EBiSC Guidance: How to Use the Catalogue Search Interface

Version 0.2

2022-08-20

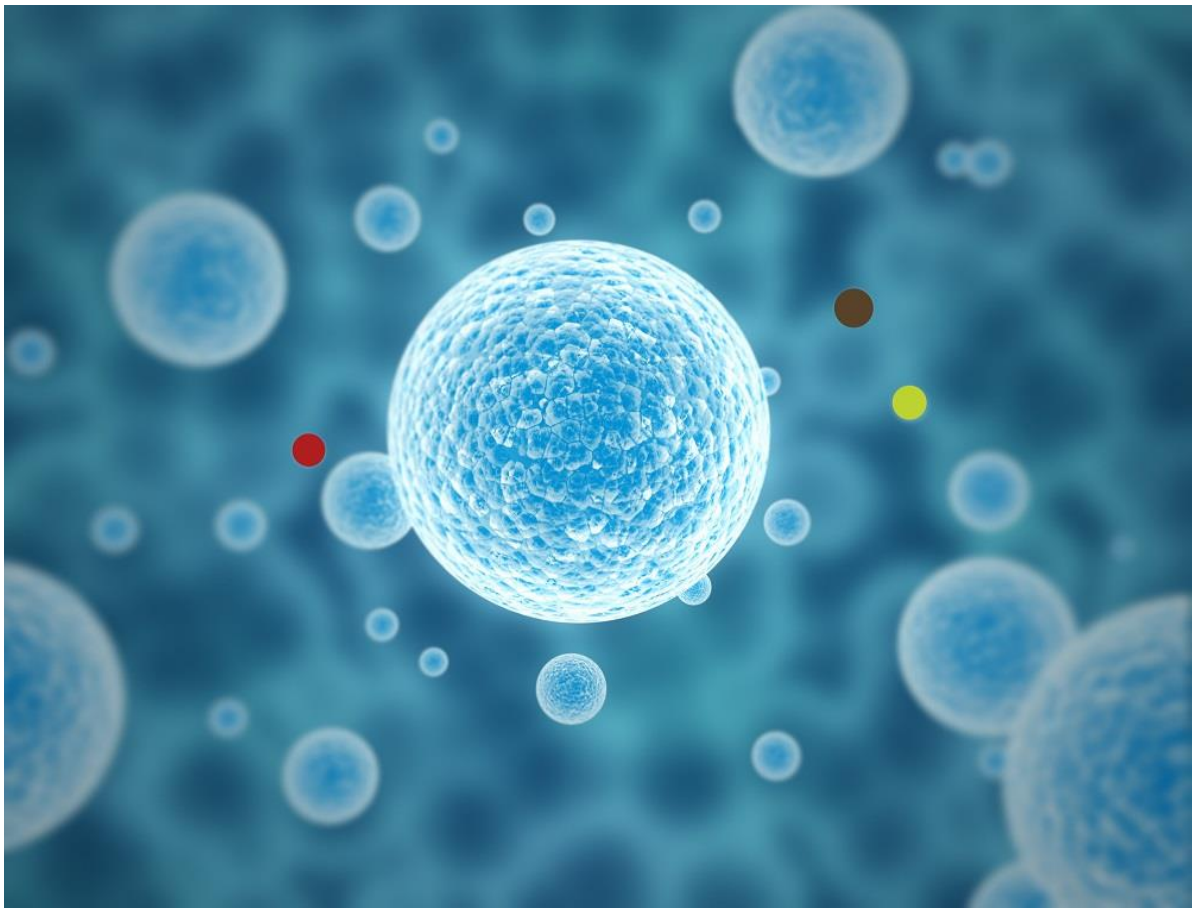


Table of Contents

1 Introduction

The European Bank for induced Pluripotent Stem Cells (EBiSC) is a not-for-profit iPS 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/).

