

Sequence search

Cortellis Drug Discovery Intelligence

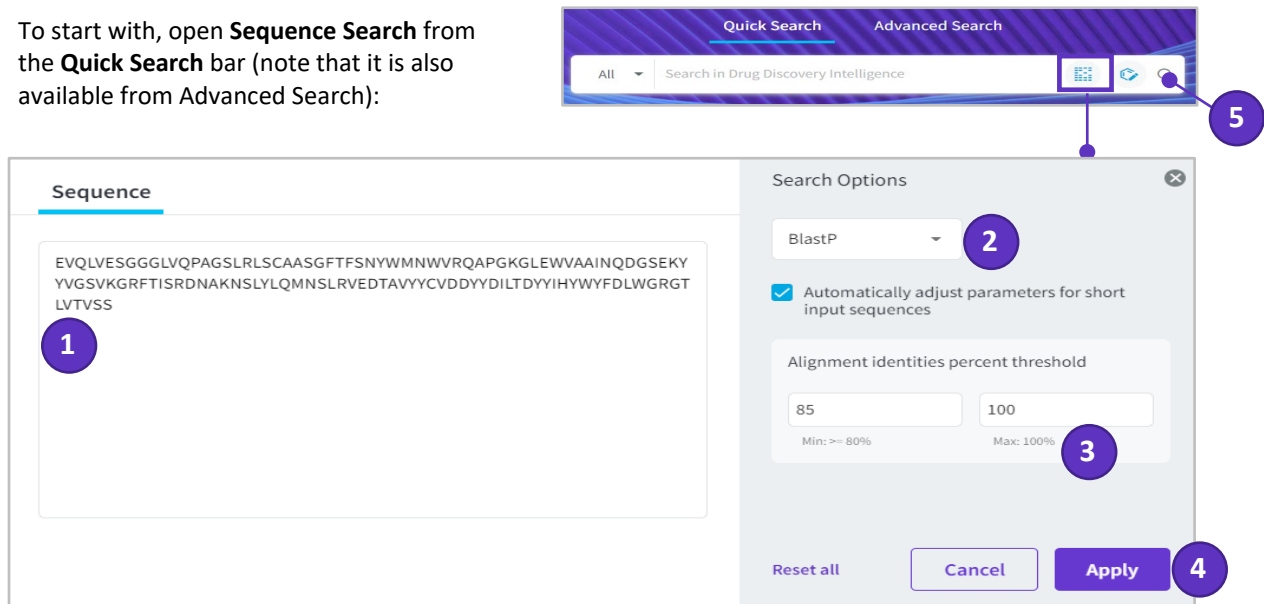
Use sequence search to:

- Find products with similar sequences to yours
- Understand competitive landscape around your sequence
- Benchmark your candidate's activity against those with similar sequences

In this example we've isolated neutralizing antibodies against IL-17 derived from mice immunized with IL17 antigens. We'd like to know if there are other antibodies with a similar sequence, and what Conditions are associated with these antibodies.

1. Find products with similar sequences to yours

To start with, open **Sequence Search** from the **Quick Search** bar (note that it is also available from Advanced Search):



The screenshot shows the 'Sequence Search' interface. At the top, there is a navigation bar with 'Quick Search' and 'Advanced Search' tabs. Below this is a search bar with a dropdown menu set to 'All' and the text 'Search in Drug Discovery Intelligence'. To the right of the search bar are three icons: a grid icon (1), a magnifying glass icon (2), and a search icon (3). Below the search bar is a 'Sequence' window containing a text area with a sequence: 'EVQLVESGGGLVQPAGSLRLSCAASGFTFSNYWMNWRQAPGKGLEWVAAINQDQSEKY YGGSVKGRFTISRDNKNSLYLQMNSLRVEDTAVYYCDDYYDILTDYYIHYYWFDLWGRGT LTVSS'. Below the sequence window is a 'Search Options' panel. It has a dropdown menu set to 'BlastP' (2), a checked checkbox for 'Automatically adjust parameters for short input sequences', and two input fields for 'Alignment identities percent threshold' with values '85' and '100' (3). Below these fields are 'Reset all', 'Cancel', and 'Apply' buttons (4). A fifth callout (5) points to the search icon in the top navigation bar.

1. Paste your sequence into the sequence window
2. Select **BlastP** for amino acid sequences or **BlastN** for nucleotide sequences
3. Set your preferred alignment percentage threshold
4. Click **Apply** to load your sequence into Quick Search
5. Click on the Search icon to run your search.

