

Supplementary Information

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.

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Description

Amyloid fibrils are formed when soluble proteins misfold into highly ordered insoluble fibrillar aggregates and affect various organs and tissues. The deposition of amyloid fibrils 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 63 diseases associated with amyloid deposition into 3 distinct categories: 1)amyloidosis, 2)clinical conditions related to amyloid deposition and 3)clinical conditions associated with amyloidosis.

Each database entry is annotated with 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:	63
Total Number of Amyloidogenic Proteins:	145

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



Search

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

The screenshot shows the AmyCo Search interface. At the top, there is a navigation bar with links: AmyCo, Search, Browse, Blast Search, Manual, Download, and Contact. Below this, the 'Search' tab is selected. The search form includes the following fields and options:

- Disease:** A text input field with the placeholder 'Disease Name or Alternative Disease Name (e.g. Alzheimer disease)'.
- Protein:** A text input field with the placeholder 'Protein Name or Alternative Protein Name (e.g. Tau)'.
- Type:** Three checkboxes:
 - ☐ Amyloidosis
 - ☐ Clinical conditions related to amyloid deposition
 - ☐ Clinical conditions associated with amyloidosis
- Gene:** A text input field with the placeholder 'Gene Name (e.g. APP)'.
- Protein Accession:** A text input field with the placeholder 'UniProt.AC or UniProt.ID (e.g. P05067)'.
- Combine searches with:** Radio buttons for AND and OR.
- Submit!** A blue button at the bottom.

The search options are:

- by Disease Name

The user may use a Name or an Alternative Disease Name (e.g. Alzheimer Disease or Alzheimer Syndrome)

- by a Protein Name associated with a disease

Proteins can be either a major or a minor (other) component.

- by Disease Type

AmyCo Disease entries are classified in three categories: **1) Amyloidosis**, when amyloid deposition is the main disease cause (e.g. AL amyloidosis), **2) Clinical conditions related to amyloid deposition**, when amyloid deposition is not the main disease cause, but amyloid deposits are present in tissues and organs, (e.g. Alzheimer disease) and **3) 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)



The search, based on disease name, protein name and gene name does not require specific keywords.

For example a user enters the word “apo” in the **disease search field**.

The screenshot shows the AmyCo search interface. At the top is a navigation bar with links: AmyCo, Search, Browse, Blast Search, Manual, Download, and Contact. Below this is a 'Search' section with the following fields:

- Disease:** A text input field containing the text 'apo'.
- Protein:** A text input field with placeholder text 'Protein Name or Alternative Protein Name (e.g. Tau)'.
- Type:** Three radio button options:
 - ☐ Amyloidosis
 - ☐ Clinical conditions related to amyloid deposition
 - ☐ Clinical conditions associated with amyloidosis
- Gene:** A text input field with placeholder text 'Gene Name (e.g. APP)'.
- Protein Accession:** A text input field with placeholder text 'UniProt AC or UniProt ID (e.g. P05067)'.
- Combine searches with:** Two radio button options: ☐ AND and ☒ OR.
- Submit!** A blue button at the bottom right of the search form.

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

The screenshot shows the search results page. At the top is a 'Results' header. Below it is a 'Show 10 entries' link and a 'Search:' input field. The main content is a table with 5 entries. Each entry has a 'Show' button to the right. The table has the following columns:

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	Associated Proteins	Show
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

At the bottom of the table, there is a 'Showing 1 to 5 of 5 entries' label and a pagination bar with 'Previous', '1', and 'Next' links.



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:

The screenshot shows the AmyCo Search interface. The search criteria are as follows:

- Disease:** dementia
- Protein:** synuclein
- Type:**
 - ☐ Amyloidosis
 - ☐ Clinical conditions related to amyloid deposition
 - ☐ 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

A blue **Submit!** button is located at the bottom right of the search form.

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

The screenshot shows the AmyCo Results page. The search criteria are: **Search:** [empty]. The results table is as follows:

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	Associated Proteins	
34	Lewy Body Disease	Clinical conditions related to amyloid deposition	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 the ICD-10 Classification for the categories 2 (clinical conditions related to amyloid deposition) and 3 (amyloidosis occurrence).

