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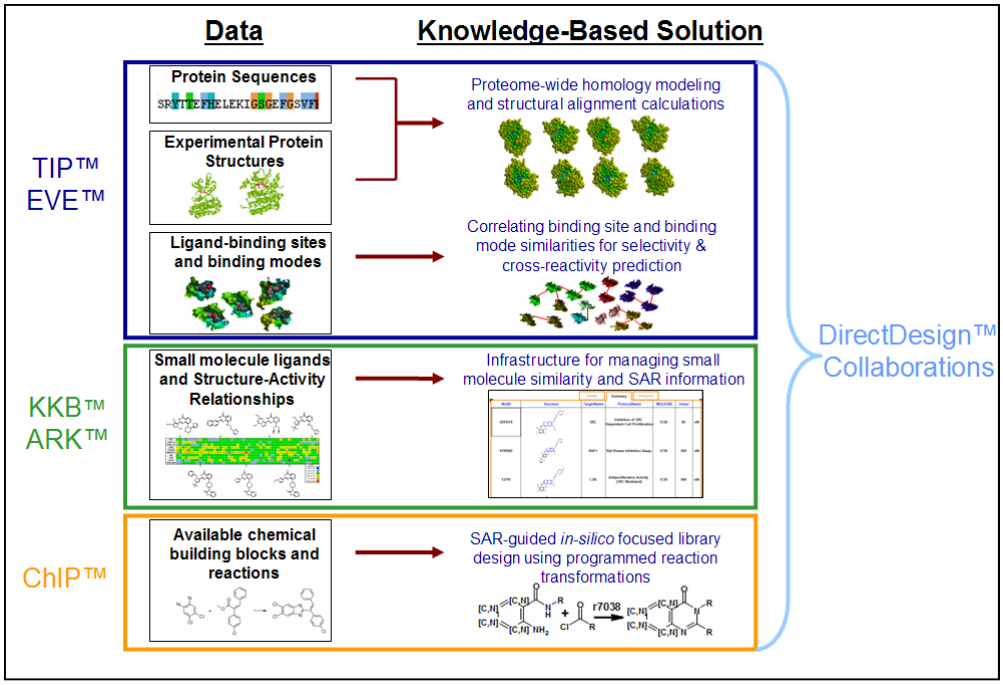
Products & Services

Eidogen-Sertanty is dedicated to delivering discovery informatics technologies that bridge the target-to-lead knowledge gap. With a unique set of ligand- and structure-based drug discovery technologies, Eidogen-Sertanty's knowledge-based software and collaborative services are designed to enhance the efficiency of your organization's lead discovery and optimization efforts.



Customers

Our discovery software and database products have a well-established customer base, including many of the largest pharmaceutical companies.

The flexibility of our software and services licensing model also makes us an ideal partner for smaller drug discovery organizations.

Example Customers & Collaborators

Pfizer, Lilly, Novartis, sanofi aventis, Takeda San Diego, Merck, Cephalon, Roche, Shionogi & Co., Ltd., K.A.I. Pharmaceuticals, genzyme, Pioneer A DuPont Business, origenis, Genomics Institute of the Novartis Research Foundation, University of Miami, Znomics, specs, University of Maryland, U.S. Food and Drug Administration Protecting and Promoting *Your* Health

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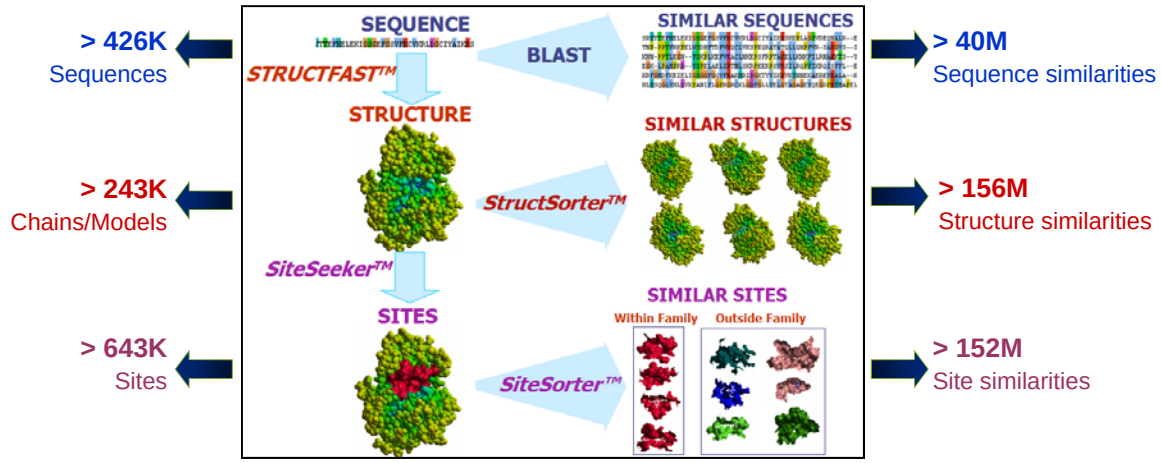
Target Informatics Platform™ (TIP™)

