EBiSC
European Bank for induced pluripotent Stem Cells

ECACC
European Collection of Authenticated Cell Cultures

EBiSC2
European Bank for induced pluripotent Stem Cells

The European Bank for induced Pluripotent Stem Cells

Operated through The European Collection of Authenticated Cell Cultures

Acknowledgements

EBiSC2 is a public-private partnership with diverse stakeholders including clinical, academic and industrial iPSC researchers and users. In this effort we would like to acknowledge the EBiSC2 partners:

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking (JU) under grant agreement No 821362. The JU receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA.

Image on front cover courtesy of Tomo Šarić, Medical Faculty, University of Cologne, Germany

Introducing the European Bank for induced Pluripotent Stem Cells (EBiSC): iPS cell lines available from ECACC

The development of human iPSC technology offers researchers the ability to more accurately generate physiologically relevant models of disease and normal tissues in the laboratory. Advances in iPSC generation have allowed many laboratories to make their own cell lines; however, researchers rarely have the resources needed to establish stocks, undertake quality control and share their own de novo iPSC lines with other laboratories. A pre-existing and established iPSC collection therefore allows iPSC researchers to obtain “off the shelf” access to a large, robust and reliable supply of iPS lines that represent diverse donor to donor variability and which include disease status, normal controls and gene edited cell lines.

EBiSC is designed to address the increasing demand for iPSC lines and has developed an extensive range of high quality, research grade, and fully consented iPSCs which are available to academic and commercial scientists for use in disease modelling and other forms of pre-clinical research. The collection currently holds iPSCs generated from a wide range of donors representing either >30 specific disease backgrounds or healthy normal donors and is growing.

Registration in the human Pluripotent Stem Cell registry (hPSCreg) is a prerequisite for depositing iPSC lines in EBiSC. After the depositor has registered the lines in hPSCreg, EBiSC reviews the consent forms used to collect the original biosamples and the hPSCreg certificate is provided as evidence that minimal ethical and scientific standards have been met. All iPSC lines in the EBiSC collection are banked and quality controlled in standardised processes following stringent standard operating procedures (SOPs), and through ECACC have the benefit of coming from a trusted and internationally recognised Culture Collection with worldwide distribution.

The EBiSC collection also contains a number of lines from StemBANCC and the Human Induced Pluripotent Stem Cells Initiative (HipSci). By ordering through EBiSC, these HipSci lines are available to commercial as well as academic customers.

Detailed information on each iPSC line can be found on the EBiSC catalogue website:
www.cells.ebisc.org

The EBiSC cell lines are available to order from the ECACC website:
www.culturecollections.org.uk/ebisc

EBiSC2
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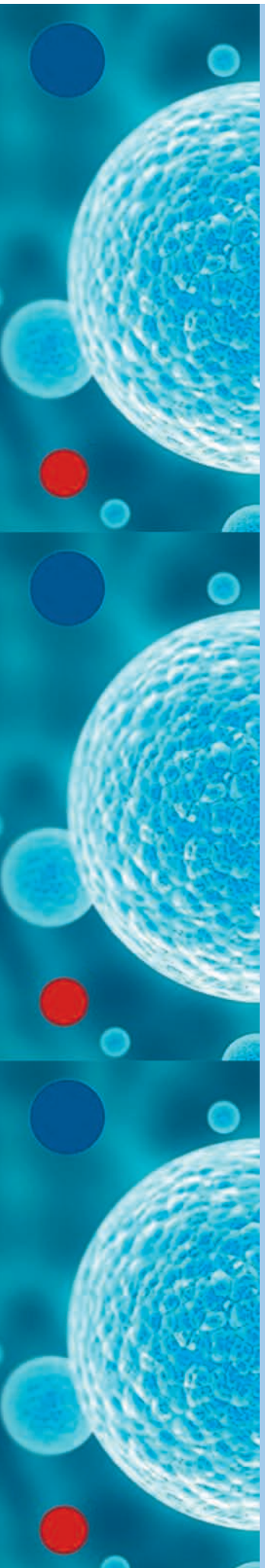
efpia

imi innovative medicines initiative



Range of diseases available

Identification of suitable iPSC lines is essential to ensure accurate research outputs. The wide range of lines from diseased and healthy backgrounds, of both genders, from a wide age range should make finding appropriate cell lines easier. In addition to EBiSC's large collection of well characterised control lines, the collection also holds many isogenic controls. Genetic background variations may confound disease traits and the use of paired isogenic controls and disease representative lines may be used to overcome this challenge. The EBiSC catalogue currently includes iPSC lines from >35 different disease backgrounds; a snapshot of the range of diseases represented is below:

Healthy Controls

The collection contains lines derived from skin fibroblasts, adipose tissue derived mesenchymal stem cells and peripheral blood derived mononuclear cells from healthy volunteers. Lines were generated with mainly non-integrating reprogramming techniques such as Sendai and Episomes. Many lines have been generated and deposited by the HipSci project so they come with extensive characterization data.