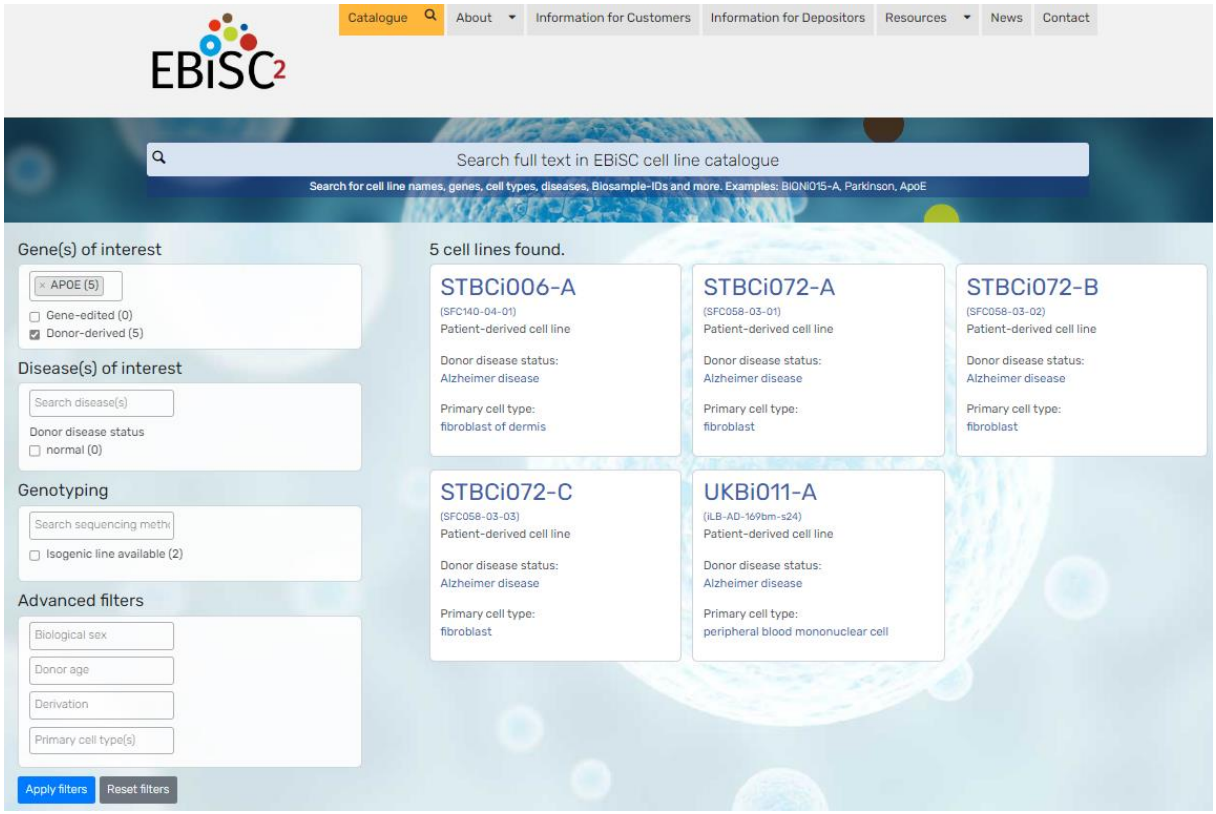
EBiSC is dedicated to supporting research through provision of a high-quality, well-characterised collection of human iPSC lines from a range of genetic backgrounds and reprogramming methods. Lines banked at EBiSC are associated with an extensive cell line data package. Search functions in the EBiSC 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.

