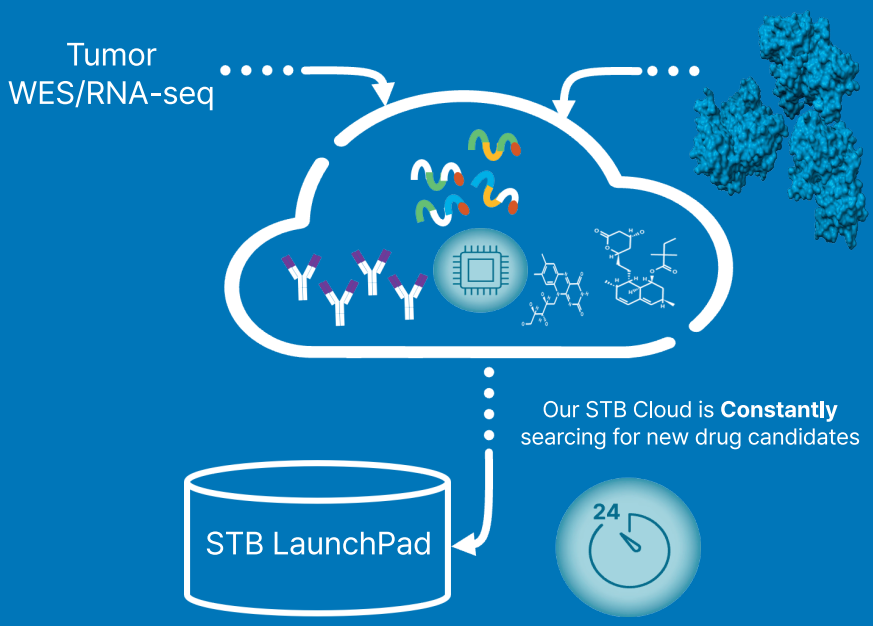
Syntekabio LaunchPad

(Pre-made Hit & Lead Inventory)

syntekabio.com



Syntekabio
AI Drug Platform as a Cloud Service

STB CLOUD

STB LaunchPad: Pre-made Hit & Lead Inventory

Syntekabio (STB) has developed a collection of AI-discovered hit and lead compounds for well-known drug targets across major therapeutic indications via our STB LaunchPad program.
This R&D project leverages our in-silico AI technology, DeepMatcher™, to develop many, concurrent drug pipelines simultaneously. We have initiated hit- and lead- discovery on over 100 priority protein targets, related to 60-70% of major disease indications, supporting our goal of making many, novel molecules available to our partners rapidly and at scale.

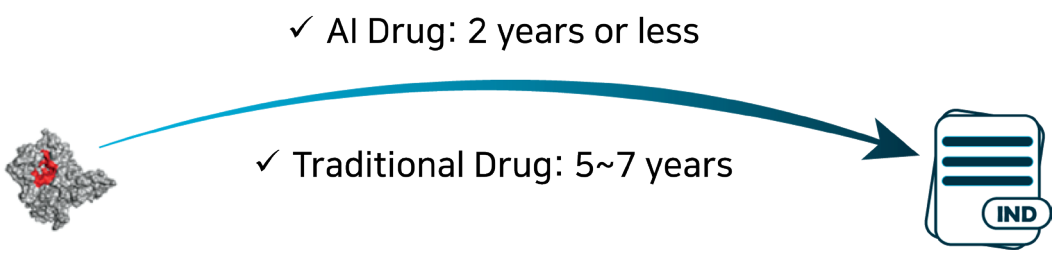
To date, our collection of candidates includes validated hits and leads, as well as compounds already in animal-stage testing. The list is inclusive of both Best-in-class and First-in-class candidates, based on the target's broader clinical development stage. The newly discovered STB LaunchPad compounds are available to biotechnology and pharmaceutical companies, interested in partnering with us to accelerate their drug discovery and preclinical phase pipelines.

Beyond our ongoing LaunchPad drug discovery efforts, STB can also provide broader AI solutions to our partners and facilitate your preclinical R&D activities via our robust in-silico platform and optimization workflows.

