

Supplementary File 2

AmyCo: the Amyloidoses Collection

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Welcome to AmyCo, a freely available, literature-curated collection of amyloidoses and other pathological conditions associated with the deposition of amyloid fibrils.

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Home

In order to visit AmyCo*, the user should enter the following address: <http://bioinformatics.biol.uoa.gr/AmyCo/>. The page contains a short description of the repository and the AmyCo statistics.

The screenshot shows the AmyCo website interface. At the top is a navigation bar with links: AmyCo, Search, Browse, Blast Search, Manual, Download, and Contact. Below this is a 'Description' section with text about amyloid fibrils and the collection. A 'Statistics' table is displayed, showing 74 diseases and 83 amyloidogenic proteins. A 'Reference' section lists a paper by Nastou et al. (2018). The footer includes the logo of the National and Kapodistrian University of Athens, the Department of Biology, and the Biophysics & Bioinformatics Laboratory.

AmyCo

The Amyloidoses Collection

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Description

Amyloid fibrils are formed when soluble proteins misfold into highly ordered insoluble fibrillar aggregates which affect various organs and tissues. **Tissue deposition of amyloid fibrils (or amyloid deposition) is the main hallmark of a group of disorders called "amyloidoses"**. Curiously, fibril deposition has been also recorded as a complication in a number of other neurodegenerative or endocrine diseases. To date, amyloidoses are roughly classified, owing to their tremendous heterogeneity.

AmyCo, a freely available collection of amyloidoses and other clinical disorders related to amyloid deposition, classifies **74** diseases into 2 distinct categories: 1) **Amyloidosis** and 2) **Clinical conditions associated with amyloidosis**.

Each database entry is annotated with the major components (causative proteins), other components of amyloid deposits and affected tissues or organs. Database entries are also supplemented with detailed annotation and are linked to **ICD-10**, **MeSH**, **OMIM**, **PubMed**, **AmyPro** and **UniProtKB** databases.


AmyCo is the largest repository containing information about amyloidoses and diseases related to amyloid deposition. It is hoped that it will aid clinical scientists and researchers, in need of a comprehensive resource, referencing biological information on amyloidoses.

Statistics

Total Number of Diseases:	74
Total Number of Amyloidogenic Proteins:	83
Database Version:	v1.1
Release Date:	2-Nov-2018

Reference

Nastou, K.C., Nasi, G.I., Tsiolaki, P.L., Litou, Z.I., Iconomidou, V.A.
AmyCo: the Amyloidoses Collection
in preparation

 National and Kapodistrian University of Athens
Department of Biology
Biophysics & Bioinformatics Laboratory

* Logo background: A photomicrograph of Congo Red stained IAPP, taken in polarized light by Dr. P.L.Tsiolaki.



Search

The search tab allows the navigation of the database. A form with multiple options appears.

A screenshot of the AmyCo website's search interface. At the top, a dark blue navigation bar contains the following links: 'AmyCo', 'Search', 'Browse', 'Blast Search', 'Manual', 'Download', and 'Contact'. Below this, a white search box is titled 'Search'. Inside the search box, there are several input fields and options: a 'Disease' field with the placeholder 'Disease Name or Alternative Disease Name (e.g. Alzheimer disease)'; a 'Protein' field with the placeholder 'Protein Name or Alternative Protein Name (e.g. Tau)'; a 'Type' section with two radio buttons: 'Amyloidosis' (selected) and 'Clinical conditions associated with amyloidosis'; a 'Gene' field with the placeholder 'Gene Name (e.g. APP)'; and a 'Protein Accession' field with the placeholder 'UniProt AC or UniProt ID (e.g. P05067)'. At the bottom of the search box, there is a radio button for 'AND' (selected) and a radio button for 'OR'. A blue 'Submit!' button is located at the bottom center of the search box.

The search options are:

- by Disease Name

The user may use a Name or an Alternative Disease Name, including the ISA name when available (e.g. Alzheimer Disease or Alzheimer Syndrome)

- by a Protein Name associated with a disease

Proteins can be either a major (precursor protein) or a minor (co-deposited protein) component.