Note: Searching in **All** areas will retrieve products with similar sequences as well as records in other knowledge areas that are associated with those products.

Go to **Drugs & Biologics** to see your results:

Product List										Development Status			Milestones			Overview		
Entry Number	Highest Phase	Name	Score	% Align	% Query	Length	E-value	Sequence	Product Category	Mechanism of Action	Organization							
SEQ 1111185	Preclinical	AdIL17-sF	614	98.42	100	127	4.05e-82	Variable heavy chain (VH)	<ul style="list-style-type: none"> Antibody Gene Therapy Cancer Immunotherapy Single-Chain V-Domain Antibody Fragment (scFv) 	Anti-IL-17A (Interleukin-17A) Signal Transduction Modulators	East China Normal University (ECNU) (Originator)							
SEQ 418942	Launched - 2015	<ul style="list-style-type: none"> AIN-457 KB-03303A NVP-AIN-457 Secukinumab 	614	98.42	100	127	4.05e-82	Variable heavy chain	<ul style="list-style-type: none"> Human Monoclonal Antibodies Polypeptides, from 41 AA 	Anti-IL-17 (Interleukin-17) Signal Transduction Modulators	<ul style="list-style-type: none"> Maruho Novartis (Originator) 							

Evaluate your results according to:

Score: Numerical value describing the overall quality of the alignment

% Align: The extent to which the sequences have the same residues at the same position in the alignment

% Query: Percentage of the query length that is included in the aligned segments

Length: Length of the target sequence that was matched with the sequence of interest

E-value: Expected number of times that the alignment score would appear randomly

Sequence: Name of the sequence matching the query

Tip: To visualize the sequence alignment, click the **SEQ** button, copy the sequence of interest, and paste it into an alignment analysis tool like [NCBI](#):

Sequence of 1111185

Variable heavy chain (VH) [Copy](#)

```
EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYWMNWRQAPGKGLEWVAAINQDQSEKYYVSVKGRFTISRDNAKNSLYLQMNSLRVEDTAVYYCVRDYYDILTDYYIHYYWF
DLWGRGTLTVSS
```

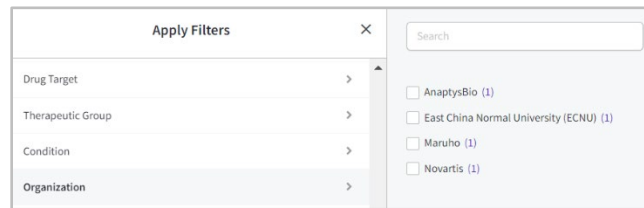
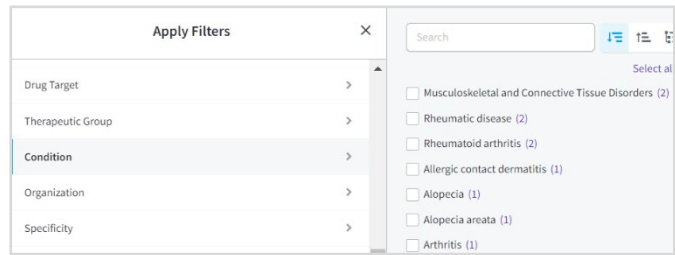
Variable light chain (VL) [Copy](#)

```
EIVLTQSPGTLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSGSGSGTDFLTISRLEPEDFAVYYCQYGGSPCTFGQGTREIKR
```

