

EBiSC Guidance: How to Use the Catalogue Search Interface

Version 0.2

2022-08-20

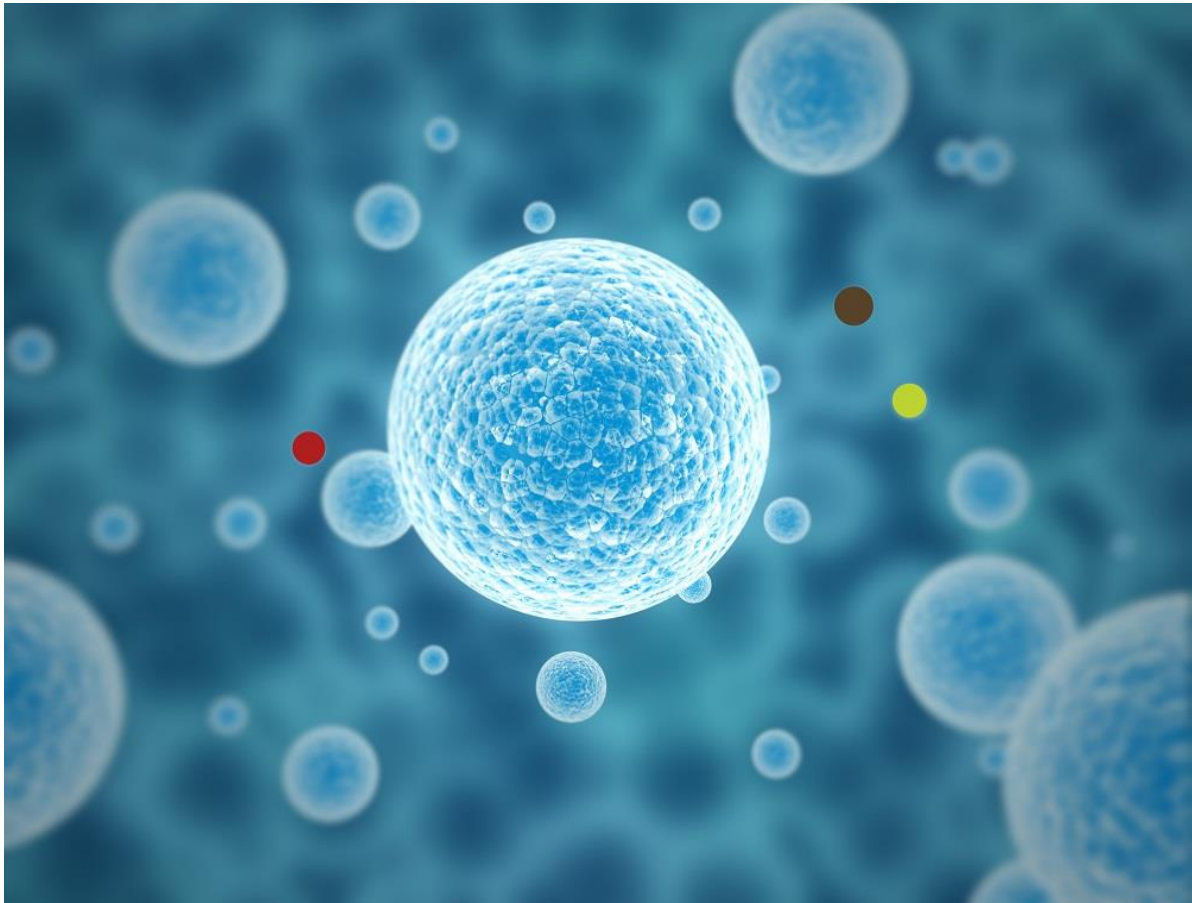


Table of Contents

1	Introduction	3
2	Using the EBiSC catalogue search functions	4
2.1	Use Case 1: Direct search for a gene-of-interest	4
2.2	Use case 2: Lines with genomic variants (from WGS) in disease-associated genes	7
2.3	Use case 3: Filter lines for karyotype	9

1 Introduction

The European Bank for induced Pluripotent Stem Cells (EBiSC) is a not-for-profit iPSC cell banking and distribution service enabling academic and commercial researchers to access quality-assured, disease relevant, research-grade iPSC lines, data and cell services (<https://ebisc.org/>). For a quick overview of the EBiSC deposition steps, please refer to the EBiSC webpage “Information for Depositors” (<https://cells.ebisc.org/depositors/>).