TIP is the industry's first structural informatics database solution. TIP efficiently manages and amplifies the continuously growing body of experimental target structural data, supplying researchers with the largest knowledgebase of drug target structural information available. The figure below summarizes the number of human target structures, sites, and similarity relationships that are pre-calculated and stored in the TIP database. With TIP, researchers have *instant access* to structural data and relationships that required more than *40 CPU years* to calculate.



Key Features and Benefits of TIP:

⇒ **STRUCTFAST™** automated homology modeling algorithm was the top comparative modeling server at CASP6[1]	TIP contains the most accurate and reliable set of alignments and protein models available
⇒ Contains >200,000 high quality protein structures/models, including one or more structures for more than 80% of the druggable human genome[2-3]	High quality structural information can be downloaded on-demand for nearly any drug target in the human proteome
⇒ All sequence, structure, and site similarities are pre-computed and stored in the TIP database for easy searching	Efficiently derive proteome-wide structural similarity information that requires hundreds of CPU hours to create
⇒ Updated monthly with new structures from the Protein Data Bank (~500 new PDB structures and hundreds of new models per month)	Automated update process keeps TIP up-to-date with the latest structure information
⇒ **SiteSeeker™** algorithm confidently annotates novel ligand-binding sites on all TIP structures	Instant identification of relevant ligand-binding hotspots and alternate binding pockets
⇒ **SiteSorter™** algorithm computes 3D similarities between binding sites, both within a target family and between unrelated target families[4]	Streamline "target hopping" research via rapid detection of target binding site similarity across the entire proteome
⇒ Open search API allows you to extract XML directly from the TIP database	Supports custom web services application development for deploying TIP data across your organization

References:

1. Debe, et al. Proteins. 2006, 64:960-967
2. Hambly, et al. Molecular Diversity. 2006
3. AL Hopkins and CR Groom. *Nat Rev Drug Discov.* **1** (9), 727-730, 2002.
4. Palmer, et al. J.Chem.Inf.Model. 2006, 46:1871-1876

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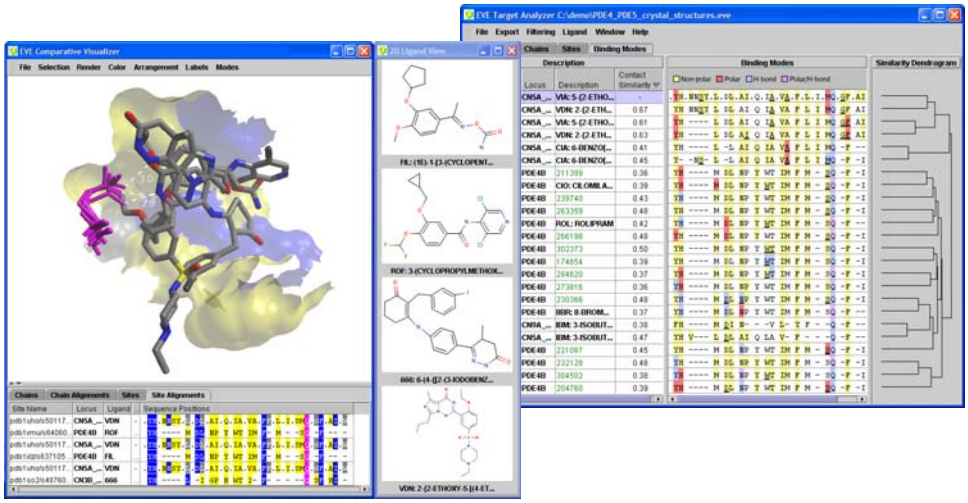
EVE™ Comparative Visualizer

EVE is our unique visualization environment for the comparative analysis of biological and chemical structures. EVE runs on your Windows or Linux desktop or laptop computer, seamlessly integrating the pre-calculated structural data in TIP with your own proprietary small molecule and protein structure data.