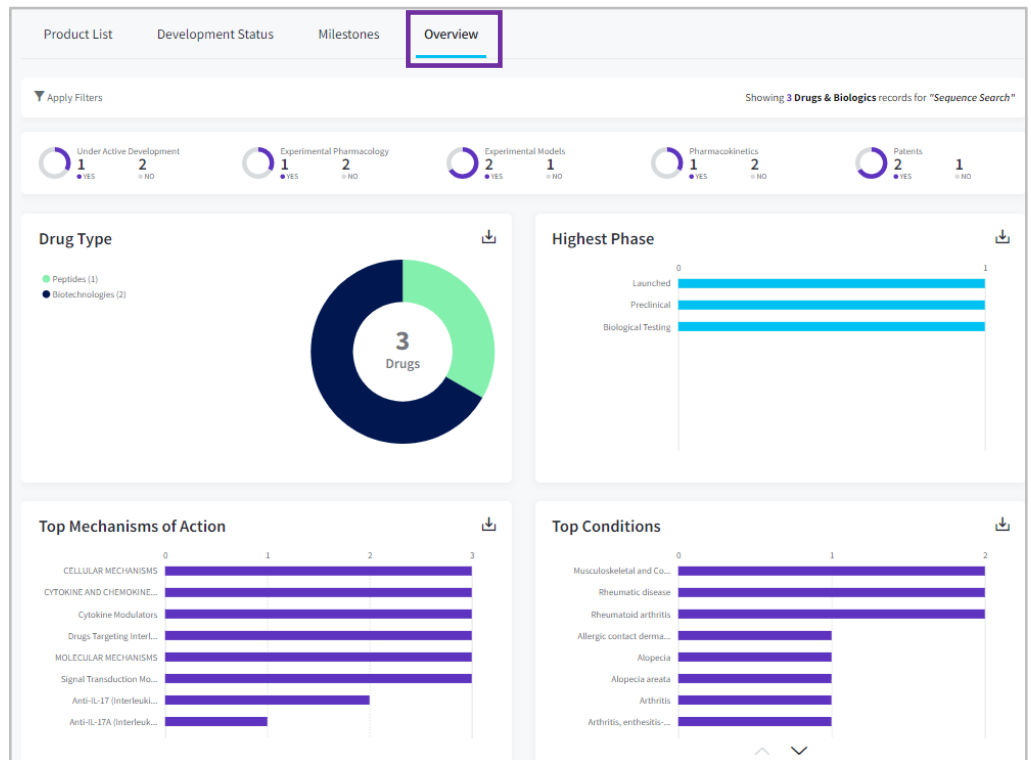
2. Understand the competitive landscape around your sequence.

Now that you have a list of candidates with sequences similar to yours, use **Apply Filters** to analyze them. As an example:

- Understand the *disease-scape* related to your results by selecting the **Conditions** filter
- Identify potential competitors and collaborators by selecting the **Organizations** filter



You may also use the **Overview** tab to visualize the distribution of your results among drug type, highest phase, mechanisms of action, conditions, organizations and regions of development.



3. Benchmark your candidate's activity against those with similar sequences

To do this, use the **Related Content** button on the top right of the page, navigate to the associated experimental pharmacology data and use the mean/median workflow to obtain the activity benchmark

Drug Name	Experimental Activity	Pharmacological Activity	Material/Experimental Model	Method	Parameter	Value	Source
Secukinumab	Interleukin 17 (IL-17) (nonspecified subtype) affinity, IN VITRO	Interleukin-17 affinity	Cynomolgus monkey protein		Kd	6 ± 0.7 nM	WO 2006013107 (2006)
Secukinumab	Interleukin 17 (IL-17) (nonspecified subtype) affinity, IN VITRO	Interleukin-17 affinity	Rhesus monkey protein		Kd	9 ± 1 nM	WO 2006013107 (2006)
Secukinumab	Interleukin 17 (IL-17) (nonspecified subtype) affinity, IN VITRO	Interleukin-17 affinity	Marmoset protein		Kd	1.2 ± 0.1 nM	WO 2006013107 (2006)
Secukinumab	Interleukin 17 (IL-17) (nonspecified subtype) affinity, IN VITRO	Interleukin-17 affinity	Human protein		Kd	227 ± 30 pM	WO 2006013107 (2006)

Hypothesize or validate potential targets for this set of candidates by clicking on the **Pharmacological activity** filter:

Apply Filters

- Experimental Activity
- Pharmacological Activity**
- Target
- Condition
- Toxicity
- Activity/Effect
- System
- Parameter
- Material
- Method

Pharmacological Activity Filter Results:

- Interleukin-17A affinity (11)
- Interleukin-17 affinity (4)
- Interleukin-17A production, inhibition (3)
- Interleukin-6 production (interleukin-17A-induced), inhibition (3)
- Chemokine (C-X-C motif) ligand 1 [CXCL1, KC] production (interleukin-17A/F-induced), inhibition (2)
- Chemokine (C-X-C motif) ligand 1 [CXCL1, KC] production, inhibition (2)
- Interleukin-17A/tumor necrosis factor-alpha production, inhibition (2)
- Interleukin-6 production, inhibition (2)
- Interleukin-8 production, inhibition (2)
- Monocyte chemoattractant protein-1 production, inhibition (2)
- Chemokine (C-X-C motif) ligand 1 [CXCL1, KC] production (interleukin-17-induced), inhibition (1)

For more information contact Customer Service at **LS Product Support**