- by Disease Type

AmyCo Disease entries are classified into two categories: **1) Amyloidosis**, when amyloid deposition is the main disease cause (e.g. AL amyloidosis) or amyloid deposits are present in tissue and organs (e.g. Alzheimer disease), and **2) Clinical conditions associated with amyloidosis**, when amyloidosis is a clinical feature of a disease or a syndrome (e.g. amyloid deposition in Waldenström's macroglobulinemia)

- by Gene Name (e.g. APP)

- by Protein Components based on a UniProt Accession or a UniProt Identifier (e.g. P05067, ***Two human UniProt ACs (P0DOX7, P0DOX8) corresponding to amyloidogenic light chains and four human UniProt ACs (P0DOX2, P0DOX4, P0DOX5, P0DOX6) corresponding to amyloidogenic heavy chains, available in AmyCo, are universal protein representatives annotated by the UniProtKB database in March 15th 2017***)



The search, based on disease name, protein name and gene name does not require specific words. For example a user enters the word “apo” in the **disease search field**.

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Search

Disease

Protein

Type
 Amyloidosis
 Clinical conditions associated with amyloidosis

Gene

Protein Accession

Combine searches with: AND OR

Submit!

The result is all diseases containing the word “apo” in the **disease search field**.

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Results

Show 10 entries Search:

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	Associated Proteins	
17	Apolipoprotein A-I associated Amyloidosis	Amyloidosis	Amyloidosis	Heart, Liver, Skin, Kidney, Intestine, Larynx, Uterus, Ovary Lymph Node, Pelvic Lymph Node	Alpha-1-antitrypsin; Apolipoprotein A-I; Serum amyloid P-component; Transthyretin; Serum albumin; Zinc-alpha-2-glycoprotein; Actin, cytoplasmic 1; Elongation factor 1-alpha 1; Hemoglobin subunit beta; Hemoglobin subunit alpha; Dermcidin; Extracellular glycoprotein lacritin	Show
22	Apolipoprotein A-II associated Amyloidosis	Amyloidosis	Amyloidosis	Kidney	Apolipoprotein E; Apolipoprotein A-II; Serum amyloid P-component; Apolipoprotein A-IV; Actin, cytoplasmic 1	Show
25	Apolipoprotein C-II associated Amyloidosis	Amyloidosis	Amyloidosis	Kidney	Apolipoprotein E; Apolipoprotein C-II; Serum amyloid P-component; Apolipoprotein A-IV	Show
26	Apolipoprotein C-III associated Amyloidosis	Amyloidosis	Amyloidosis	Kidney, Spleen, Salivary Gland, Intestine, Heart	Apolipoprotein A-I; Apolipoprotein E; Apolipoprotein C-III; Serum amyloid P-component; Apolipoprotein A-IV	Show
28	Apolipoprotein A-IV associated Amyloidosis	Amyloidosis	Amyloidosis	Kidney, Heart, Intestine, Lung, Skin	Apolipoprotein E; Serum amyloid P-component; Apolipoprotein A-IV	Show
ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	Associated Proteins	

Showing 1 to 5 of 5 entries Previous 1 Next



All searches can be combined with logical operators (AND/OR), in order to make the search result as specific as possible.

For example if we proceed to the following combined search:

AmyCo Search Browse Blast Search Manual Download Contact

Search

Disease
dementia

Protein
synuclein

Type
 Amyloidosis
 Clinical conditions associated with amyloidosis

Gene
Gene Name (e.g. APP)

Protein Accession
UniProt AC or UniProt ID (e.g. P05067)

Combine searches with: AND OR

Submit!

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We will get only the disease, which is classified as dementia and is associated with synuclein.

AmyCo Search Browse Blast Search Manual Download Contact

Results

Show 10 entries Search: [input]

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	Associated Proteins
34	Lewy Body Disease	Amyloidosis	Diseases of the Nervous System	Central Nervous System (CNS)	Alpha-synuclein Show

Showing 1 to 1 of 1 entries Previous 1 Next



Browse

The **browse tab** allows the browsing of the database. User can apply filters and browse the database by selecting the disease Type or/and the ICD-10 Classification.