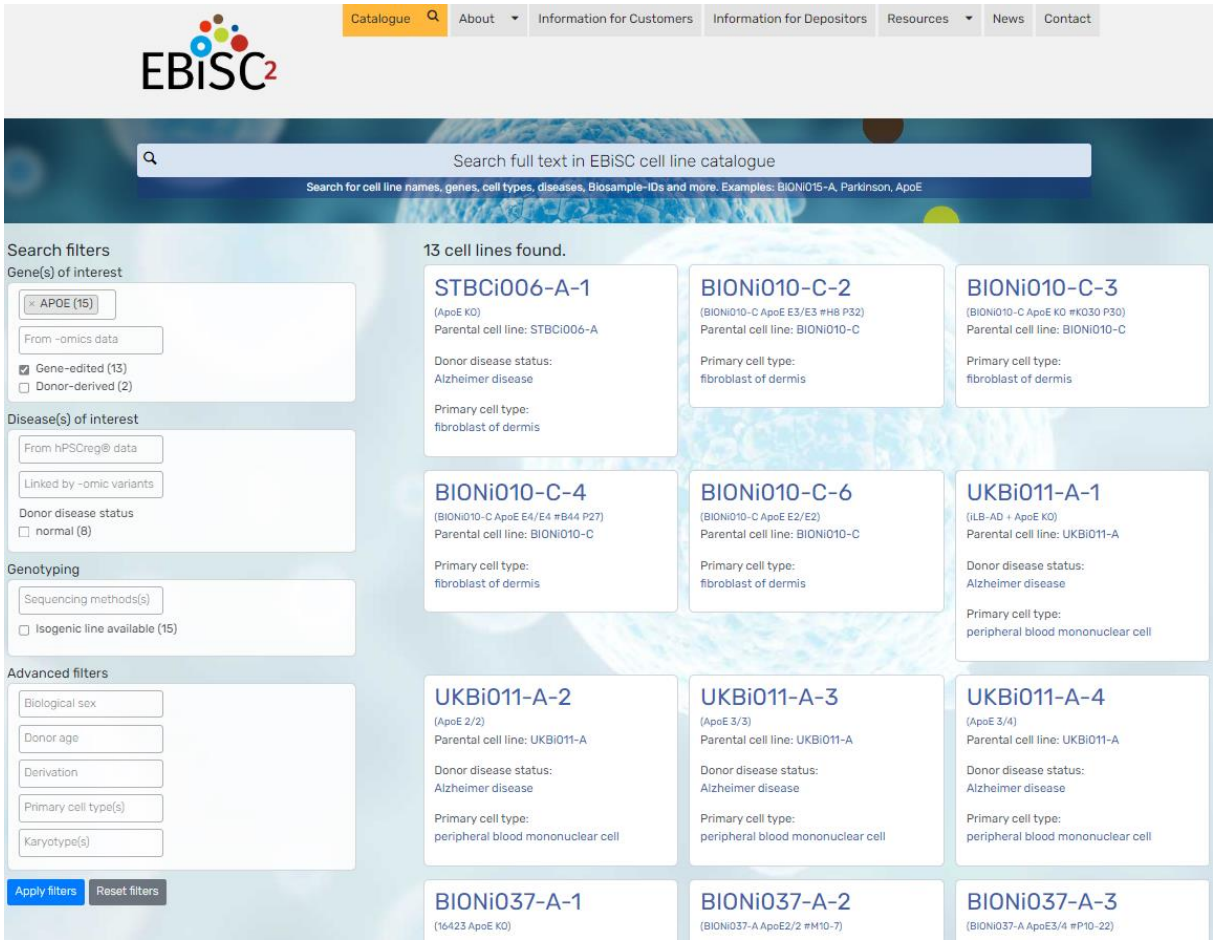
2 Using the EBiSC catalogue search functions