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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:
Clinical conditions related to amyloid deposition
Show selected entries

Select based on ICD-10 Classification:
Endocrine, Nutritional and Meta
Show selected entries

Show 10 entries
Search:

ID	Disease Name	Disease Type	ICD-10 Classification	Tissue	
1	Alzheimer Disease	Clinical conditions related to amyloid deposition	Diseases of the Nervous System	Central Nervous System (CNS)	Show
2	Diabetes Mellitus, Type 2	Clinical conditions related to amyloid deposition	Endocrine, Nutritional and Metabolic Diseases	Pancreas (Islets of Langerhans)	Show
3	Huntington Disease	Clinical conditions related to amyloid deposition	Diseases of the Nervous System	Central Nervous System (CNS)	Show
4	Parkinson Disease	Clinical conditions related to amyloid deposition	Diseases of the Nervous System	Central Nervous System (CNS)	Show
5	Creutzfeldt-Jakob Syndrome	Clinical conditions related to amyloid deposition	Certain Infectious and Parasitic Diseases	Central Nervous System (CNS)	Show
6	Kuru	Clinical conditions related to amyloid deposition	Certain Infectious and Parasitic Diseases	Central Nervous System (CNS)	Show
7	Gerstmann-Strausler-Scheinker Disease	Clinical conditions related to amyloid deposition	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	Clinical conditions related to amyloid deposition	Diseases of the Circulatory System	Central Nervous System (CNS), Skin, Lymph Node, Spleen, Salivary Gland, Seminal Vesicle	Show
10	Dementia, familial British	Clinical conditions related to amyloid deposition	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 63 entries
Previous
1
2
3
4
5
6
7
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	Clinical conditions related to amyloid deposition	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	-
2	Clinical conditions related to amyloid deposition	Endocrine, Nutritional and Metabolic Diseases
		Diseases of the Circulatory System
		Chromosomal Abnormalities
		Diseases of the Nervous System
		Neoplasms
		Certain Infectious and Parasitic Diseases
		Diseases of the Eye and Adnexa
3	Clinical conditions associated with amyloidosis	Endocrine, Nutritional and Metabolic Diseases
		Diseases of the Respiratory System
		Diseases of the Musculoskeletal System and Connective Tissue
		Neoplasms
		Diseases of the Skin and Subcutaneous Tissue
		Diseases of the Digestive System
		Disease of the blood and blood-forming organs and certain disorders involving the immune mechanism
		Other

For example if the user selects **Clinical conditions related to amyloid deposition** as the disease type and **Neoplasms** as the ICD-10 classification

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:

Clinical conditions related to amyloid deposition
Amyloidosis
Clinical conditions related to amyloid deposition
Clinical conditions associated with amyloidosis

Select based on ICD-10 Classification:

Neoplasms

Show selected entries

The selected diseases are :

Results

Show 10 entries

Search:

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

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. 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.

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Basic Information

Disease Name:	Alzheimer Disease	
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:	Clinical condition related to amyloid deposition	
ICD-10 Classification	Diseases of the Nervous System	
Tissue:	Central Nervous System (CNS)	
Major Components:	<div>P05067: Amyloid-beta A4 protein</div>	
Other Components:	<div> <div>P01011: Alpha-1-antichymotrypsin</div> <div>P01034: Cystatin-C</div> <div>P02649: Apolipoprotein E</div> <div>P02743: Serum amyloid P-component</div> <div>P07339: Cathepsin D</div> <div>P07858: Cathepsin B</div> <div>P10909: Clusterin</div> <div>P98160: Basement membrane-specific heparan sulfate proteoglycan core protein</div> <div>P10636: Tau</div> </div>	
Additional Information:	<div>Show</div>	

Interaction Network

Right click on Protein Nodes to go to UniProt.
Red Colored Edges Indicate a connection between the disease and a Major Component, while Blue Colored Edges indicate a connection with Other Components

Cross-References

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



In 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)
- ✓ 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
- ✓ Major Components of Amyloid Deposits
- ✓ Other Components of Amyloid Deposits

Basic Information	
Disease Name:	Alzheimer Disease
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:	Clinical condition related to amyloid deposition
ICD-10 Classification	Diseases of the Nervous System
Tissue:	Central Nervous System (CNS)
Major Components:	P05067: Amyloid-beta A4 protein
Other Components:	<div>P01011: Alpha-1-antichymotrypsin</div> <div>P01034: Cystatin-C</div> <div>P02649: Apolipoprotein E</div> <div>P02743: Serum amyloid P-component</div> <div>P07339: Cathepsin D</div> <div>P07858: Cathepsin B</div> <div>P10909: Clusterin</div> <div>P98160: Basement membrane-specific heparan sulfate proteoglycan core protein</div> <div>P10636: Tau</div>
Additional Information:	Show



Additional information about *alternative names* or any other *comments* regarding a specific disease can be found when a user presses the green show button

Additional Information	
Alternative Names:	<ul style="list-style-type: none"> • Cerebral Amyloid Angiopathy, Ibm2b-Related, 1 • Cerebral amyloid angiopathy, British type • Presenile dementia with spastic ataxia • Familial dementia, British type • Dementia Familial British • Bri Amyloidosis • Familial British Dementia (FBD) • ABri amyloidosis
Comment:	Familial British Dementia is an autosomal dominant form of cerebral amyloid angyopathy (CAA). The disease is typified by progressive dementia, spastic tetraparesis and cerebral ataxia(PMID:11193180). Neuropathologically is characterised by amyloid deposition and tau aggregation(PMID: 10391242;10781099;11159188). Affected individuals develop symptoms in the fourth to fifth decade of life (PMID:11193180)

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 major or other components a new page opens with information about the proteins.