Key Features and Benefits of EVE:

⇒ Easy visualization of sequence, structure, site, and binding mode similarity relationships	Common structure-based comparative analysis workflows are accomplished with a single mouse click.
⇒ 2D sequence viewer and 3D structure viewer are fully linked	Easily select and manipulate regions of interest
⇒ Instantly overlay proteins based on structure and binding site similarity, or user-defined residue subsets	Flexible overlaying capabilities allow you to quickly focus on the precise regions you wish to compare
⇒ **Site-Ligand Contact (SLiC)** feature enables sophisticated analysis and comparison of binding modes for bound ligands (based on SIFt[1])	- Understand ligand selectivity across multiple targets - Enables rescoring of docking results based on binding mode fingerprint comparison, improving docking enrichments by 5 to 10X
⇒ **LigandCross** feature enables automated creation of novel ligand scaffolds from known target-ligand complexes (based on BREED[2])	Automatic recombination of known ligand binding fragments enables rapid creation of novel ligand structures with a high probability of activity
⇒ One-click annotation and comparison of important binding site properties such as hydrophobicity, charge, hydrogen bonding, shape, and chemical character	Selectivity analysis is a breeze with EVE's fast comparative binding site analysis tools
⇒ Saves families of structural data as projects rather than individual structure files	Enables easy sharing of all relevant data between members of a project team
⇒ Import your own proprietary structures, sites, and ligands, and compare them to data exported from TIP	Instant comparison of proprietary structures and sites versus all other structures in the family
⇒ Complete macro language and batch-mode analysis compatibilities	Carry out customized, automated large scale comparative analyses
⇒ Complete menu customization capabilities	Supports custom application development for data and idea sharing across entire project teams

References:
1. Deng *et al. J. Med. Chem.* **47** (2), 337-344, 2004.
2. Pierce *et al. J. Med. Chem.* **47** (11), 2768-2775, 2004.

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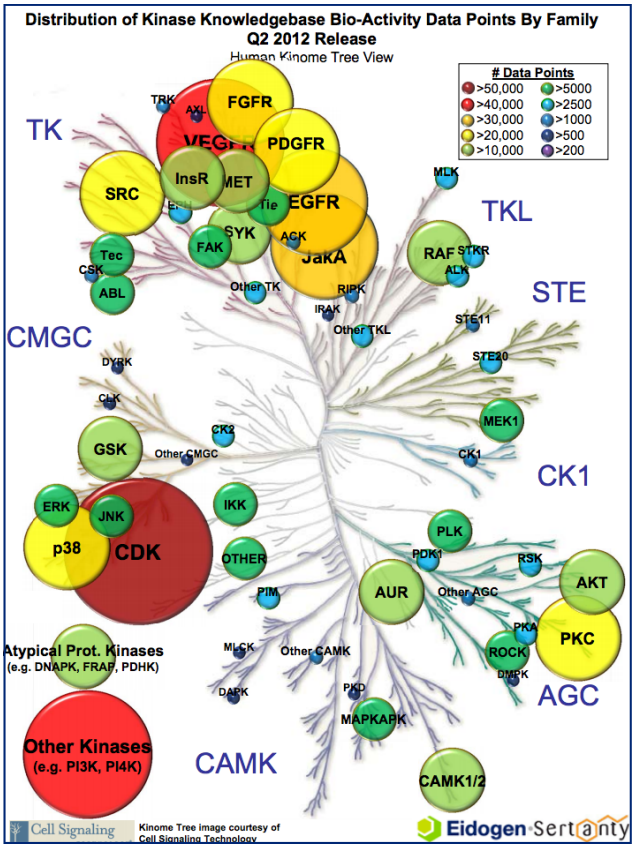
The Kinase Knowledgebase™ (KKB™)

The Kinase Knowledgebase is Eidogen-Sertanty's database of structure-activity relationship (SAR) and chemical synthesis data focused on protein kinases. The KKB contains over **649,000** SAR data points on over **241,000** unique small molecule kinase modulators, which have been curated from **>7915** journal articles and patents. The KKB can either be accessed online through Eidogen-Sertanty's ARK™ platform or licensed in a variety of formats for integration into in-house databases.