Pharma Challenges	Syntekabio LaunchPad
✓ First or Best in Class Drugs	✓ Save time with Pre-made Hits and Leads
✓ IND-enabled Drug Candidates	✓ Take Advantage of Factory-Level Drug Discovery
	✓ Experimental Validation by Global CRO Network

STB LaunchPad for Life Sciences

STB LaunchPad is an optimal solution for pharmaceutical and biotechnology companies looking for well-validated compounds – hits and/or leads – for their disease target(s) of interest. Partners can also accelerate their preclinical R&D process by quickly securing best-in-class or first-in-class compounds from our internally developed library in two years or less.



To accelerate the drug discovery process by making drug candidates readily available

STB LaunchPad-2024 Program

STB LaunchPad leverages Syntekabio's deep experience in AI drug discovery, in-silico optimization, machine learning and deep learning to generate our proprietary pipeline of robust candidates for disease targets of interest. Whether you are looking to expand your company's existing pipeline or to unlock new value, the STB Launchpad can be your trusted AI partner to augment R&D opportunities that are important to your portfolio strategy.

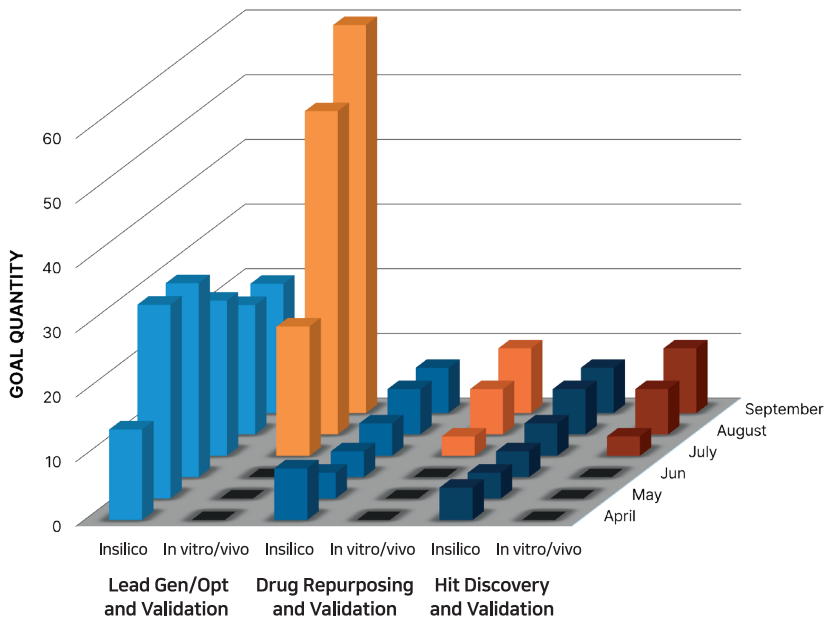
[STB LaunchPad-2024] ~130 protein targets covering 60~70% for major indications

Disease Indications			Target #	Aim to Best in Class			Aim to First in class	
				Validated Hits or Leads		Under development	Validated Hits or Leads	Under development
				Drug repurposing	New Chemical Entity		Drug repurposing	
1	Psoriasis		7	**ULK2***, DYRK1A	ITK	NTRK1, S1PR1		SGK1, PRRT2
2	Atopic Dermatitis							
3~7	Alopecia, Lupus, Bowel Disease, Spondylarthritis & Rheumatoid		10	**JAK3***, IRAK4, TYK2, IRAK1,		JAK1, JAK2, SYK	TBK1	BTLA, ICOS
8	Cancer	Breast Cancer	12	DYRK1A, ErbB2, ErbB4,	**CLK2***, CDK7	CDK4, CDK6, CK2, CLK1, TNIK		DYRK2
9		Blood Cancer	11	MKNK2	ABL1, LYN, FLT3 ITD/F691L,	]BCL2, IDH1, IDH2, DNMT3A	KC1D, PKN1,	NPM1
10		Solid Cancer	58	ALK, BRAF V600E, CSF1R, FGFR2, MERTK1, **MET M1250T***, PI3KCA, RET, TGFR1, TIE2, ULK1, **JAK3***,	CDK7, DDR1 KDM4D, KIT, SRC,	AKT1, AKT2, AR, AURKA, BCL2, CDK4, CDK6, DNMT3A, FNTA, FNTB, HDAC4, HDAC6, JAK1, JAK2, KRAS G12D, MEK1, MEK2, mTOR, PLK1	EPHB1, HASP, KDM4A, KDM5B, KGP2, PAK6, PI3KC3,	ARID1A, ARID1B, ATK3, CASP8, CDKN2A, DNMT1, HDAC2, KDM5A, KDM6A, KDM7, MAP3K1, MLL3, SETD2, TP53-Y220C
11		Immune Checkpoint Inhibitors	10		IDO/TDO			BTLA, CD112R, HAVCR2, ICOS, NKG2A, TIGIT, TNFRSF18, VISTA
12	Major Depression		7	SLC6A4, DRD3		CACNA2D1, DRD2, SLC6A2		CACNA1E, PXDNL
13	Alzheimer's Diseases		13	ACES, PDE2A, ROCK2,	**CLK2***	PDE9A, PARP1, CK2, GSK3B	MLKL, PDE10A,	CASP8, FADD, FAF1
14	Parkinson's Diseases							
15	Others		11	ACM2(Peptic Ulcer),	MMP12(COPD),	AGTR1 (Hypertension)	PI4KB(Infection), TNI3K(I/R injury), NEK7(Gout),	ACE2 (Hypertension), KDM2 (COPD), KDM7 (COPD)