EBiSC is dedicated to supporting research through provision of a high-quality, well-characterised collection of human iPSC lines from a range of genetic backgrounds and reprogramming methods. Lines banked at EBiSC are associated with an extensive cell line data package. Search functions in the EBiSC catalogue have been implemented to allow customers to find appropriate cell line products for their research according to selected genetic attributes, whilst taking measures to protect the data privacy of the cell line donors.

This guidance document illustrates the EBiSC catalogue search functions through use cases.

2 Using the EBiSC catalogue search functions

2.1 Use Case 1: Direct search for a gene-of-interest

Query 1A

“I want to find all cell lines with a genetic variant in APOE gene. I am only interested in lines with genotyped mutations in the donor.”

Search interface input

- In the “Gene(s) of interest” section, enter gene symbol “APOE” in the “From hPSCreg® data” search box
- Select the “Donor-derived” check box. This will select all genes that have been genotyped at the donor level. Typically, these genetic variants have been confirmed by the EBiSC line Generator/Depositor.

Result

There are five lines that have a been genotyped for a mutation in the APOE gene. The cell lines are named in the results.

The screenshot shows the EBiSC2 website interface. At the top, there is a navigation bar with 'Catalogue' highlighted, and links for 'About', 'Information for Customers', 'Information for Depositors', 'Resources', 'News', and 'Contact'. Below this is a search bar with the text 'Search full text in EBiSC cell line catalogue' and a subtext 'Search for cell line names, genes, cell types, diseases, Biosample-IDs and more. Examples: BiONi015-A, Parkinson, ApoE'. The main content area is divided into several sections:

- Gene(s) of interest:** A search box containing 'APOE (5)'. Below it are two checkboxes: 'Gene-edited (0)' (unchecked) and 'Donor-derived (5)' (checked).
- Disease(s) of interest:** A search box for disease names. Below it is a checkbox for 'Donor disease status' with 'normal (0)' selected.
- Genotyping:** A search box for sequencing methods. Below it is a checkbox for 'Isogenic line available (2)' which is unchecked.
- Advanced filters:** Four input fields for 'Biological sex', 'Donor age', 'Derivation', and 'Primary cell type(s)'. At the bottom of this section are 'Apply filters' and 'Reset filters' buttons.
- 5 cell lines found:** A grid of five cell line cards:
 - STBCi006-A:** (SFC140-04-01) Patient-derived cell line. Donor disease status: Alzheimer disease. Primary cell type: fibroblast of dermis.
 - STBCi072-A:** (SFC058-03-01) Patient-derived cell line. Donor disease status: Alzheimer disease. Primary cell type: fibroblast.
 - STBCi072-B:** (SFC058-03-02) Patient-derived cell line. Donor disease status: Alzheimer disease. Primary cell type: fibroblast.
 - STBCi072-C:** (SFC058-03-03) Patient-derived cell line. Donor disease status: Alzheimer disease. Primary cell type: fibroblast.
 - UKBi011-A:** (ILB-AD-169bm-s24) Patient-derived cell line. Donor disease status: Alzheimer disease. Primary cell type: peripheral blood mononuclear cell.

Query 1B

"I want to find all cell lines with a gene edit in APOE gene."

Search interface input

- In the "Gene(s) of interest" section, enter gene symbol "APOE" in the "From hPSCreg® data" search box
- Select the "Gene-edited" checkbox. This selects all genes that were involved in a genetic engineering event.

Result

There are 13 lines that have a been gene-edited in the APOE gene. The cell lines are listed in the results.

The screenshot displays the EBiSC2 website's search interface. At the top, there is a navigation menu with links for 'Catalogue', 'About', 'Information for Customers', 'Information for Depositors', 'Resources', 'News', and 'Contact'. Below this is a search bar with the text 'Search full text in EBiSC cell line catalogue' and a subtext 'Search for cell line names, genes, cell types, diseases, Biosample-IDs and more. Examples: BIONi015-A, Parkinson, ApoE'. The main content area is divided into search filters on the left and search results on the right.

Search filters:

- Gene(s) of interest:** APOE (15) (selected), From -omics data, Gene-edited (13) (checked), Donor-derived (2) (unchecked).
- Disease(s) of interest:** From hPSCreg® data, Linked by -omic variants, Donor disease status: normal (8) (unchecked).
- Genotyping:** Sequencing methods(s), Isogenic line available (15) (unchecked).
- Advanced filters:** Biological sex, Donor age, Derivation, Primary cell type(s), Karyotype(s).

