



MASTERMIND[®]

Use Case Scenario:
Searching Mastermind by Disease

Searching Mastermind by Disease

Mastermind can be used to obtain a comprehensive, up-to-date list of all of the genes associated with a given disease and their associated genetic variants. These results can be used to inform gene panel design by cataloguing genes and/or variants that are linked to a particular genetic disease.

To search by disease, enter your search term in the “Disease” search box on the Mastermind home page at <http://mastermind.genomenon.com>. Note that you will first need to login to the software with the username and password that was provided to you via email from GENOMENON at the start of your trial or license.

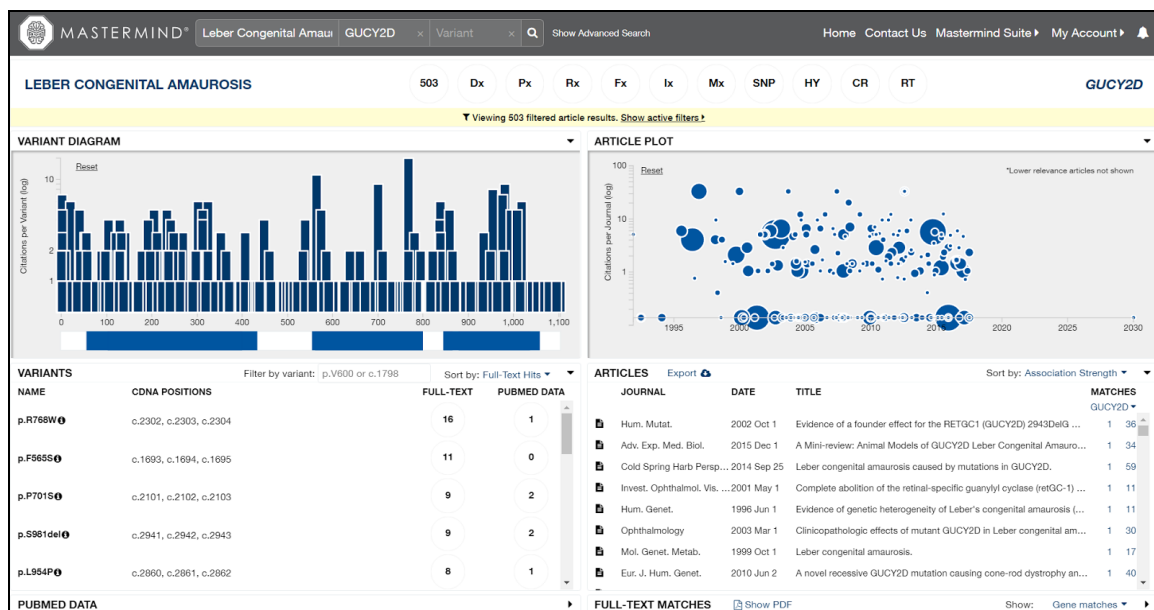
In this example, we will search for information on “Leber Congenital Amaurosis”. As you enter the search term in the text box, the auto-fill drop-down menu will allow you to select the desired search term.

The screenshot shows the Mastermind web application interface. At the top, there is a navigation bar with links: Home, Contact Us, Mastermind Suite, My Account, and a notification bell icon. The main header features the Mastermind logo (a blue octagon with a white geometric design) and the text "MASTERMIND By: GENOMENON". Below the header is the subtitle "Comprehensive Database of Genomic Knowledge". The search interface consists of three input fields: "Disease", "Gene", and "Variant". The "Disease" field contains the text "Leber" and has a dropdown menu open showing a list of suggestions: "Optic Atrophy, Hereditary, Leber", "Leber Congenital Amaurosis", "Amaurosis congenita of Leber, type 5", "Amaurosis congenita of Leber, type 9", "Leber Congenital Amaurosis 10", and "Leber Congenital Amaurosis 10". The "Gene" and "Variant" fields are empty. To the right of the input fields is a blue "Search" button with a magnifying glass icon. Below the input fields is a link that says "Show Advanced Search". At the bottom of the page, there is a footer with the copyright notice "© 2017 GENOMENON®" and links for "Terms of Service" and "Privacy Policy".

After clicking “Search” a results summary page will be shown. This list represents all genes that are associated with Leber Congenital Amaurosis (LCA) from the medical literature. Results are ordered by the number of publications citing the listed the gene-disease association. In this example, *GUCY2D*, which is associated with LCA type 1, has the highest number of publications showing an association between this gene and LCA. Less-documented or new/novel gene-disease associations are listed below in descending order of article count.

| Disease | Articles | Gene |
|----------------------------|----------|-------------------------|
| LEBER CONGENITAL AMAUROSIS | 503 | GUCY2D |
| LEBER CONGENITAL AMAUROSIS | 436 | PTPRC |
| LEBER CONGENITAL AMAUROSIS | 428 | RPE65 |
| LEBER CONGENITAL AMAUROSIS | 295 | RPE |
| LEBER CONGENITAL AMAUROSIS | 251 | RHO |
| LEBER CONGENITAL AMAUROSIS | 234 | CRB1 |
| LEBER CONGENITAL AMAUROSIS | 216 | AIPL1 |
| LEBER CONGENITAL AMAUROSIS | 214 | CRX |
| LEBER CONGENITAL AMAUROSIS | 203 | RPGRIPI |
| LEBER CONGENITAL AMAUROSIS | 176 | CEP290 |
| LEBER CONGENITAL AMAUROSIS | 148 | PLXNA2 |

Clicking on the entry for *GUCY2D* allows you to see the full list of publications citing this association as well as all associated variants in *GUCY2D*. The "Variant Diagram" can be used to view the distribution of the reported variants along the linear access of the protein. In some instances, you may see a large pile-up of hits at a given location on the protein/cDNA, which indicates that multiple articles described the same variant. In this example, the range of reported genetic variants for *GUCY2D* span the entire length of the protein.