AmyCo Search Browse Blast Search Manual Download Contact

Browse Database

You are viewing the entire database. If you want to inspect a specific category of diseases select one from the dropdown menu below

Select based on Disease Type: Amyloidosis Show selected entries

Select based on ICD-10 Classification: Diseases of the Nervous System Show selected entries

Show 10 entries Search:

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	
1	Alzheimer Disease	Amyloidosis	Diseases of the Nervous System	Central Nervous System (CNS)	Show
2	Diabetes Mellitus, Type 2	Amyloidosis	Endocrine, Nutritional and Metabolic Diseases	Pancreas (Islets of Langerhans)	Show
3	Huntington Disease	Amyloidosis	Diseases of the Nervous System	Central Nervous System (CNS)	Show
4	Parkinson Disease	Amyloidosis	Diseases of the Nervous System	Central Nervous System (CNS)	Show
5	Creutzfeldt-Jakob Syndrome	Amyloidosis	Certain Infectious and Parasitic Diseases	Central Nervous System (CNS)	Show
6	Kuru	Amyloidosis	Certain Infectious and Parasitic Diseases	Central Nervous System (CNS)	Show
7	Gerstmann-Strausler-Scheinker Disease	Amyloidosis	Certain Infectious and Parasitic Diseases	Central Nervous System (CNS)	Show
8	Immunoglobulin Light-chain Amyloidosis	Amyloidosis	Amyloidosis	Kidney, Heart, Peripheral Nervous System (PNS), Autonomic Nervous System (ANS), Liver, Gastrointestinal Tract, Lung, Soft Tissues, Urinary Tract, Larynx	Show
9	Hereditary Cerebral Amyloid Angiopathy, Icelandic Type	Amyloidosis	Diseases of the Circulatory System	Central Nervous System (CNS), Skin, Lymph Node, Spleen, Salivary Gland, Seminal Vesicle	Show
10	Dementia, familial British	Amyloidosis	Diseases of the Circulatory System	Central Nervous System (CNS), Pancreas, Heart	Show
ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	

Showing 1 to 10 of 71 entries Previous 1 2 3 4 5 ... 8 Next

At first all entries appear. Each page shows 10 entries by default but this can be altered from the dropdown menu at the top left corner of the table to 25, 50 or all entries. Moreover, users can perform non-specific searches using the search option at the top right corner of the data table.

Show 10 entries Search:

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	
1	Alzheimer Disease	Amyloidosis	Diseases of the Nervous System	Central Nervous System (CNS)	Show

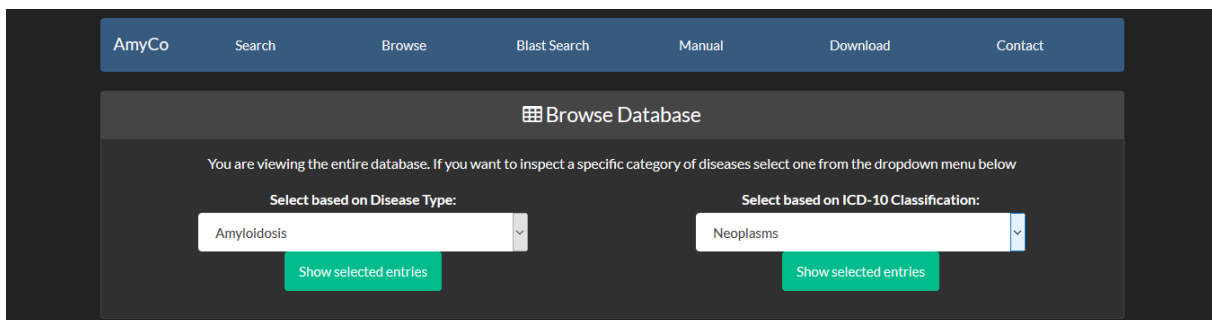


Filters and browsing can be applied according to the classification below.

Disease type and ICD-10 classification

	Disease Type	ICD-10 Classification
1	Amyloidosis	Amyloidosis
		Endocrine, Nutritional and Metabolic Diseases
		Diseases of the Circulatory System
		Diseases of the Nervous System
		Neoplasms
		Certain Infectious and Parasitic Diseases
		Diseases of the Eye and Adnexa
2	Clinical conditions associated with amyloidosis	Endocrine, Nutritional and Metabolic Diseases
		Diseases of the Respiratory System
		Chromosomal Abnormalities
		Diseases of the Musculoskeletal System and Connective Tissue
		Neoplasms
		Diseases of the Skin and Subcutaneous Tissue
		Diseases of the Digestive System
		Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
Other		

For example, if the user selects **Amyloidosis** as the disease type and **Neoplasms** as the ICD-10 classification and presses *Show Selected Entries*.