Alzheimer's Disease (AD) and Frontotemporal Dementia (FTD)

Cohorts of isogenic ApoE variants (2/2, 3/3, 4/3, 4/4 and knockout) are available through the catalogue, generated both from healthy individuals and individuals diagnosed with Alzheimer's Disease, in addition to lines carrying mutations in TREM2 (knockout, p.R47H and p.T66M) and CD33 (exon2-deletion). IPSCs associated with FTD include genetic variants within C9orf72 (hexanucleotide expansions), MAPT (P301S and/or exon IVS10+16 splice mutants), TDP-43 (A382T) Progranulin (R493X).

Neurological conditions

IPSC lines representing a number of neurological conditions including Migraine, Neuropathy, Pain agnosia, Erythromelalgia and Dravet syndrome (childhood epilepsy) are available through EBiSC due to a number of wide ranging collaborations, including the StemBANCC project.

Mental illness

The EBiSC catalogue includes lines derived from patients diagnosed with unipolar or bipolar forms of major depressive disorder including some familial controls and Schizophrenia.

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Diabetes Research

The EBiSC catalogue contains iPSC lines derived from patients with monogenic diabetes, Familial Type 2 Diabetes and Mature Onset Diabetes of the Young, including access to exome and RNA sequencing data, methylation, genotyping and expression array data for specific cohorts. An age/sex matched cohort of lines developed by Bioneer associated with normal and low birth weights and isogenic variant iPSCs with HNF1A mutations are also available.

Eye Diseases

The EBiSC catalogue contains a number of iPSC lines from patients with retinitis pigmentosa or age-related macular degeneration.

Heart Disease

The University of Cologne has deposited a number of iPSC lines derived from patients with Brugada syndrome, hypertrophic cardiomyopathy, familial long QT syndrome and catecholaminergic polymorphic ventricular tachycardia. The collection includes iPSC lines containing mutations in the *MYH7*, *SCN5A, RYR2* or *KCNH2* genes.

Huntington's Disease and other Trinucleotide Repeat Disorders

EBiSC stocks lines from patients with varying CAG repeat numbers in the Huntington gene (*HTT*). With recent advances in genome editing technologies such as CRISPR, there is great interest in studying diseases like HD to test gene editing applications that can reduce the number of trinucleotide repeats and thus hopefully restore a disease-free phenotype. Other diseases in which this could be applied are spinocerebellar ataxia is the disease ataxia Type 3 and myotonic dystrophies (CTG expansion in the DMPK gene or CCTG expansion in the ZNF9 gene), both also represented in the EBiSC collection, Friedreich's ataxia (GAA expansion in the Frataxin gene), and fragile X (CGG expansion in *FMR1* gene).

Parkinson's Disease

EBiSC stocks lines from Parkinson's Disease (PD) patients carrying a number of mutations including the p.N370S mutation in glucocerebrosidase (*GBA*) and the p.G2019S mutation in leucine-rich repeat kinase 2 (*LRRK2*). A gene-edited cohort is also available, consisting of an alpha-synuclein (SNCA) triplication line (4 alleles) which when differentiated into neural cells, shows a two-fold higher concentration of intracellular α-synuclein, with a set of isogenic controls in which the SNCA triplication has either been partially (3 alleles) or fully (2 alleles) corrected, anda familial control lines. The collection also includes iPSC lines derived from donors with sporadic PD.

Case study: Fully humanised neuronal and astrocyte co-culture platform

The possibility to generate an unlimited amount of mature and functionally active neurons from human-induced pluripotent stem cells (iPSCs) has the potential to radically accelerate neuroscience research & development. However, differentiation protocols can be lengthy, expensive and often produce batch-to-batch inconsistencies in terms of yield, molecular and functional properties.

Neurogenin 2 encodes a neural-specific transcription factor (NGN2), which is expressed in neural progenitors during embryonic development. NGN2 overexpression has been shown to transdifferentiate somatic and pluripotent stem cells towards a neuronal fate bypassing the lengthy process of neuronal differentiation *in vitro*. To simplify and accelerate neuronal differentiation, researchers at Bioneer used CRISPR-Cas9 to genetically modify two new iPSC lines to include a doxycycline inducible cassette in the AAVS1 locus, forcing expression of NGN2 (BIONi010-C-13) and NGN2-T2A-GFP (BIONi010-C-15). When maintained in pluripotent medium, both lines retain expression of self-renewal markers NANOG, TRA-1-60 and POU5F1 with no gain of karyological abnormalities.

