$	342 ± 0.07 nM	300 ± 4.27 nM	124 ± 0.93 nM	278 ± 4.99 nM	2.01 ± 0.32 nM
$K_{on}$ (1/Ms)	1.594 ± 1.592	1.164 ± 1.202	5.894 ± 1.893	2.184 ± 0.632	7.863 ± 1.073
$K_{off}$ (1/s)	5.49 ± 3.446	3.47 ± 0.256	7.26 ± 0.976	6.33 ± 0.456	1.64 ± 0.136

Fully kinetic binding profiles of the hit compounds identified in the CA2 selections, obtained without resynthesis. All compounds offer improved binding, with the exception of the negative control, compound #146.

### Functional Analysis

#### pNPA Assay for the original binder and off-DNA Linked Hit Compound



As a final analysis step the best hit compound, #63, was linked off-DNA with the original CBS binder and analyzed in a pNPA-based inhibition assay for CAII. The new linked compound outperformed the original binder, with an enhanced  $IC_{50}$ .