"First or Best in class" definition: target on Preclinical R&D stage or clinical and approved stage (phase 1~). *: IC50<10nM.

STB LaunchPad Roadmap for 2024

STB LaunchPad program is dedicated to continuously identifying New Chemical Entities (NCEs) for 100+ protein targets. In the immediate near-term, we will prioritize lead generation and optimization on the 110 hits we have discovered (first and second rows from the left). In parallel, we will be identifying new protein targets for known drugs and validating them via in-vitro and in vivo testing (middle two rows). Alongside this work, we will be continuously adding new protein targets to the hit discovery stage, in order to feed the later development and optimization stages (two rows on the far right).

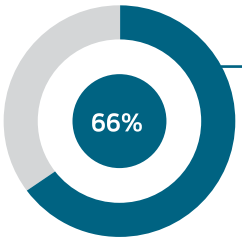


STB LaunchPad Covers Major Indications

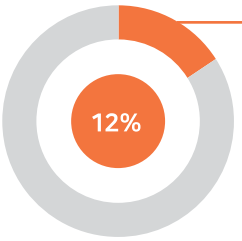
STB LaunchPad includes many well-known targets in autoimmune, cancer, CNS, metabolic and rare diseases, where the unmet need in the market remains. In the interest in progress for patients and their families, STB LaunchPad is de-risking these targets and compounds are ready for partners to bring to the IND and clinical phases.

Choose your target and disease to get started

~130 protein targets covering 60~70& of current drugs for major indications

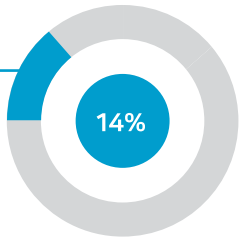


Cancer
Cancer is caused when cells in the body grow in a way that is uncontrolled and not normal, killing normal cells and often causing death. **(91 targets)**

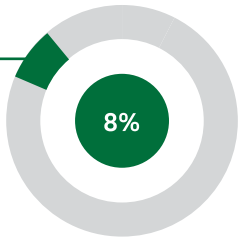


Autoimmune Disease
Autoimmune disease happens when the body's natural defense system can't tell the ditterence between your own cells and foreign cells, causing the body to mistakenly attack normal cells.
(17 targets)

CNS
CNS diseases include a broad spectrum Of disorders in which brain or spinal cord function is diminished or impaired. resulting in diminished motor, sensory, or cognitive performance. **(20 targets)**