Scroll down towards the end of the list to the entry for *NMNAT1* and click on the gene name to see the list of publications and associated genetic variants. There are 49 publications with reported variants associated with *NMNAT1*. Mutations in *NMNAT1* are associated with LCA type 9 in affected individuals.

| | | |
|----------------------------|----|---------|
| LEBER CONGENITAL AMAUROSIS | 53 | GRK1 |
| LEBER CONGENITAL AMAUROSIS | 52 | MYO7A |
| LEBER CONGENITAL AMAUROSIS | 50 | TREH |
| LEBER CONGENITAL AMAUROSIS | 49 | NMNAT1 |
| LEBER CONGENITAL AMAUROSIS | 48 | NRL |
| LEBER CONGENITAL AMAUROSIS | 46 | ARPP21 |
| LEBER CONGENITAL AMAUROSIS | 46 | CES2 |
| LEBER CONGENITAL AMAUROSIS | 46 | PHLDA2 |
| LEBER CONGENITAL AMAUROSIS | 45 | ALDH7A1 |
| LEBER CONGENITAL AMAUROSIS | 44 | CNGA3 |
| LEBER CONGENITAL AMAUROSIS | 44 | GUCA1A |
| LEBER CONGENITAL AMAUROSIS | 43 | BCO2 |

<https://mastermind.genomenon.com/#/detail?gene=arpp21&disease=leber%20congenital%20amaurosis>

To find position at which the highest number of variants has been reported, move to the “Variants” panel of the report, which by default is sorted by “Full-Text Hits”.

MASTERMIND® Leber Congenital Amaurosis NMNAT1 Variant Show Advanced Search Home Contact Us Mastermind Suite My Account

LEBER CONGENITAL AMAUROSIS 49 Dx Px Rx Fx Ix Mx SNP HY CR RT NMNAT1

Viewing 49 filtered article results. Show active filters

VARIANT DIAGRAM

VARIANTS Filter by variant: p.V600 or c.1798 Sort by: Full-Text Hits

| NAME | CDNA POSITIONS | FULL-TEXT | Pubmed Hits | Total Hits | Position |
|---------|---------------------|-----------|-------------|------------|----------|
| p.E257K | c.769, c.770, c.771 | 11 | | | |
| p.V9M | c.25, c.26, c.27 | 5 | 3 | | |
| p.R237C | c.709, c.710, c.711 | 5 | 0 | | |
| p.R66W | c.196, c.197, c.198 | 4 | 1 | | |
| p.R207W | c.619, c.620, c.621 | 4 | 0 | | |

ARTICLE PLOT

ARTICLES Export Sort by: Association Strength

| JOURNAL | DATE | TITLE | MATCHES |
|----------------------------|-------------|--|---------|
| J. Biol. Chem. | 2015 May 27 | Characterization of Leber Congenital Amaurosis-associated NMNAT1... | 1 240 |
| Am. J. Pathol. | 2016 May 18 | Mouse Models of NMNAT1-Leber Congenital Amaurosis (LCA9) Rec... | 1 42 |
| Nat. Genet. | 2012 Jul 29 | NMNAT1 mutations cause Leber congenital amaurosis. | 1 91 |
| Mol. Vis. | 2014 Jun 2 | Novel compound heterozygous NMNAT1 variants associated with L... | 1 49 |
| Nat. Genet. | 2012 Jul 29 | Mutations in NMNAT1 cause Leber congenital amaurosis and identf... | 1 31 |
| Gene | 2015 May 16 | A novel missense NMNAT1 mutation identified in a consanguineous ... | 1 28 |
| Graefes Arch. Clin. Exp... | 2015 Oct 13 | Clinical and genetic findings in a family with NMNAT1-associated Le... | 1 26 |
| Nat. Genet. | 2012 Jul 29 | Exome sequencing identifies NMNAT1 mutations as a cause of Lebe... | |

PUBMED DATA FULL-TEXT MATCHES Show PDF Show: Gene matches

There are 11 full-text publications associated with the p.E257K variant. For future access, a file containing the PubMed Identification number, the title and the journal name for each article in the article list can be exported from Mastermind by clicking on the "Export" icon at the upper right of the Articles panel. To view the PDF of any publication, click on the title you are interested in, then click "Show PDF" header bar of the "Full-Text Matches" panel. In instances where the full-text article is not freely-available, you will need to either have an institutional subscription to the online journal, or pay a one-time fee to the Publisher to access and download the article directly from the publisher's website.

In summary, searching Mastermind by Disease will enable you to: 1) see all genes associated with a given disease; 2) view the reported genetic variants for a given gene associated with a genetic disease; and 3) obtain (where applicable) the underlying, supporting publication from the biomedical literature.



MASTERMIND

We are pleased that you are interested in our software and we look forward to learning from your experience.

If any questions arise, please do not hesitate to contact us.

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