As of Sep 2012, the Kinase Knowledgebase covers the following data:

- Journal articles and patents: >7915
- Biological Activity Data Points: >649,000
- Unique molecules w/annotated assay data: >241,000
- Unique molecules from patents and articles: >586,000
- Kinase targets with assay data: ~484
- Annotated assay protocols: >25,472
- Annotated chemical reactions: >2,365



Key Features and Benefits of the KKB:

⇒ >649,000 SAR data points from >241,000 unique molecules	Largest archive of reported structure-activity data for kinase inhibitors
⇒ Data readily mined through variety of sources (ARK, Daylight, Symyx-ISIS,Accelrys-Accord, Scitegic-PipelinePilot, ChemAxon), with customizable exporting options to enable easy merging into other programs	Flexible data access model allows different users to interface with the KKB data in different ways, depending on the application
⇒ Optional integrated **eScreen®** QSAR models supplement experimental assay data with predicted activity data and selectivity analysis across 150 common kinase targets	Quickly assess potential activity and selectivity for all molecules in the KKB even if biological data is not available
⇒ Released quarterly, with growth rate of ~150 publications, 20-30K unique molecules, and 15-20K SAR data points *per quarter*	Stay up-to-date with the latest reported structure-activity data for kinase targets of interest
⇒ Enumerated products from common kinase inhibitor synthetic schemes found in patents are incorporated into the database	Obtain a broadened view of covered scaffold space for many patents, even if biological activity data is not reported
⇒ Streamlined curation process enables rapid response to customer data requests	Customer-driven prioritization ensures that the highest value data is added to the KKB in a timely manner
⇒ Extensive standardization, classification and quality control of primary assay data	Easily navigate the knowledgebase to find the data you want, and then use the data with confidence

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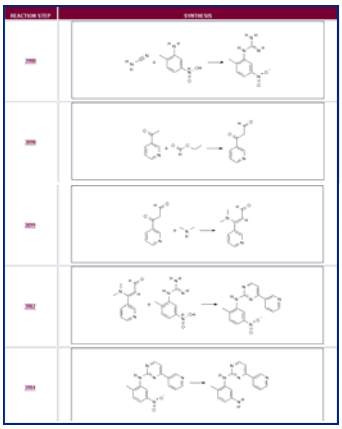
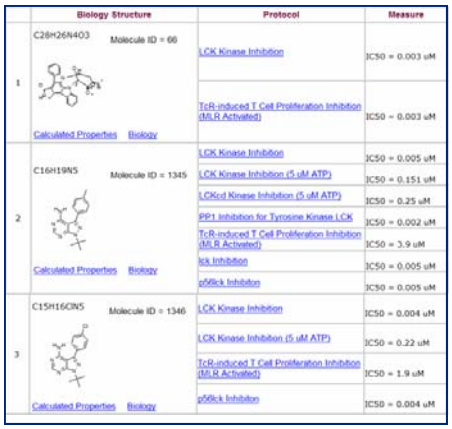
Activity and Reaction Knowledgebase™ (ARK™)

The **ARK** platform is a web-based chemistry "white-boarding" environment which captures synthetic information and structure-activity data, enabling scientists to simultaneously build computational QSAR models and explore chemical hypotheses through virtual library enumeration followed by QSAR-based prioritization. ARK's unique Reaction and SAR Archival system efficiently captures and links chemical and biological data in a centralized infrastructure. Coupled with the Virtual Library Enumeration module, ARK provides a convenient way to both archive experimental work and virtually explore new synthetic ideas, all through an easy-to-use web-based interface.

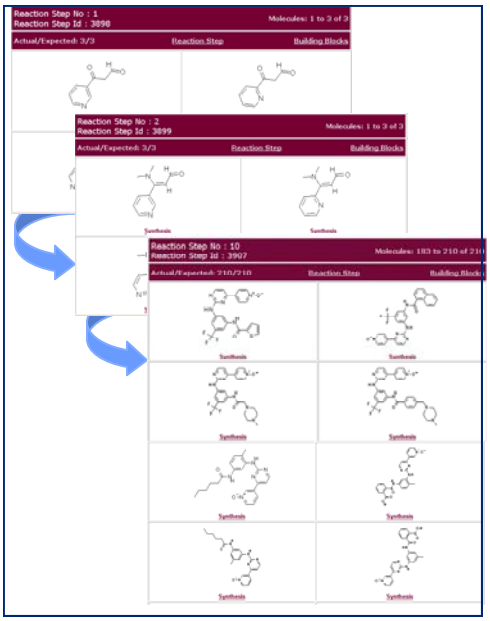
Reaction Archive



SAR Archive



Virtual Library Enumeration



Key Features and Benefits of ARK:

⇒ Integrates chemical synthesis information (reactions), biological activity information (SAR), and informatics (predictions) in a centralized infrastructure	Conveniently explore ideas and published knowledge by navigating between synthetic protocols, and known and predicted activities
⇒ Enumeration engine leverages and expands upon Daylight technology, correctly handling highly complex reaction sequences	Virtually explore products of complex reaction sequences where other enumeration technologies often fail
⇒ High-throughput reaction chemistry starter-set available with over 14,000 archived, validated reactions	Process and evaluate millions of virtual molecules at the early design stage
⇒ All content is searchable by structure, substructure, similarity, specific and generic transformations, experimental procedure, reaction conditions, yield, etc.	Easily search and mine data from the knowledgebase that are specific to the scaffolds and reactions you are interested in
⇒ Intuitive web-based interface for entering and archiving reaction chemistry and synthetic protocols	Reaction chemistry can be entered the same way as it would in a laboratory notebook

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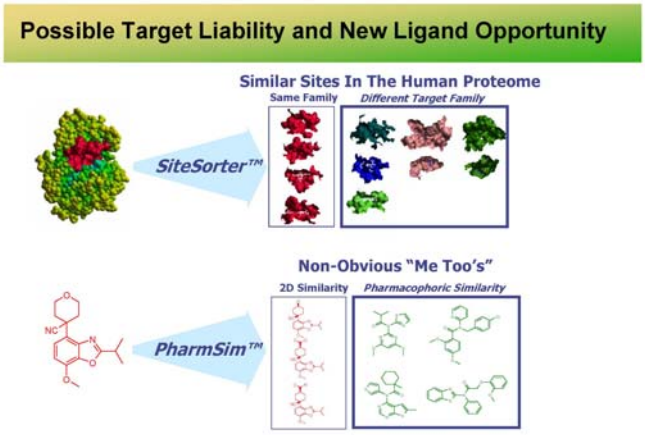
DirectDesign™ Discovery Collaborations

Eidogen-Sertanty's **DirectDesign** Discovery Collaborations utilize our entire suite of informatics technologies in collaborative drug discovery engagements. The broad scope and high integration of our *in silico* tools for target and ligand similarity assessment and prioritization make Eidogen-Sertanty an ideal partner for organizations seeking novel approaches for challenging **target and scaffold-hopping** projects.

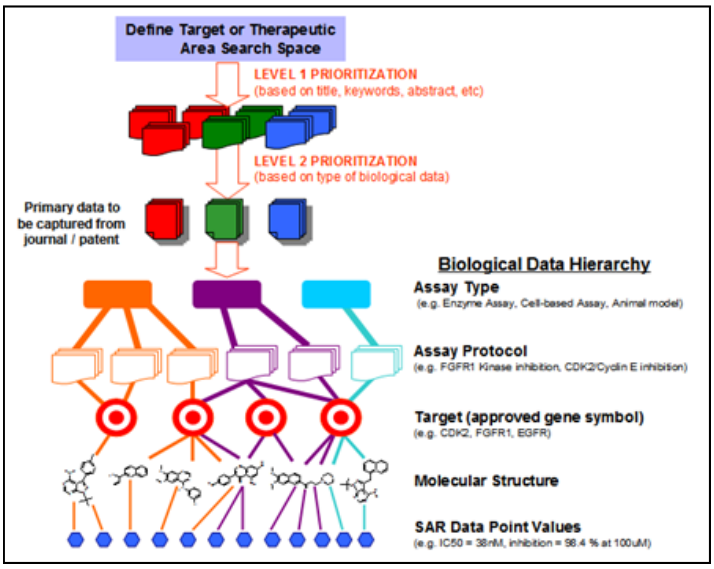


Example DirectDesign projects range from **Custom Data Curation**, to **Knowledge-Based Lead Design** (directed *de novo* design of novel, patentable compounds or target-focused libraries), to **Virtual Target Screening** ("fishing" for likely targets given known bio-active compounds, revealing new opportunities and potential liabilities), to **Compound Prioritization** for in-licensing efforts.

Custom Content Curation

The Eidogen-Sertanty content development team has extensive experience in mining, prioritizing, and categorizing structure-activity relationship (SAR) and chemistry data from patents and journal articles for any target class or therapeutic category. Using the Activity & Reaction Knowledgebase (ARK) archival system, our team is able to streamline such data mining efforts, efficiently compiling and presenting data in formats that are most useful for our partners within a few weeks of project initiation.