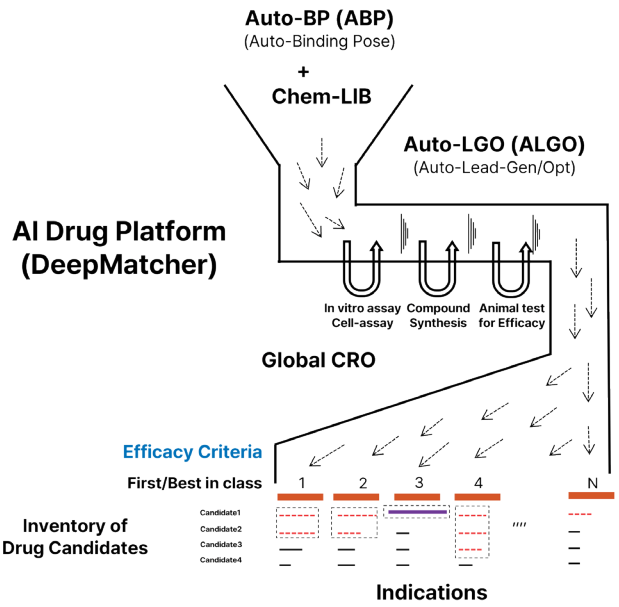
Other
This categories is included the targets which is metabolic disease, inflammatory diseases and rare diseases. **(11 targets)**



STB LaunchPad is Powered by the STB CLOUD

Our robust AI infrastructure includes cloud-based supercomputing, strategic learning models, and scalable end-to-end automated solutions for drug discovery, compound synthesis, and validation in the lab. This can seamlessly integrate into our partner's development processes while accelerating overall project speed and efficiency. Our custom workflows are supported by our proprietary STB CLOUD within the AI Bio Supercomputing Center.

Factory-Level AI Drug Discovery



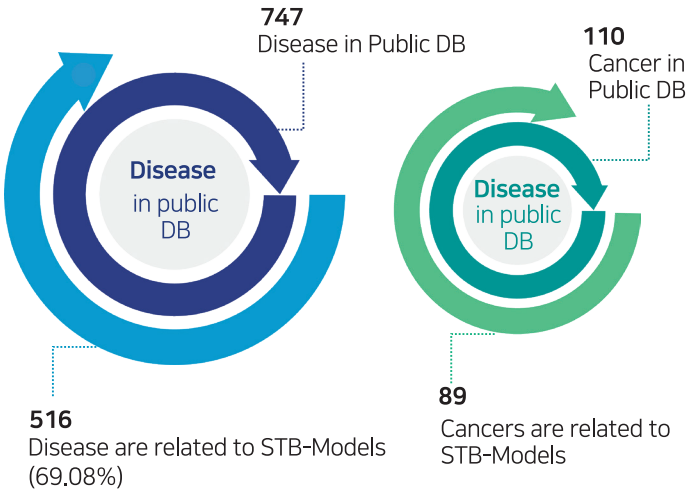
AI Bio Supercomputing Center

Facility dedicated to bio application like AI/ML, MD, Structural Biology, and Genomics Big Data

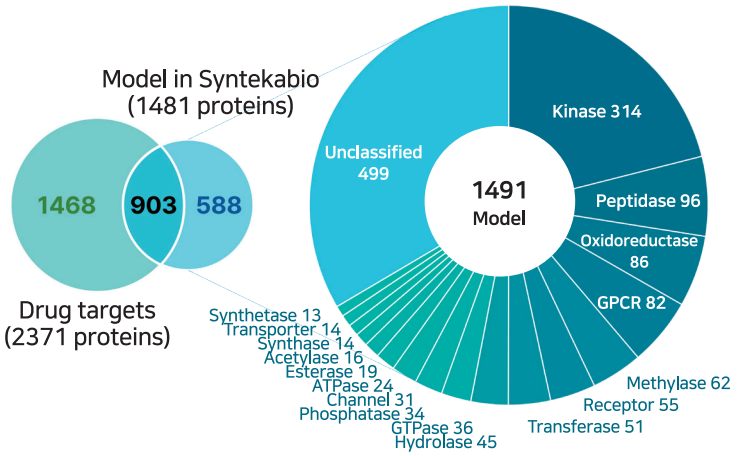
DeepMatcher® AI Drug Discovery Platform

DeepMatcher™ is a comprehensive fully automated AI drug discovery and development platform developed to find the most compatible drug candidate for any given target protein. DeepMatcher™ provides a suite of drug discovery tools from hit identification, lead generation, lead optimization, ADMET/PK analyses, and off-target screening.

