



# MASTERMIND®

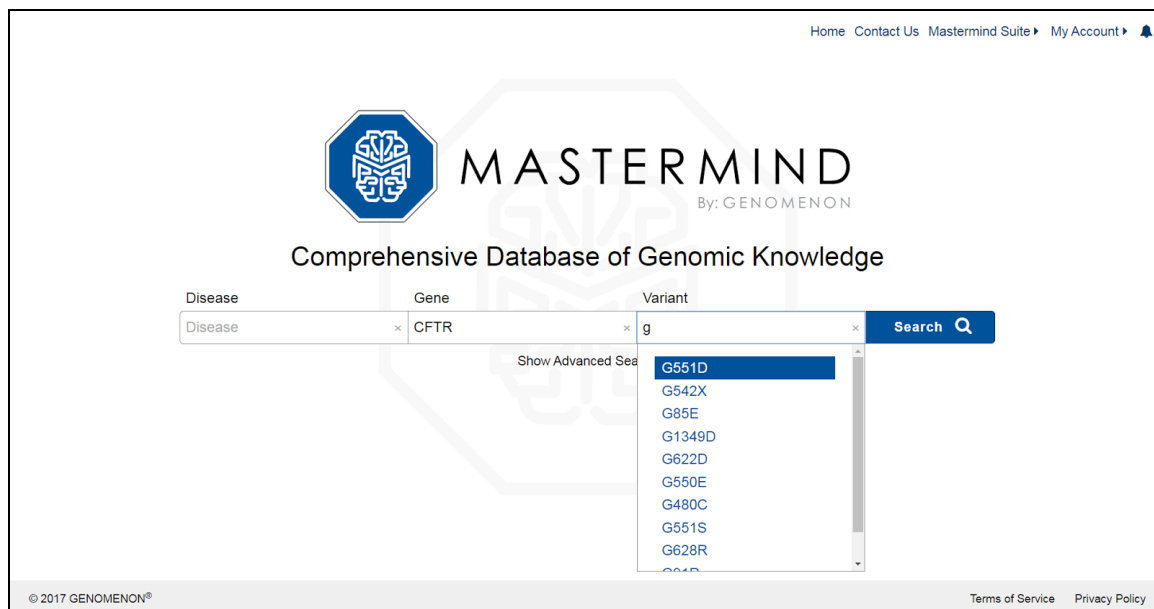
Use Case Scenario:  
Searching Mastermind by Variant

## Searching Mastermind by Variant

Mastermind can be used to search for all publications associated with a known, previously reported genetic variant. As new articles describing a specific disease-causing variant are being published daily, using Mastermind to keep up-to-date with the latest information and clinical findings can help guide and accelerate precision medicine initiatives in the clinic.

In the following example, we will use Mastermind to search for the p.G551D variation in the *CFTR* gene. The p.G551D variant, in which the amino acid glycine is replaced with aspartic acid at position 551 in the protein, results in a dysfunctional cell surface protein that is unable to transport chloride through a channel.

From the Mastermind home page, enter "CFTR" in the Gene field to automatically enable the Variant query box.



The screenshot displays the Mastermind website interface. At the top right, there are navigation links: Home, Contact Us, Mastermind Suite, and My Account. The main header features the Mastermind logo (a blue octagon with a white brain-like pattern) and the text "MASTERMIND By: GENOMENON". Below the header is the tagline "Comprehensive Database of Genomic Knowledge". The search interface consists of three input fields: "Disease", "Gene", and "Variant". The "Gene" field contains "CFTR" and is marked with an "x". The "Variant" field contains "g" and is also marked with an "x". A blue "Search" button with a magnifying glass icon is to the right of the "Variant" field. A dropdown menu is open below the "Variant" field, listing several variants: G551D (highlighted in blue), G542X, G85E, G1349D, G622D, G550E, G480C, G551S, G628R, and G64D. Below the search fields is a "Show Advanced Search" link. At the bottom left, there is a copyright notice: "© 2017 GENOMENON®". At the bottom right, there are links for "Terms of Service" and "Privacy Policy".

The results page will show you a list of MeSH disease terms where this gene-variant pair has been described in the full text, title, and abstract of any corresponding publications. The results are also sorted with the highest number of publications appearing at the top.

Next, click on the disease term "CYSTIC FIBROSIS" to go to an overview page with information about this specific disease-gene-mutation association.