Content mining, prioritization, and data capture process



In addition to the ongoing curation of the Kinase Knowledgebase™, our content development offers custom data curation services for specific targets or therapeutic areas of interest to our partners. Our rigorous prioritization, quality control, and data archival processes ensure that we deliver the highest value data in a timely manner.

Example custom target-directed SAR compilation projects that have been completed to date include:

- ⇒ Kinase inhibitors
- ⇒ GPCR antagonists
- ⇒ Protease inhibitors
- ⇒ Radioprotective agents

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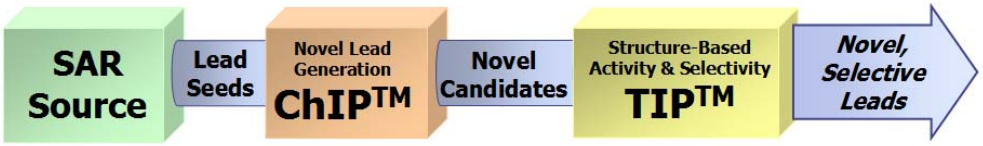
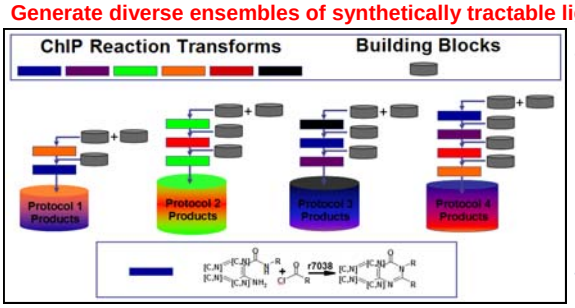
DirectDesign™ Discovery Collaborations, continued

Knowledge-Based Lead Design (*De-"Know"-vo Design) Collaborations*

Eidogen-Sertanty's Knowledge-Based Lead Design service incorporates all of our ligand- and structure-based technologies for the *in silico* design and activity assessment of novel small molecules. Our unique **De-"Know"-vo Design** approach utilizes knowledge from known active molecules to direct the design and prioritization of novel and synthetically accessible molecules that meet predicted activity, selectivity, and patentability criteria.

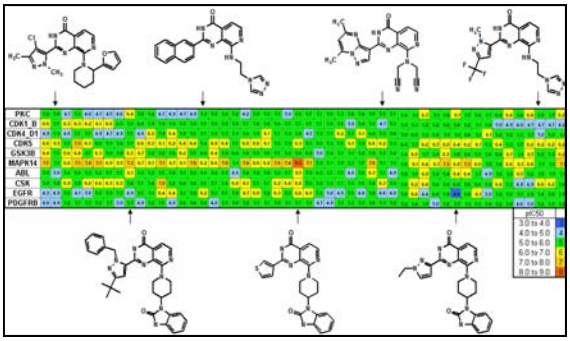


Generate diverse ensembles of synthetically tractable ligands



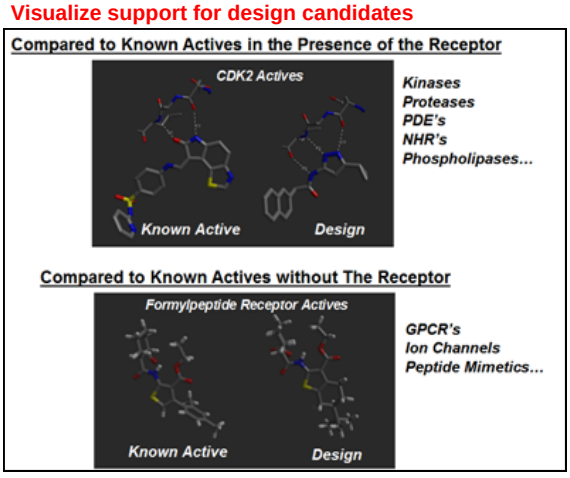
The **Chemical Intelligence Platform (ChIP™)** is the key enabling technology behind our De-"Know"-vo Design platform. ChIP utilizes reaction transformations containing both empirical reactivity and compatibility information to dynamically assemble plausible reaction sequences supported by commercially available chemical building blocks. The result is a diverse ensemble of synthetically tractable small molecules.