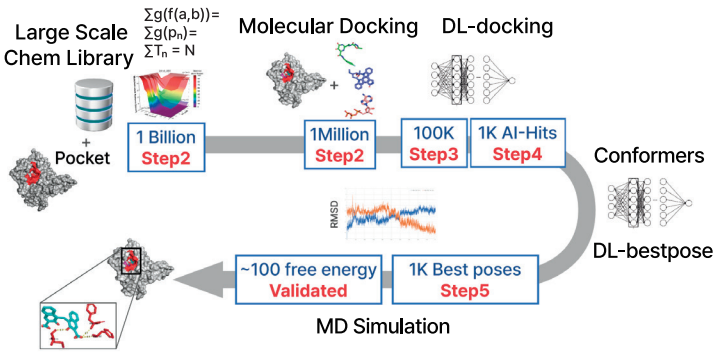
Diverse Disease Indications and Target Proteins



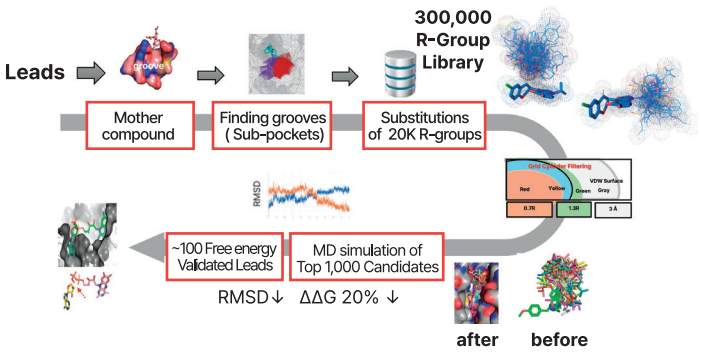
1,491 Ready-to-be-screened Targets



Auto-BP (Auto-Binding Pose)



Auto-LGO (Auto-Lead Gen/Opt)

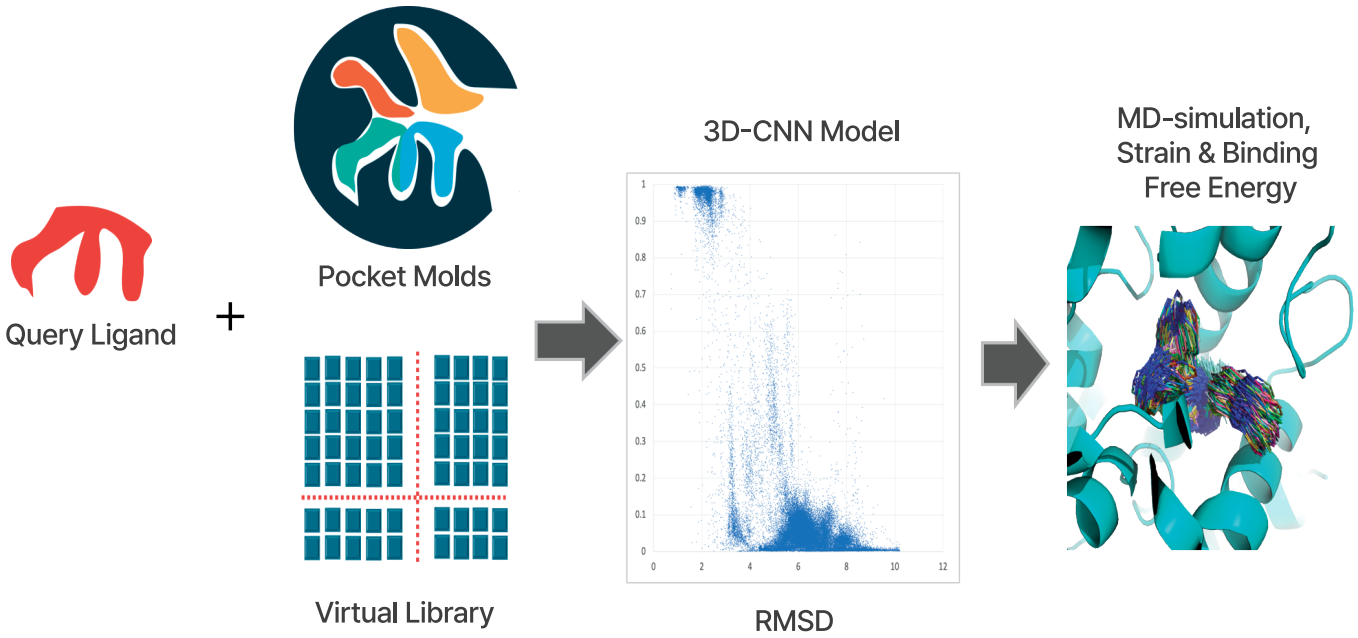


Auto-Binding Pose Pose by DeepMatcher™ initiatedby pre-screening hit compounds from the library, followed by molecular docking and two consecutive steps of DL-dockings. The optimal pose is selected before conducting MD simulation, completing the hit identification in five steps.