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

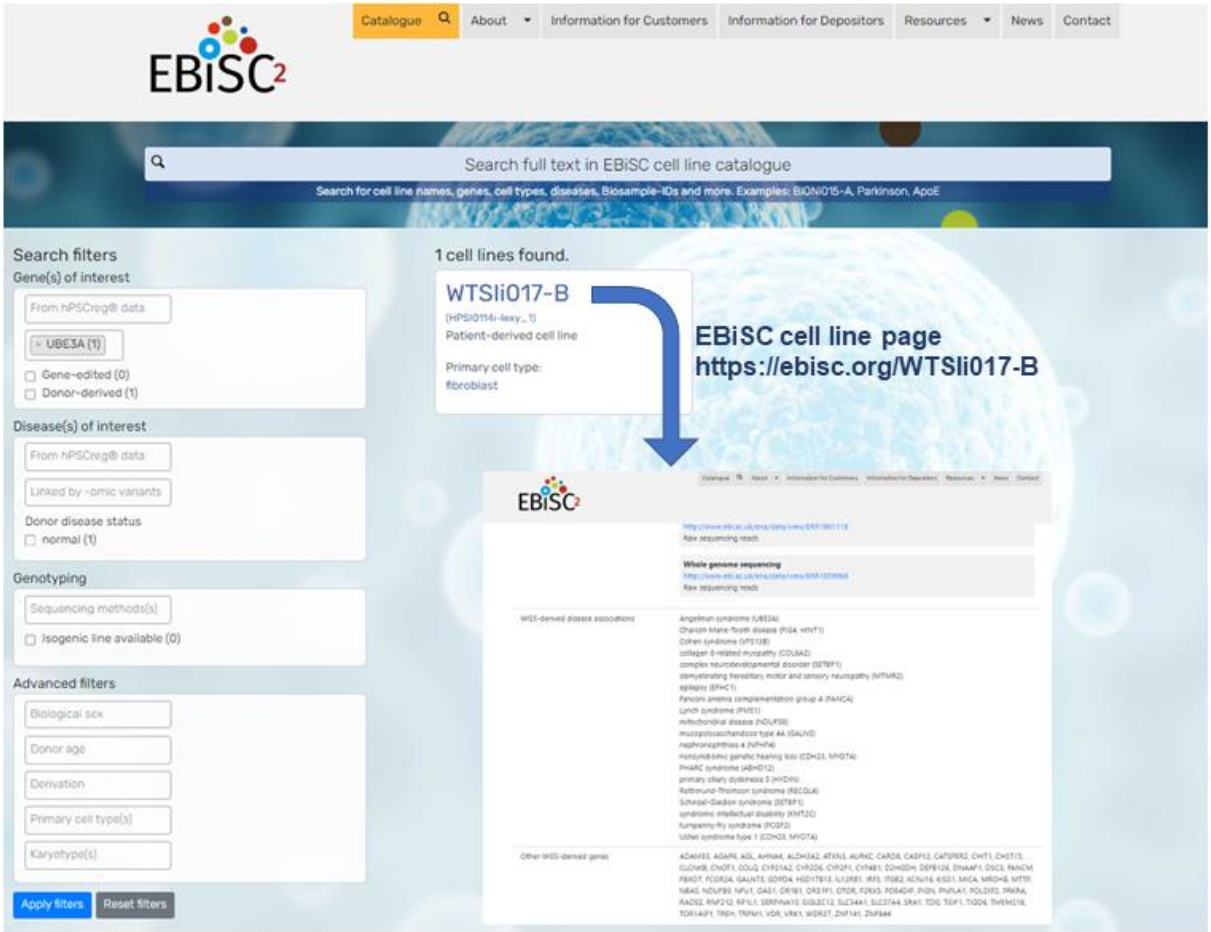
Query 1A
"I want to find all cell lines with a genetic variant in APOE gene. I am only interested in lines with genotyped mutations in the donor."
Search interface input
• In the "Gene(s) of interest" section, enter gene symbol "APOE" in the "From hPSCreg® data" search box • Select the "Donor-derived" 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.



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.