Prioritize designs based on predicted activity and selectivity



The novel compositions of matter generated by ChIP are then filtered and prioritized using highly flexible, researcher-defined selection functions. Common selection functions include 3D-shape and pharmacophoric similarity, QSAR potency/selectivity scores, and binding mode similarity to known active co-crystallized or docked compounds. Directing ChIP simulations via these selection functions facilitates scaffold hopping into novel small molecule space, while at the same time addressing potential selectivity concerns.

Visualize support for design candidates



Our De-Know-vo Design projects are highly collaborative. The flexible and iterative design process enables us to incorporate our clients' specific prioritization criteria into the final designs, such as desirable building blocks or synthetic schemes, undesired chemical functionality, etc.

In addition, we have found that our ability to provide direct visualization of the underlying structure- and/or ligand-based support for any of our design candidates is a very powerful way to engage project team members to engage in the final prioritization and synthesis of the proposed designs.

Finally, we provide optional patentability assessments for any or all of our design candidates as part of every De-Know-vo Design collaboration.

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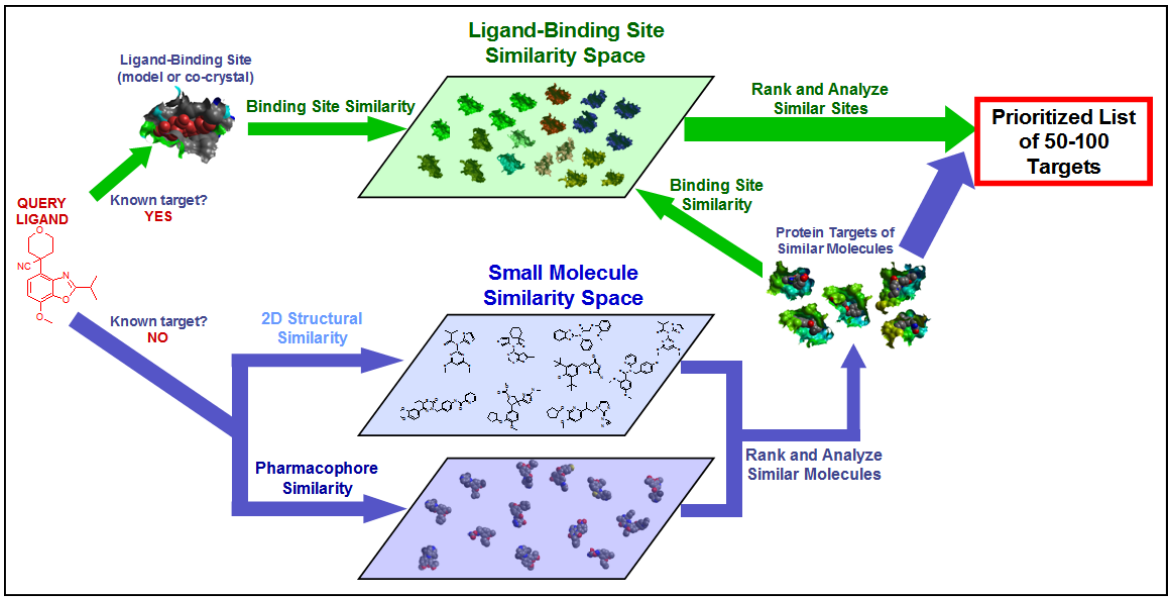
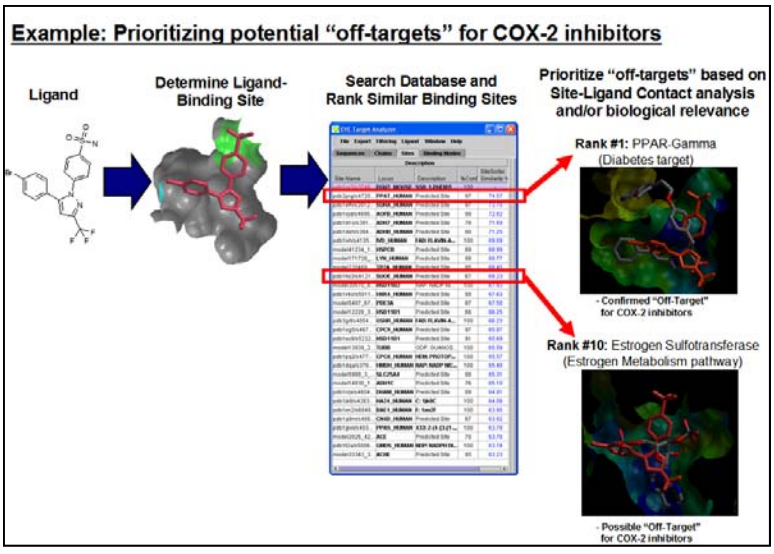
DirectDesign™ Discovery Services, continued