Auto-Lead Generation/**Opt**imization by DeepMatcher™. 20,000 R-groups are substituted and perturbed at the scaffold of a mother compound, and the top 1,000 candidates are selected for MD simulation to complete the process.

Hit: Auto-BP (Auto-Binding Pose)

Auto-BP begins by generating pocket molds that fit protein pockets with fragments of small molecule (molds). Next, all virtual protein-ligand conformational poses are generated and evaluated using a 3D-CNN model to identify the most promising pose candidates. Molecular dynamics (MD) simulations followed by calculations of strain and binding free energy to measure the strength of the interaction between the protein and the ligand at the atomic level.



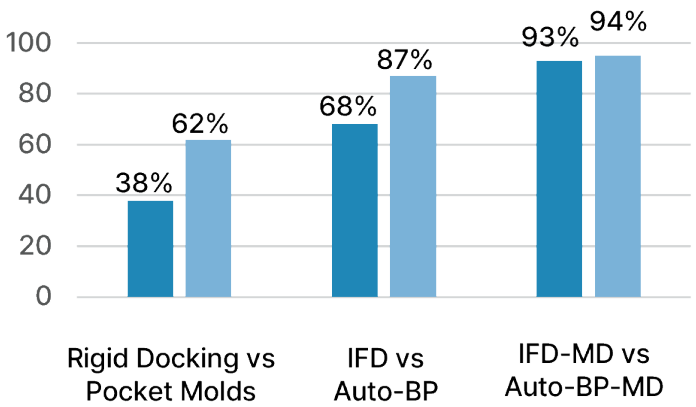
Case Studies

Auto-BP was evaluated using two different benchmarks. The first is the IFD-MD method, in which docking was attempted in three steps using approximately 190 protein-ligand interaction data. A comparison of pocket mold-based docking with IFD-MD shows that the ability to select the best is far superior. The second benchmark data is 25 peptide docking data. In the case of peptides, accurate docking is difficult because the size is more than 5 times larger, but DINC (MD Anderson/Rice University) attempted thorough docking using AutoDock Vina and proved that the root mean square deviation (RMSD) is smaller than 2.5 angstroms or less. The results of comparing DINC and Auto-BP also show that Auto-BP is far superior.

Auto-BP Accuracy with 190 protein-ligands

J. Chem. Theory Comput | (2021) 17: 2630–2639

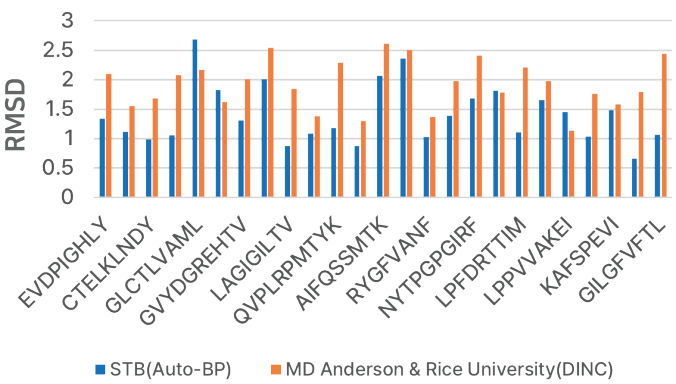
(190 Protein-ligand complexes, *RMSD<2.5)



Auto-BP Accuracy with 25 MHC-Peptides

Scientific Report | (2018) 8:4327

(25 Protein-peptides complexes, *RMSD<2.5)

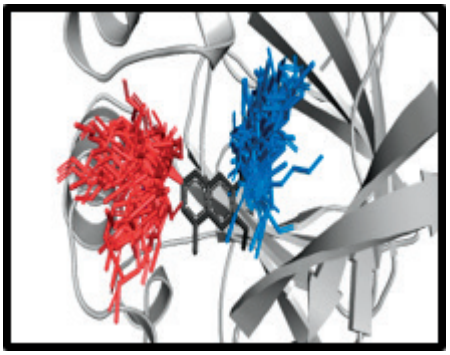


Lead: Auto-LGO (Auto-Lead Gen/Opt)

Auto-LGO is set to automatically generate 1 to 3 million derivatives when the scaffold in the pocket and the anchor atom to be substituted are determined. And, through five filters in between, about 20 candidates that can be synthesized are finally predicted.