The selected diseases are:

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	
15	Prolactinoma	Amyloidosis	Neoplasms	Pituitary Gland	Show
21	Thyroid Cancer, Medullary	Amyloidosis	Neoplasms	C-cell thyroid tumors	Show
35	Calcifying Epithelial Odontogenic Tumor	Amyloidosis	Neoplasms	Mandible, Maxilla, Gingiva	Show

Showing 1 to 3 of 3 entries

Previous 1 Next

Through browsing the database or after a search is submitted, a list of diseases appears, as the shown above. The list contains the Disease Name, the ICD-10 Classification, the disease type and the tissue(s), in which deposits are located. When the user presses the Show button they are redirected to the Entry page of a Disease.



Disease Entry

The Entry page contains information about the disease. CytoscapeJS is integrated to visualize the relationship between the disease and proteins found on amyloid deposits.

AmyCo
The Amyloidoses Collection

Search
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Blast Search
Manual
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Basic Information

Disease Name:	Alzheimer Disease												
ISA Name:	Aβ Amyloidosis												
Alternative Names:	<ul style="list-style-type: none"> • Acute Confusional Senile Dementia • Alzheimer Dementia • Alzheimer Disease, Early Onset • Alzheimer Disease, Late Onset • Alzheimer Sclerosis • Alzheimer Syndrome • Alzheimer Type Senile Dementia • Alzheimer's Disease • Alzheimer's Disease, Focal Onset • Alzheimer-Type Dementia (ATD) • Dementia, Alzheimer Type • Dementia, Presenile • Dementia, Primary Senile Degenerative • Dementia, Senile • Early Onset Alzheimer Disease • Familial Alzheimer Disease (FAD) • Focal Onset Alzheimer's Disease • Late Onset Alzheimer Disease • Presenile Alzheimer Dementia • Primary Senile Degenerative Dementia • Senile Dementia, Acute Confusional • Senile Dementia, Alzheimer Type • Presenile and Senile Dementia 												
MeSH Description:	A degenerative disease of the brain characterized by the insidious onset of dementia. Impairment of memory, judgment, attention span, and problem solving skills are followed by severe apraxias and a global loss of cognitive abilities. The condition primarily occurs after age 60, and is marked pathologically by severe cortical atrophy and the triad of senile plaques; neurofibrillary tangles; and neuropil threads.												
Type:	Amyloidosis												
ICD-10 Classification:	Diseases of the Nervous System												
Tissue:	Central Nervous System (CNS)												
Precursor Proteins:	P05067: Amyloid-beta A4 protein												
Co-deposited Proteins:	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td>P01011: Alpha-1-antichymotrypsin</td> <td>P01034: Cystatin-C</td> </tr> <tr> <td>P02649: Apolipoprotein E</td> <td>P02743: Serum amyloid P-component</td> </tr> <tr> <td>P07339: Cathepsin D</td> <td>P07858: Cathepsin B</td> </tr> <tr> <td>P10909: Clusterin</td> <td>P98160: Basement membrane-specific, heparan sulfate proteoglycan core protein</td> </tr> <tr> <td>P10636: Tau</td> <td>P01023: Alpha-2-macroglobulin</td> </tr> <tr> <td>P05231: Interleukin-6</td> <td></td> </tr> </table>	P01011: Alpha-1-antichymotrypsin	P01034: Cystatin-C	P02649: Apolipoprotein E	P02743: Serum amyloid P-component	P07339: Cathepsin D	P07858: Cathepsin B	P10909: Clusterin	P98160: Basement membrane-specific, heparan sulfate proteoglycan core protein	P10636: Tau	P01023: Alpha-2-macroglobulin	P05231: Interleukin-6	
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P05231: Interleukin-6													

Interaction Network

Right click on Protein Nodes to go to UniProt.
Red Colored Edges Indicate a connection between the disease and a precursor protein, while Blue Colored Edges indicate a connection with co-deposited proteins

Cross-References

MeSH:	D000544
ICD:	G30
OMIM:	104300
PubMed:	8713166 6375662 3159021 17065112

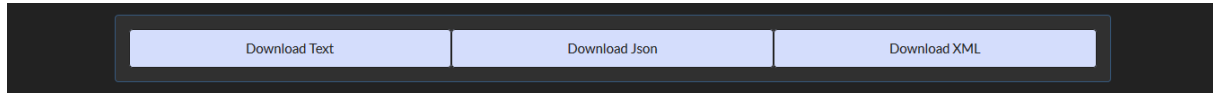
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At the top of the page the user can find three buttons; *Download Text*, *Download Json* and *Download XML*. By pressing these buttons the user can download all page information in text, Json or XML format respectively.