Virtual Target Screening (Target "Fishing") Collaborations

The broad view into both target similarity and 2D/3D ligand similarity provided by Eidogen-Sertanty's suite of discovery informatics tools offers a unique capability to virtually "screen" the entire proteome for potential targets for our client's query ligands. These **Virtual Target Screening —** or Target "Fishing" — collaborations utilize both target-based and ligand-based *in silico* predictions and comparisons to prioritize a set of potential primary and/or secondary targets in the human proteome that are likely to bind a given query ligand, as shown in the figure below.



The Virtual Target Screening approach facilitates the efficient identification of potential **off-target opportunities** (e.g. applying known bio-active compounds to other targets or indications) as well as potential **off-target liabilities** (e.g. identifying potential binding interactions that may lead to undesirable *in vivo* effects). An example of this application is shown here, for the COX-2 inhibitor celecoxib.



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DirectDesign™ Discovery Services, continued

Compound Prioritization Collaborations

Compound prioritization is a strong core competency at Eidogen-Sertanty. We have developed a broad and effective set of computational tools and human resources for compound prioritization and in-licensing. During our compound in-licensing research collaborations, we work closely with our partner to ensure maximum ROI via high compound activity rates and reduced software licensing costs and human resource expenditures.

The broad scope and high integration of our *in-silico* tools makes Eidogen-Sertanty unique among collaboration partners in this area. We are further differentiated from our competitors, because we have implemented a variety of effective approaches to target and scaffold hopping which have only recently been published in the 2004 and 2005 scientific literature.

Depending on the target class and purchasing objectives, we apply our human resources and technologies in order to achieve project goals as efficiently as possible. Coupled with our significant computer hardware resources, compound purchasing guidelines can be delivered within *one month* of project initiation. A sample outline of project steps and timelines is summarized below.

1. SAR Data Compilation

- ⇒ Continuously productive literature and patent curation team
- ⇒ Human Kinome SAR data resource (Kinase Knowledgebase™), and druggable target structure resource (Target Informatics Platform™)

2. Chemical Starting Point Evolution, Proliferation, & Enrichment

- ⇒ Chemical Intelligence Platform (ChIP™) Directed *In Silico* Synthesis[1]
- ⇒ LigandCross™ (using co-crystal structures and docked actives)[2]

3. 2D– and 3D-Ligand based *In Silico* Screening & Clustering

- ⇒ Custom pharmacophore modeling and screening[3]
- ⇒ Custom QSAR modeling and screening

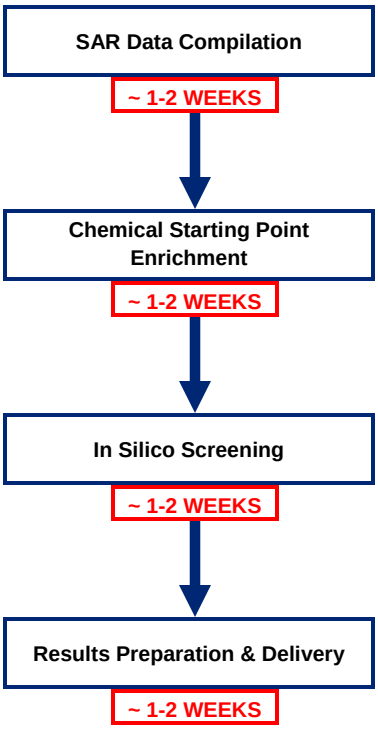
4. 3D-Ligand+Target Receptor-based Screening & Clustering

- ⇒ Knowledge-based docking of known actives
- ⇒ Enhanced enrichments via SLiC™ interaction analysis and clustering[4]

5. Chemical-Biological Data Management

- ⇒ Synthetic strategies and summary biological data archived and explored in ARK™
- ⇒ Simultaneous prioritization of acquisition costs and expected activity

Example Project Workflow



References:
1. Schurer *et al. J. Chem. Inf. Model*. **45** (2), 239-248, 2005.
2. Pierce *et al. J. Med. Chem*. **47** (11), 2768-2775, 2004.
3. McGregor *et al. J. Chem. Inf. Comput. Sci*. **39** (3), 569 -574, 1999.
4. Deng *et al. J. Med. Chem*. **47** (2), 337-344, 2004.