Upon DOX induction, both lines show rapid transition to a neural morphology and displayed expression of pan-neuronal markers such as MAPT and TUJ1. After co-culture with hiPSC derived astrocytes, functional properties of iNGN2 neurons were assessed by patch clamp and in multi-electrode arrays and subsequently compared to mouse primary neurons. NGN2-induced neurons (iNGN2) display a resting membrane potential, input resistance and evoked action potential amplitude as well as frequencies that are comparable to murine primary neurons. Hence, BIONi010-C-13 and BIONi010-C-15 can be co-cultured with hiPSC-derived astrocytes to establish a “fully humanised” in vitro neuronal cell model that displays functional properties comparable to the gold standard used in electrophysiology.

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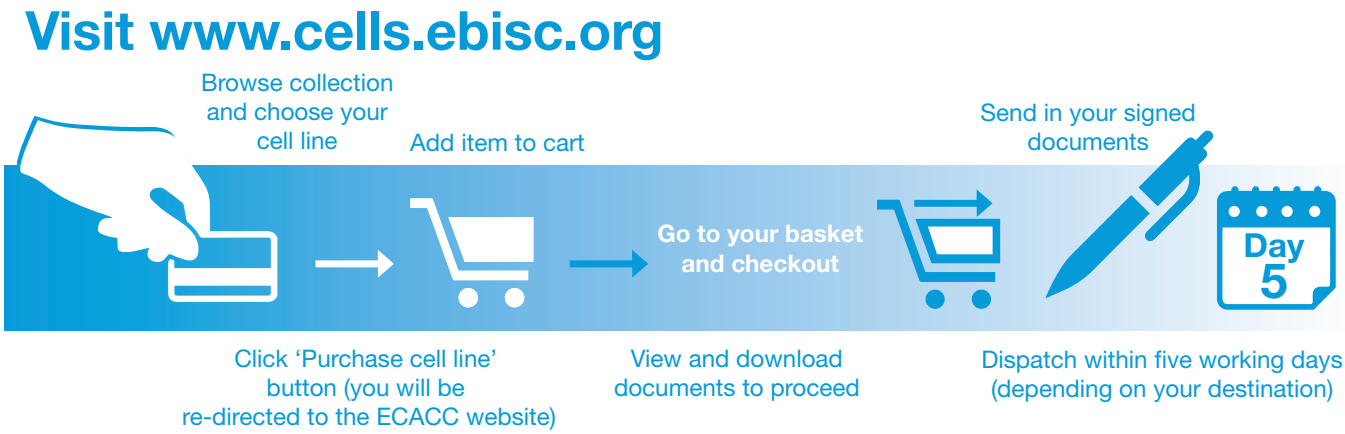
How to order

ECACC is a global distributor of authenticated cell lines. There are a number of different methods for ordering ECACC products. The fastest way to order is online either via Credit Card or Credit Account. Once you have chosen your lines from the EBiSC catalogue you will be redirected to the ECACC website for purchase.



For more information please visit www.culturecollections.org.uk/orderinginfo

ECACC also has an established working partnership with Merck (formerly Sigma Aldrich) for global distribution of ECACC cell lines including EBiSC iPSCs.

What's to come?

EBiSC2 continues to collaborate with iPSC research centres and projects worldwide, ensuring safe long term storage of generated iPSC lines and distribution to other researchers.

Additionally, this second project phase will provide iPSC derived differentiated products, use improved automation strategies for upscaling iPSCs and progenitors, supply iPSCs for commercial use and develop the services currently provided by EBiSC, including iPSC reprogramming, gene-editing, custom bulk banking and iPSC line characterisation.

About EBiSC2

The EBiSC2 consortium is a public-private partnership project supported by the Innovative Medicines Initiative Joint Undertaking 2 (IMI), consisting of, in addition to ECACC, a further 15 organisations, comprising pharmaceutical companies who are members of the European Federation of Pharmaceutical Industries and Associations (EFPIA), small and medium-sized enterprises (SMEs) and academic institutions.

To keep up to date with the arrival of new lines and other developments, please follow us:
Twitter: @EBiSC_cells
LinkedIn: www.linkedin.com/company/ebisc

For specific cell line information requests, please contact Enquiries@ebisc.com

Access to the iPSC Catalogue: www.cells.ebisc.org

About ECACC

ECACC was established in 1985 as a cell culture collection to service the research community and provide an International Depository Authority recognised patent depository for Europe. Over the last 30 years ECACC has expanded and diversified to become one of the premier collections of authenticated cell cultures in the world and this remains the core of ECACC's business. The collection currently holds cell lines representing 45 different species, 50 tissue types, 300 HLA types, 450 monoclonal antibodies and at least 800 genetic disorders as well as over 1000 iPSC lines.

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