Search results (13 cell lines found):

Cell Line ID	Gene Edit	Parental Cell Line	Donor Disease Status	Primary Cell Type
STBCi006-A-1	(ApoE KO)	STBCi006-A	Alzheimer disease	fibroblast of dermis
BIONi010-C-2	(BIONi010-C ApoE E3/E3 #H8 P32)	BIONi010-C		fibroblast of dermis
BIONi010-C-3	(BIONi010-C ApoE KO #K030 P30)	BIONi010-C		fibroblast of dermis
BIONi010-C-4	(BIONi010-C ApoE E4/E4 #B44 P27)	BIONi010-C		fibroblast of dermis
BIONi010-C-6	(BIONi010-C ApoE E2/E2)	BIONi010-C		fibroblast of dermis
UKBi011-A-1	(ILB-AD + ApoE KO)	UKBi011-A	Alzheimer disease	peripheral blood mononuclear cell
UKBi011-A-2	(ApoE 2/2)	UKBi011-A	Alzheimer disease	peripheral blood mononuclear cell
UKBi011-A-3	(ApoE 3/3)	UKBi011-A	Alzheimer disease	peripheral blood mononuclear cell
UKBi011-A-4	(ApoE 3/4)	UKBi011-A	Alzheimer disease	peripheral blood mononuclear cell
BIONi037-A-1	(16423 ApoE KO)			
BIONi037-A-2	(BIONi037-A ApoE2/2 #M10-7)			
BIONi037-A-3	(BIONi037-A ApoE3/4 #P10-22)			

Query 1C – implemented as a proof-of-principle

“I want to find all cell lines with variants in the gene UBE3A, as analysed from -omic data.”

- Please refer to [EBiSC Information Sheet: Genomic data processing for catalogue search](#) for details on how the variants have been compiled from selected datasets.

Search interface input

- In the “Gene(s) of interest” section, enter gene symbol “UBE3A” in the “From -omics data” search box.

Result

There is a genetic variant (as detected in WGS data) in one line (WTSli017-B), and all other genomic variants, as well as the associated diseases, are shown for this cell line at the bottom of the [EBiSC cell line page](#). As a supplementary information, all genes with omic variants, which did not have any associations to disease according to ClinGen, are listed on the EBiSC cell line page under the heading “Other WGS-derived genes”.



2.2 Use case 2: Lines with genomic variants (from WGS) in disease-associated genes

Query 2A

“I want to find all cell lines that have potentially clinically significant variants in epilepsy.”

Search interface input

- Under the heading “Disease(s) of interest”, select “epilepsy” in the “Linked by -omic variants” box.

Result

There are two named cell lines in the EBiSC catalogue that have *potentially* clinically significant variants in epilepsy. In this case, the lines are from the same donor, who has no diagnosed disease. **As a very conservative data privacy measure, the exact genetic variants that were found in the WGS data of these cell lines are not shown on the EBiSC search result.** Further information about the epilepsy-associated gene variants can be requested from EBiSC.

The screenshot displays the EBiSC2 search interface. At the top, there is a navigation bar with links for Catalogue, About, Information for Customers, Information for Depositors, Resources, News, and Contact. Below this is a search bar with the text "Search full text in EBiSC cell line catalogue" and a subtext "Search for cell line names, genes, cell types, diseases, Biosample-IDs and more. Examples: BION015-A, Parkinson, ApoE".

The search filters section on the left includes:

- Gene(s) of interest:** A dropdown menu set to "From hPSCreg@ data" and a checkbox for "From -omics data". Below these are checkboxes for "Gene-edited (0)" and "Donor-derived (2)".
- Disease(s) of interest:** A dropdown menu set to "From hPSCreg@ data" and a button for "epilepsy (2)". Below this is a checkbox for "Donor disease status" set to "normal (2)".
- Genotyping:** A dropdown menu set to "Sequencing methods(s)" and a checkbox for "Isogenic line available (0)".
- Advanced filters:** A section with dropdown menus for "Biological sex", "Donor age", "Derivation", "Primary cell type(s)", and "Karyotype(s)".

At the bottom of the filters are "Apply filters" and "Reset filters" buttons.