The basic disease information available is:

- ✓ Disease Name (MeSH name, when the disease is a MeSH entry)
- ✓ ISA Name (International Society of Amyloidosis name, when available)
- ✓ Alternative Names
- ✓ Disease Description (a short description from MeSH)
- ✓ Disease Type (see [here](#))
- ✓ Disease Association (from ICD-10, when available)
- ✓ Tissue(s) where amyloid deposits are located (Tissues corresponding to “Clinical conditions associated with amyloidosis” were manually collected from the scientific literature)
- ✓ Precursor Proteins of Amyloid Deposits
- ✓ Co-deposited Protein of Amyloid Deposits

Basic Information													
Disease Name:	Alzheimer Disease												
ISA Name:	AB Amyloidosis												
Alternative Names:	<ul style="list-style-type: none"> • Acute Confusional Senile Dementia • Alzheimer Dementia • Alzheimer Disease, Early Onset • Alzheimer Disease, Late Onset • Alzheimer Sclerosis • Alzheimer Syndrome • Alzheimer Type Senile Dementia • Alzheimer's Disease • Alzheimer's Disease, Focal Onset • Alzheimer-Type Dementia (ATD) • Dementia, Alzheimer Type • Dementia, Presenile • Dementia, Primary Senile Degenerative • Dementia, Senile • Early Onset Alzheimer Disease • Familial Alzheimer Disease (FAD) • Focal Onset Alzheimer's Disease • Late Onset Alzheimer Disease • Presenile Alzheimer Dementia • Primary Senile Degenerative Dementia • Senile Dementia, Acute Confusional • Senile Dementia, Alzheimer Type • Presenile and Senile Dementia 												
MeSH Description:	A degenerative disease of the brain characterized by the insidious onset of dementia. Impairment of memory, judgment, attention span, and problem solving skills are followed by severe apraxias and a global loss of cognitive abilities. The condition primarily occurs after age 60, and is marked pathologically by severe cortical atrophy and the triad of senile plaques; neurofibrillary tangles; and neurofibrillary threads.												
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The panel at the bottom of the page contains references to other databases. The databases are:

- MeSH
- ICD
- OMIM
- PubMed

Cross-References	
MeSH:	D000544
ICD:	G30
OMIM:	104300
PubMed:	20061647

When the user presses on the buttons of precursor or co-deposited components a new page opens with information about the proteins.

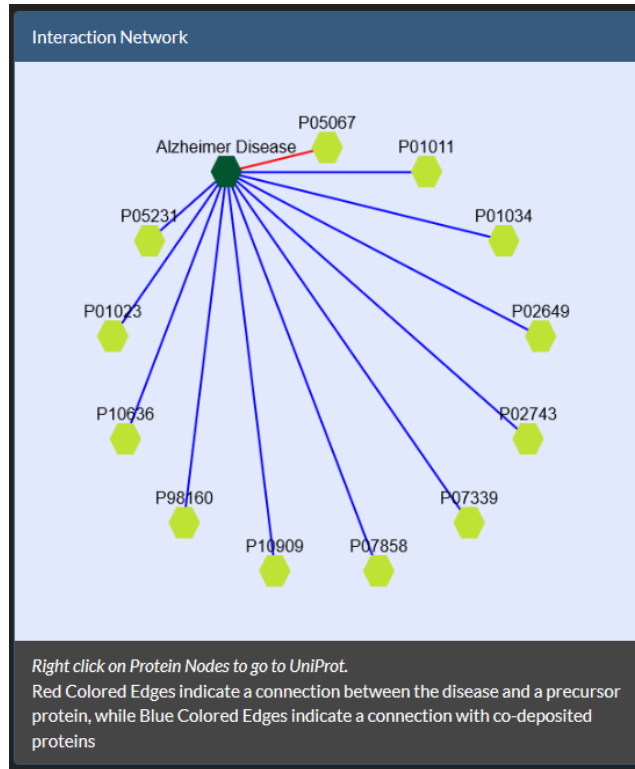
- Primary Name
- Gene Name
- Other Protein Names
- Protein Sequence
- Protein Length
- Uniprot AC
- Uniprot ID

For precursor proteins an external link to AmyPro is given when available. For co-deposited proteins the peer reviewed publication (*Association Source*) of disease is also provided.