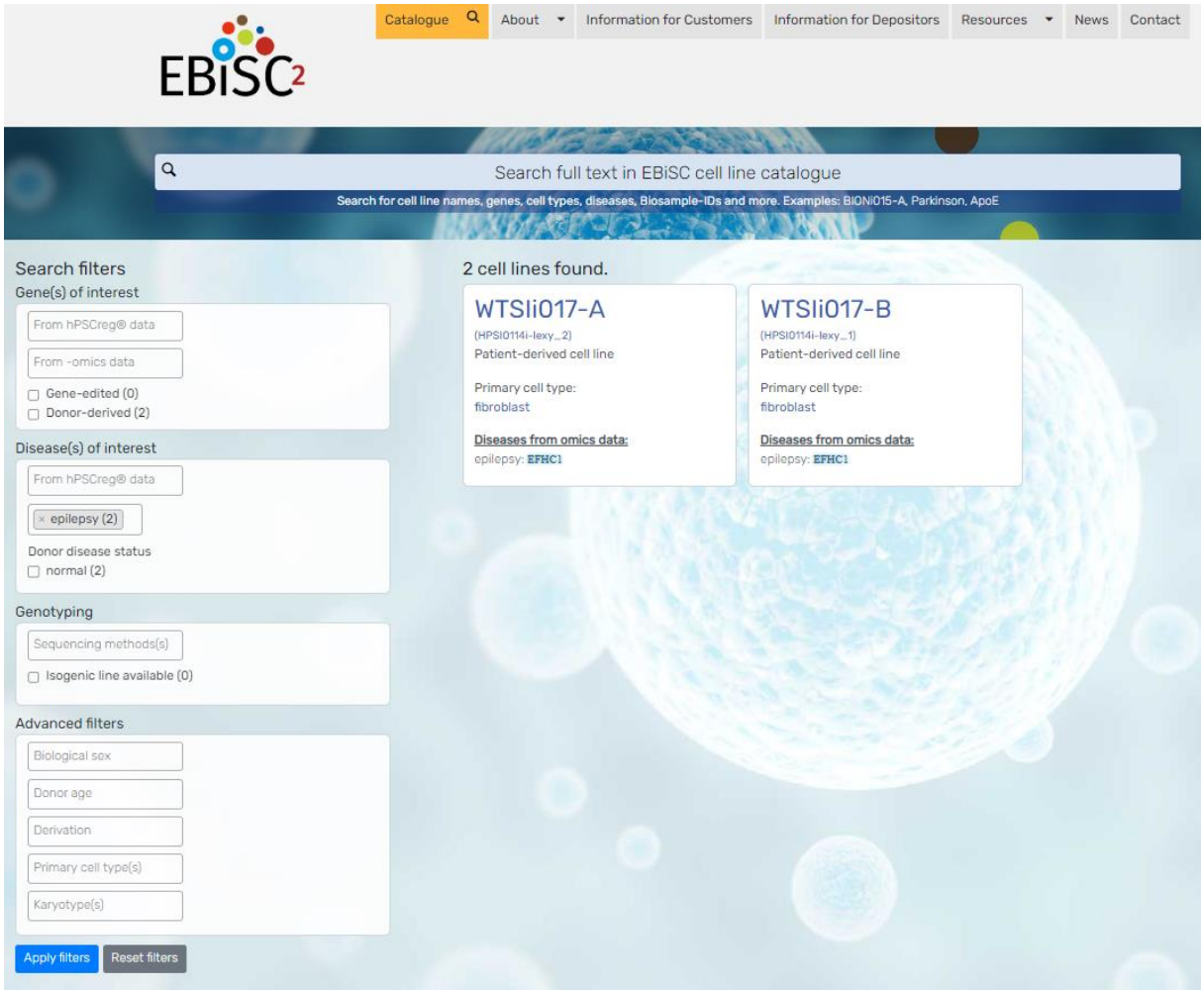


Query 1C – implemented as a proof-of-principle
"I want to find all cell lines with variants in the gene UBE3A*, as analysed from -omic data."* • Please refer to EBiSC Information Sheet: Genomic data processing for catalogue search for details on how the variants have been compiled from selected datasets.
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 (WSTIi017-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".