The search results section on the right shows "2 cell lines found.":

- WTSii017-A:** (HPSi0114i-lexy...2) Patient-derived cell line. Primary cell type: fibroblast. Diseases from omics data: epilepsy: [EPHC1](#).
- WTSii017-B:** (HPSi0114i-lexy...1) Patient-derived cell line. Primary cell type: fibroblast. Diseases from omics data: epilepsy: [EPHC1](#).

Query 2B

“I want to find all cell lines that have omic variants associated to 3-hydroxyisobutyryl-CoA hydrolase deficiency.”

Search interface input

- Under the heading “Disease(s) of interest”, select “3-hydroxyisobutyryl-CoA hydrolase deficiency” in the “Linked by -omic variants” box.

Result

There are 87 named cell lines in the EBiSC catalogue that have omic variants associated to the disease 3-hydroxyisobutyryl-CoA hydrolase deficiency. The disease-related genes, which have genomic variants related to the specified disease, are listed. In this case, it is only one gene (HIBCH). The [ClinGen online report](#) for this gene states that the disease mechanism is homozygous loss-of-function. Since the zygosity of the -omic gene variant in the cell lines is not known, the functional consequence of having a variant in this gene is unknown.

The screenshot displays the EBiSC2 website interface. At the top, there is a navigation menu with 'Catalogue' highlighted. Below the menu is a search bar with the text 'Search full text in EBiSC cell line catalogue'. Underneath the search bar, it says 'Search for cell line names, genes, cell types, diseases, Biosample-IDs and more. Examples: BION015-A, Parkinson, ApoE'. On the left side, there are several filter sections: 'Search filters', 'Gene(s) of interest' (with 'From hPSCreg@ data' and 'From -omics data' options), 'Disease(s) of interest' (with 'From hPSCreg@ data' and a selected '3-hydroxyisobutyryl-CoA hydrolase deficiency (87)' option), 'Donor disease status' (with 'normal (87)' selected), 'Genotyping' (with 'Sequencing methods(s)' and 'Isogenic line available (1)' options), and 'Advanced filters' (with 'Biological sex', 'Donor age', 'Derivation', 'Primary cell type(s)', and 'Karyotype(s)' options). On the right side, there are 12 result cards for cell lines: WTSli002-A, WTSli003-A, WTSli004-A, WTSli004-B, WTSli005-A, WTSli006-A, WTSli006-B, WTSli007-A, WTSli009-A, WTSli010-A, WTSli010-B, and WTSli011-B. Each card includes the cell line name, HPSI ID, patient-derived status, primary cell type, and a link to 'Diseases from omics data' for HIBCH.

2.3 Use case 3: Filter lines for karyotype

Query 3A

"I want to find all cell lines with an abnormal karyotype from donors with Alzheimer disease."

Search interface input

- Under the heading "Advanced filters", select "otherwise" in the "Karyotype" search box.
- Under the heading "Disease(s) of interest", select "Alzheimer disease" in the "From hPSCreg® data" box.

Result

There are 13 lines from AD patients that have at least some kind of chromosomal abnormality in the karyotype.

The screenshot displays the EBiSC2 website search interface. At the top, there is a navigation bar with 'Catalogue' highlighted, and links for 'About', 'Information for Customers', 'Information for Depositors', 'Resources', 'News', and 'Contact'. A search bar is present with the text 'Search full text in EBiSC cell line catalogue' and a subtext 'Search for cell line names, genes, cell types, diseases, Biosample-IDs and more. Examples: BION015-A, Parkinson, ApoE'.

The search filters section on the left includes:

- Gene(s) of interest:** 'From hPSCreg® data' (selected), 'From -omics data', 'Gene-edited (0)', and 'Donor-derived (13)'.
- Disease(s) of interest:** 'Alzheimer disease (13)' (selected), 'Linked by -omic variants', and 'Donor disease status: normal (0)'.
- Genotyping:** 'Sequencing methods(s)', 'Isogenic line available (0)'.
- Advanced filters:** 'Biological sex', 'Donor age', 'Derivation', 'Primary cell type(s)', and 'otherwise (13)' (selected).

 Buttons for 'Apply filters' and 'Reset filters' are at the bottom of the filter section.

The results section shows '13 cell lines found.' and displays a grid of 12 cell line cards (STBCi010-A through STBCi071-C). Each card provides the cell line name, ID, type, donor disease status (Alzheimer disease), and primary cell type (fibroblast).