



MASTERMIND[®]

Use Case Scenario: Searching Mastermind by Disease

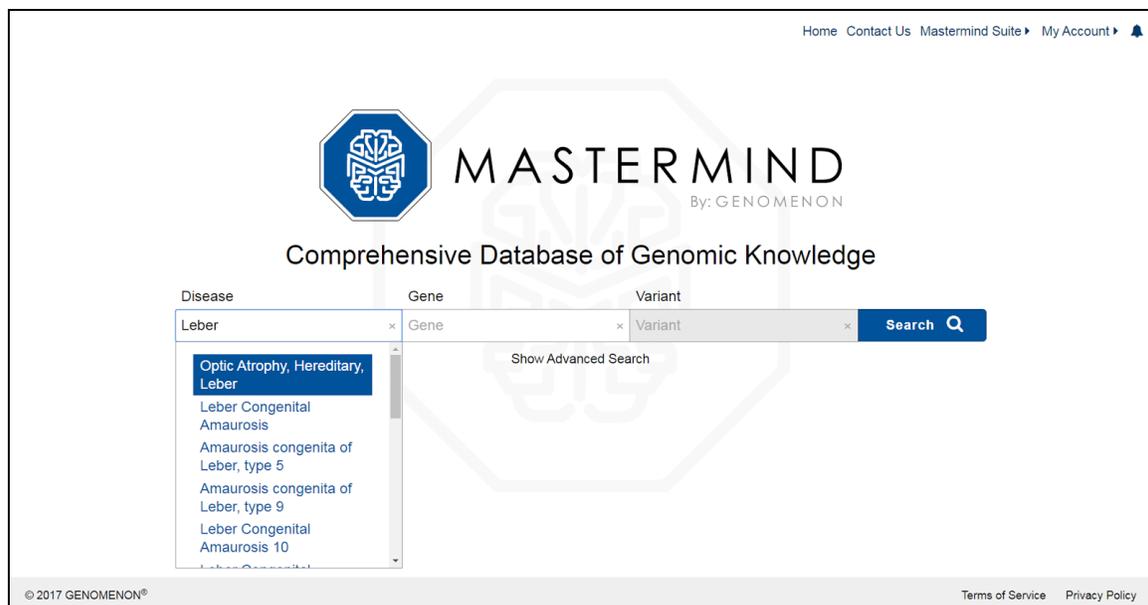
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Searching Mastermind by Disease

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.



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	<i>GUCY2D</i>
LEBER CONGENITAL AMAUROSIS	436	<i>PTPRC</i>
LEBER CONGENITAL AMAUROSIS	428	<i>RPE65</i>
LEBER CONGENITAL AMAUROSIS	295	<i>RPE</i>
LEBER CONGENITAL AMAUROSIS	251	<i>RHO</i>
LEBER CONGENITAL AMAUROSIS	234	<i>CRB1</i>
LEBER CONGENITAL AMAUROSIS	216	<i>AIPL1</i>
LEBER CONGENITAL AMAUROSIS	214	<i>CRX</i>
LEBER CONGENITAL AMAUROSIS	203	<i>RPGRIP1</i>
LEBER CONGENITAL AMAUROSIS	176	<i>CEP290</i>
LEBER CONGENITAL AMAUROSIS	148	<i>PLXNA2</i>

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.

The screenshot displays the MASTERMIND interface for Leber Congenital Amaurosis (LCA) associated with the *GUCY2D* gene. The interface includes a variant diagram, an article plot, a list of variants, and a list of articles.

VARIANT DIAGRAM: A bar chart showing the distribution of reported variants along the linear access of the protein. The x-axis represents the position (0 to 1,100) and the y-axis represents the number of citations per variant (log scale, 1 to 10). The chart shows a high density of variants across the entire length of the protein.

ARTICLE PLOT: A scatter plot showing the distribution of articles over time. The x-axis represents the year (1995 to 2030) and the y-axis represents the number of citations per journal (log scale, 1 to 100). The plot shows a significant increase in the number of articles published over time, with a peak around 2010.

VARIANTS: A table listing the variants associated with *GUCY2D*. The table includes columns for NAME, CDNA POSITIONS, FULL-TEXT, and PUBMED DATA.

NAME	CDNA POSITIONS	FULL-TEXT	PUBMED DATA
p.R766W	c.2302, c.2303, c.2304	16	1
p.F565S	c.1693, c.1694, c.1695	11	0
p.P701S	c.2101, c.2102, c.2103	9	2
p.S981del	c.2941, c.2942, c.2943	9	2
p.L954P	c.2880, c.2881, c.2882	8	1

ARTICLES: A table listing the articles associated with *GUCY2D*. The table includes columns for JOURNAL, DATE, TITLE, and MATCHES.

JOURNAL	DATE	TITLE	MATCHES
Hum. Mutat.	2002 Oct 1	Evidence of a founder effect for the RETGC1 (GUCY2D) 2943DelG ...	1 36
Adv. Exp. Med. Biol.	2015 Dec 1	A Mini-review: Animal Models of GUCY2D Leber Congenital Amauro...	1 34
Cold Spring Harb Persp...	2014 Sep 25	Leber congenital amaurosis caused by mutations in GUCY2D.	1 59
Invest. Ophthalmol. Vis. ...	2001 May 1	Complete abolition of the retinal-specific guanylyl cyclase (retGC-1) ...	1 11
Hum. Genet.	1996 Jun 1	Evidence of genetic heterogeneity of Leber's congenital amaurosis (...)	1 11
Ophthalmology	2003 Mar 1	Clinicopathologic effects of mutant GUCY2D in Leber congenital am...	1 30
Mol. Genet. Metab.	1999 Oct 1	Leber congenital amaurosis.	1 17
Eur. J. Hum. Genet.	2010 Jun 2	A novel recessive GUCY2D mutation causing cone-rod dystrophy an...	1 40

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

ARTICLE PLOT

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	3	14	
p.V9M	c.25, c.26, c.27	5	3	8	
p.R237C	c.709, c.710, c.711	5	0	5	
p.R66W	c.196, c.197, c.198	4	1	5	
p.R207W	c.619, c.620, c.621	4	0	4	

ARTICLES Export

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 identif...	1 31
Gene	2015 May 16	A novel missense NMNAT1 mutation identified in a consanguineous ...	1 31
Graefes Arch. Clin. Exp...	2015 Oct 13	Clinical and genetic findings in a family with NMNAT1-associated Le...	1 28
Nat. Genet.	2012 Jul 29	Exome sequencing identifies NMNAT1 mutations as a cause of Lebe...	1 26

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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