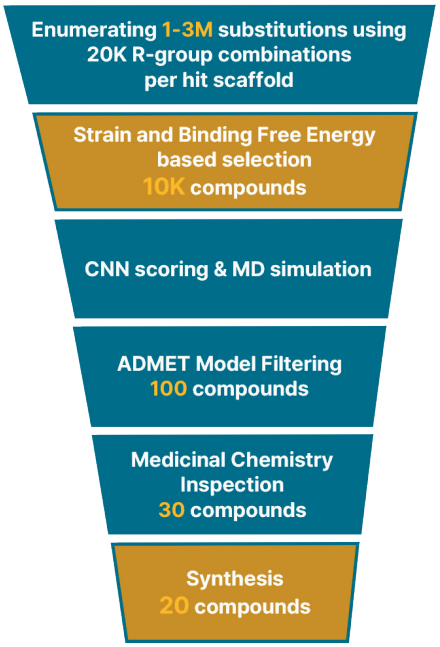
Auto-LGO high-throughput design

1-3 million R-groups enumerations to generate and optimize leads for specific protein targets.



No prior knowledge required to use our system

Auto-LGO Steps

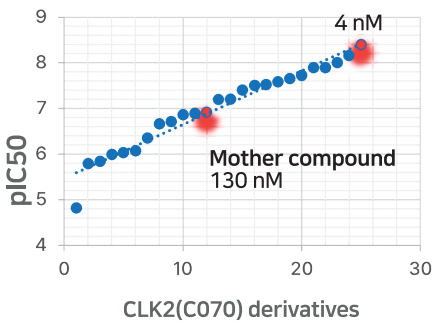


Case Studies

Finally, synthesis was performed using 10 to 20 synthesizable compounds, and when the final result was performed in vitro assay, the IC50 was improved 32 folds for CLK2 compared to the mother compound, and for FLT3, was improved by 6.5 folds, and 6 out of 7 synthesized were improved, and in the case of dual inhibitors like IDO/TDO, it was also improved by about 14 folds.

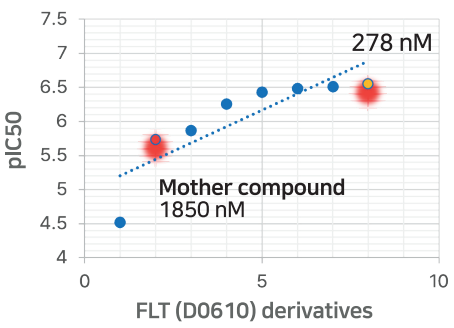
CLK2(STB_C070)

32 folds improved



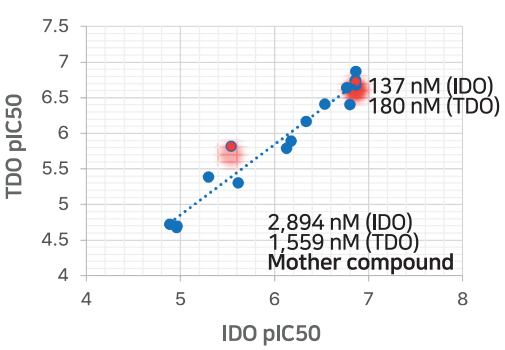
FLT3(STB_D0610)

6.5 folds & 6/7 improved



IDO/TDO(STB_C017): Dual Hit

14 folds improved



*pIC50 = -Log (IC50),
Log(1/1,000,000,000) = 1(nm) = 9 (pIC50)
Log(1/30,000) = 30(um) = 4.5 (pIC50)

Kim et. al., Oncoimmunology, 2021

STB CLOUD

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