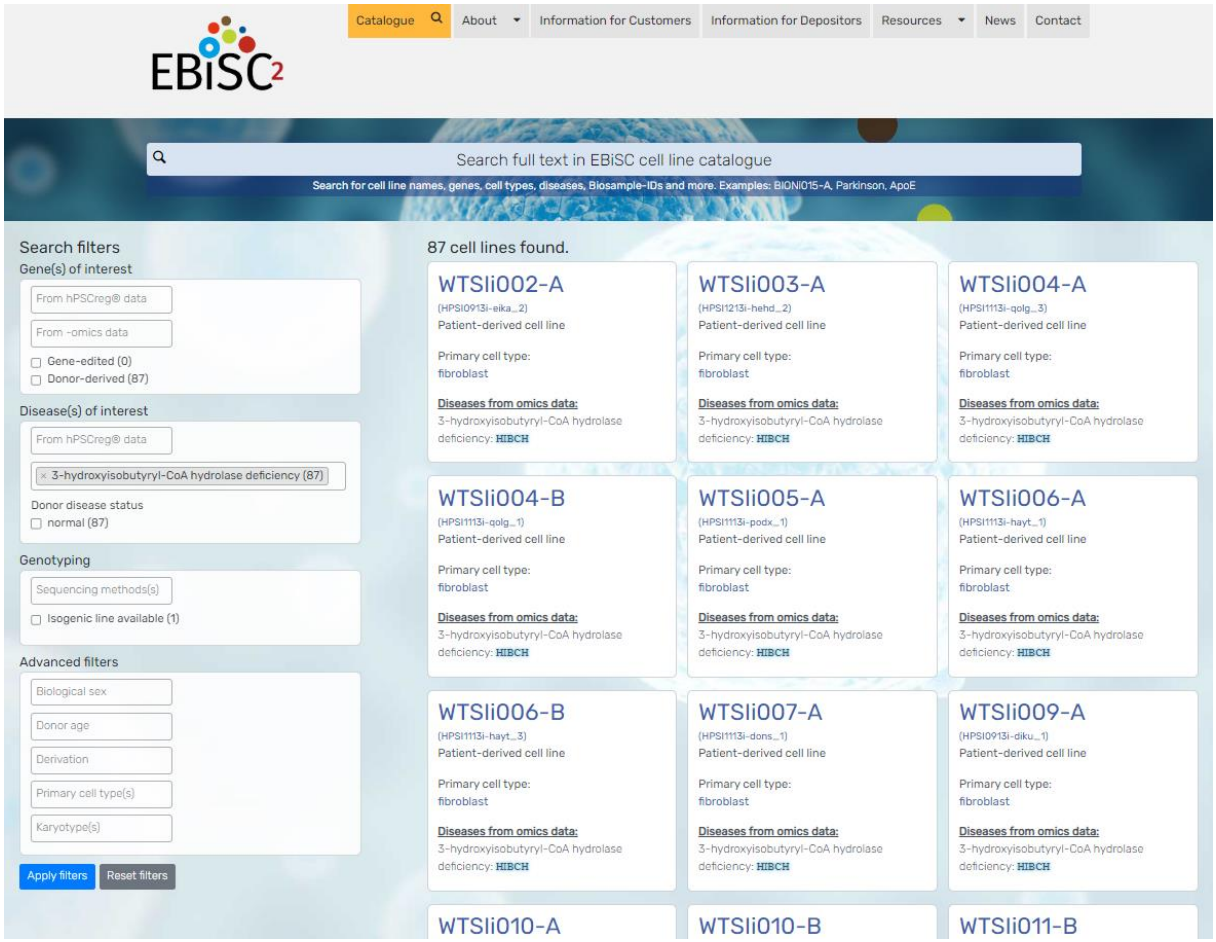


2.2 Use case 2: Lines with genomic variants (from WGS) in disease-associated genes

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.



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.



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.