Protein Information	
Primary Name:	Cystatin-C
Gene Name:	CST3
Association Source:	11202179
Protein Names:	Cystatin-C (Cystatin-3) (Gamma-trace) (Neuroendocrine basic polypeptide) (Post-gamma-globulin)
Protein Length:	146
Protein Sequence:	MAGPLRAPLLLLLAILAVALAVSPAAGSSPGKPPRLVGGPMDASVEEIEGVRRALDFAVGEYNKASNDMYHSRALQVVRARKQIVAGVNYFLDVELGRITCTKTQPNLDNCPFDQPHLKRKAFCSFQIVAVPWQGTMTLSKSTCQDA
UniProt AC:	P01034



A CytoscapeJS viewer is integrated in the page for the visualization of bipartite graphs, showing the association between **each disease with precursor and co-deposited proteins**.



The diseases are colored green and the protein components yellow. Red Colored Edges indicate a connection between the disease and a Precursor Protein, while Blue Colored Edges indicate a connection with Co-deposited Proteins. Each protein node is also a hyperlink to UniProt.

If your browser prevents you from opening pop-up windows, please select *Allow pop-ups for this site*.



If during scrolling through the page you accidentally lose the network view, please reload the page to see it again.



BLAST Search

With the BLAST search tool, the user may submit a sequence and search the database for homologous protein molecules.

The input for the BLAST application is a sequence in the standard FASTA format.

```
>sp | P01034 | 27-146
SSPGKPPRLVGGPMDASVEEEGVRR
```

The result page of the BLAST search shows a list of the Blast hits with significant alignment on the query sequence. The list is in a table format including the target protein, the Length of the target sequence and the Query and finally, Target align range.

Blast Search Results											
Align with	Hit Number	Length	Score	E-value	Query Align Range	Hit Align Range	Identities	Positives	Gaps	Align Length	Show/Hide Alignment
P10997 IAPP_HUMAN	1	89	460	5.07544e-64	1-89	1-89	89	89	0	89	Show/Hide
P06881 CALCA_HUMAN	2	128	107	5.27101e-10	19-73	60-122	27	34	16	67	Show/Hide

The BLAST results can be compared through the Score, the E-value, the Identities and Positives.

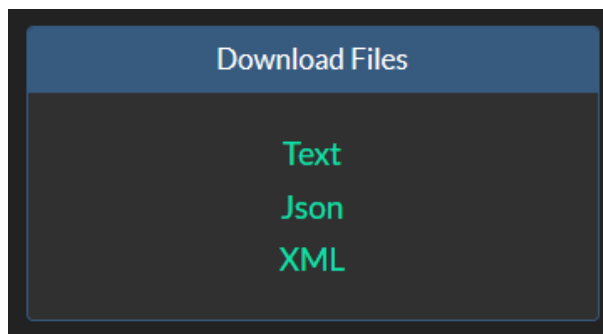


Furthermore, the user can have a more detailed view of each alignment through the Show button at the end of each line:

Align with	Hit Number	Length	Score	E-value	Query Align Range	Hit Align Range	Identities	Positives	Gaps	Align Length	Show/Hide Alignment
P06881 CALCA_HUMAN	2	128	107	5.27101e-10	19-73	60-122	27	34	16	67	Show/Hide
<pre> hsp_qseq: 19 HLKATPIESHQ-----VEKRFKONTATCATQRLANFLVHSS---NNFGAILLSSTNVG 79 hsp_hseq: 60 QMKASELEBQEQEREGSRIIAQKFRACDTATCVTHRLAGLLSRSGGVVKNNF---VPTNVG 120 hsp_midl: +KA+ +E Q +KR C+TATC T RLA L S NNF TNVG hsp_qseq: 79 SNTYGRR 85 hsp_hseq: 120 SKAFGRR 126 hsp_midl: S +G+R </pre>											

Download

User can download all database files in Text, JSON or XML format.



Contact

Users can contact us for more information at the emails specified at the contact page.

Contact:	
<i>Scientific questions:</i>	veconom[at]biol.uoa.gr
<i>Database administration:</i>	katnastou[at]biol.uoa.gr
<i>Data submission:</i>	gnasi[at]biol.uoa.gr



Users are encouraged to submit data by using the form below. Data will be reviewed and later will be added to the database by the authors.

Submit Data:

Send an email regarding the annotation of data in the database

Your Name

Your Email Address

Your Message

Send e-mail

Related publications to the current work are also presented.

Database Technologies

AmyCo is based on modern technologies. User should have Javascript enabled on the web browser.



AmyCo follows the General Data Protection Regulation ([EU 2016/679](#) ("GDPR")) regulation. See the [Privacy](#) page for more information.



References

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