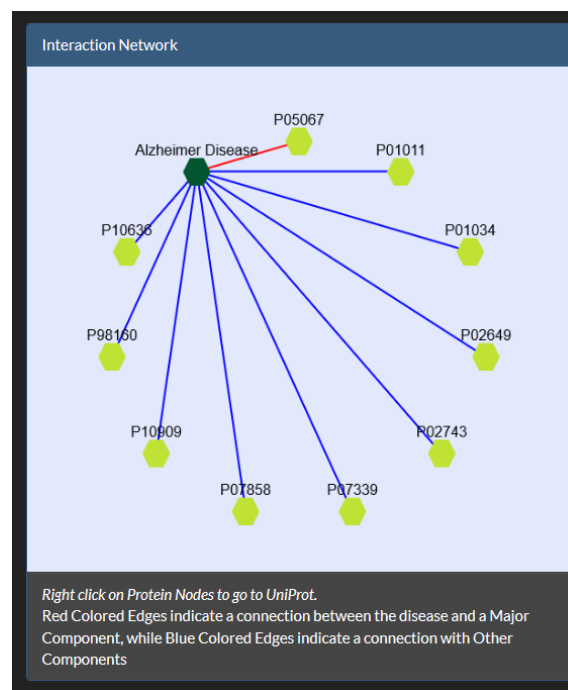
- Primary Name
- Gene Name
- Other Protein Names
- Protein Sequence
- Protein Length
- Uniprot AC
- Uniprot ID



For major components an external link to AmyPro is given when available. For other components the peer reviewed publication (*Association Source*) of disease is also provided.

Protein Information	
Primary Name:	Cystatin-C
Gene Name:	CST3
Association Source:	11202172
Protein Names:	Cystatin-C (Cystatin-3) (Gamma-trace) (Neuroendocrine basic polypeptide) (Post-gamma-globulin)
Protein Length:	146
Protein Sequence:	MAGPLRAPLLLLAILAVALAVSPAAGSSPGKPPRLVGGPMDASVEEGVRRALDFAVGEYNKASNDMYHSRALQVVRARKQIVAGVNYFLDVELGRTTCTKTQPNLDNCPFDQPHLKRKAFCSFQIYAVPWQGTMTLSKSTCQDA
UniProt AC:	P01034

A CytoscapeJS viewer is integrated in the page for the visualization of bipartite graphs, showing the association between **each disease** with **major and other protein components**.



The diseases are colored green and the protein components yellow. Red Colored Edges indicate a connection between the disease and a Major Component. Blue Colored Edges indicate a connection with Other Protein Components. Each protein node is also a hyperlink to UniProt.



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
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

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

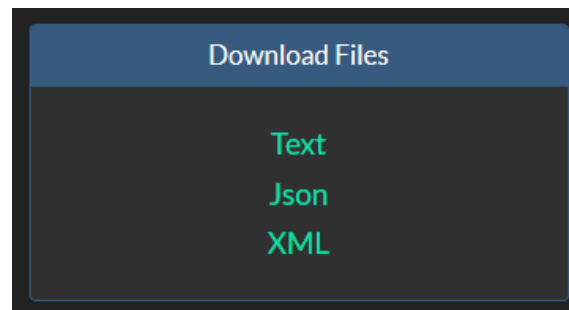


Furthermore, the user can have a more detailed view of each alignment through the Show button at the end of each line:

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> hap_qseq: 19 HLKATPIESHQ-----VEKRKCNATCATQRLANFLVHSS----NNFGAILSSTNVG 79 hap_hseq: 60 QMKASELEQEGEREGSRIIAQKRACDTATCTVTHRLAGLLSRSGGVVKMNF----VPTNVG 120 hap_midl: +KA+ +E Q +KR C+TATC T RLA L S NNF TNVG hap_qseq: 79 SNTYGKR 85 hap_hseq: 120 SKAFGRR 126 hap_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:	
Scientific questions:	veconom[at]biol.uoa.gr
Database administration:	katnastou[at]biol.uoa.gr
Data submission:	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

Database Technologies

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





References

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