Disease	Articles	Gene
ALL	2.0k	CFTR
FIBROSIS	1.8k	CFTR
CYSTIC FIBROSIS	1.8k	CFTR
HUMANISM	326	CFTR
LUNG DISEASES	258	CFTR
INDIVIDUALITY	240	CFTR
INDIVIDUATION	240	CFTR
PANCREATITIS	220	CFTR
GENERALIZATION (PSYCHOLOGY)	217	CFTR
SWEATING	217	CFTR
INHIBITION (PSYCHOLOGY)	197	CFTR

In the bottom left panel, labeled "Variants", you will see the p.G551D variant, along with p.G551del, since our search term did not exclude this variant.

At the top of this detail page you will see a toolbar with abbreviated terms that further qualify the publications by various subcategories. This will be handy since even when searching by a Disease-Gene-Variant trio, there are still 1.7k articles to sort through. Mousing over each term will reveal the full names of each subcategory. The treatment category (Rx) itemizes those publications where a therapeutic treatment is likely to have been described. To view these publications, click on the "Rx" ico. This will open a menu with additional search terms that can be used to further filter your results.

The “drug” field will generate a list of publications (counted in parenthesis) that describe a specific drug therapy administered in CF patients harboring the *CFTR*-p.G551D variant. To generate this list, you will first need to click on the “Disable All” option to deselect all search terms, then click on “drug”.

The screenshot displays the Mastermind search interface for Cystic Fibrosis. The search criteria are set to Cystic Fibrosis, CFTR, and G551D. The 'Rx' (Drug) category is selected, showing 208 results. The interface includes a navigation bar, a filter menu, and a main content area with 'Enable All' and 'Disable All' buttons. The 'Drug' category is active, showing 208 results. Below this, there are tables for 'VARIANTS', 'ARTICLES', and 'PUBMED DATA'. The 'ARTICLES' table lists several publications with their titles, dates, and match counts. The 'PUBMED DATA' section shows a detailed view of a specific article with its abstract text.

NAME	CDNA POSITIONS	FULL-TEXT	PUBMED DATA
p.G551D	c.1651, c.1652, c.1653	1.7k	266
p.G551del	c.1651, c.1652, c.1653	33	0

JOURNAL	DATE	TITLE	MATCHES
J. Biol. Chem.	2005 Nov 25	Differential sensitivity of the cystic fibrosis (CF)-associa...	1 127 1 89
Sheng Li Xue Bao	2015 Apr 25	[Polymethoxylated flavonoids activate cystic fibrosis tr...	1 184 1 1
Assay Drug Dev Technol	2010 Nov 4	Identification of synergistic combinations of F508del cy...	1 122 1 1
Ann Pharmacother	2012 Jun 26	Cystic fibrosis transmembrane conductance regulator-...	1 99 1 21
J. Biol. Chem.	2007 Dec 30	Mechanism of G551D-CFTR (cystic fibrosis transmemb...	1 31 1 98

**PUBMED DATA** PMID: 16311240  
 Differential sensitivity of the cystic fibrosis (CF)-associated mutants G551D and G1349D to potentiators of the cystic fibrosis transmembrane conductance regulator (CFTR) Cl<sup>-</sup> channel. J. Biol. Chem. 2005 Nov 24

**FULL-TEXT MATCHES** PMID: 16311240 Show: Gene matches

The genetic disease **cystic fibrosis** (CF) is caused by loss of function of the **cystic fibrosis transmembrane conductance regulator** (CFTR) Cl<sup>-</sup> channel. Two CF mutants, G551D and G1349D, affect equivalent residues in the highly conserved LSGGG motifs that are essential components of the ATP-binding sites of CFTR. Both mutants severely disrupt CFTR channel gating by decreasing mean burst duration (MBD) and prolonging greatly the interburst interval (IBI). To identify small molecules that rescue the gating defects of G551D- and G1349D-CFTR and understand better how these agents work, we used the patch clamp technique to study the effects on G551D- and G1349D-CFTR of phloxine B, pyrophosphate (PPi), and 2'-deoxy ATP (2'-dATP).

Publications can then be browsed in the “Articles” panel in the center right. The default view rank orders the publications by the strength of the term associations in the full text, title, and abstract, but they can also be sorted by Publication Date, Journal Name, and Impact Factor. Clicking on the “Export” icon will then export the list of filtered publications (PubMed ID, Title, and Journal in .csv format) which can be saved locally.

In summary, searching Mastermind with a gene name and known variant will enable you to 1) see all publications associated with a gene-variant-disease association and 2) filter the search results by subcategory to identify subsets of publications describing a particular treatment, therapy or biological outcome (among others).



# 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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