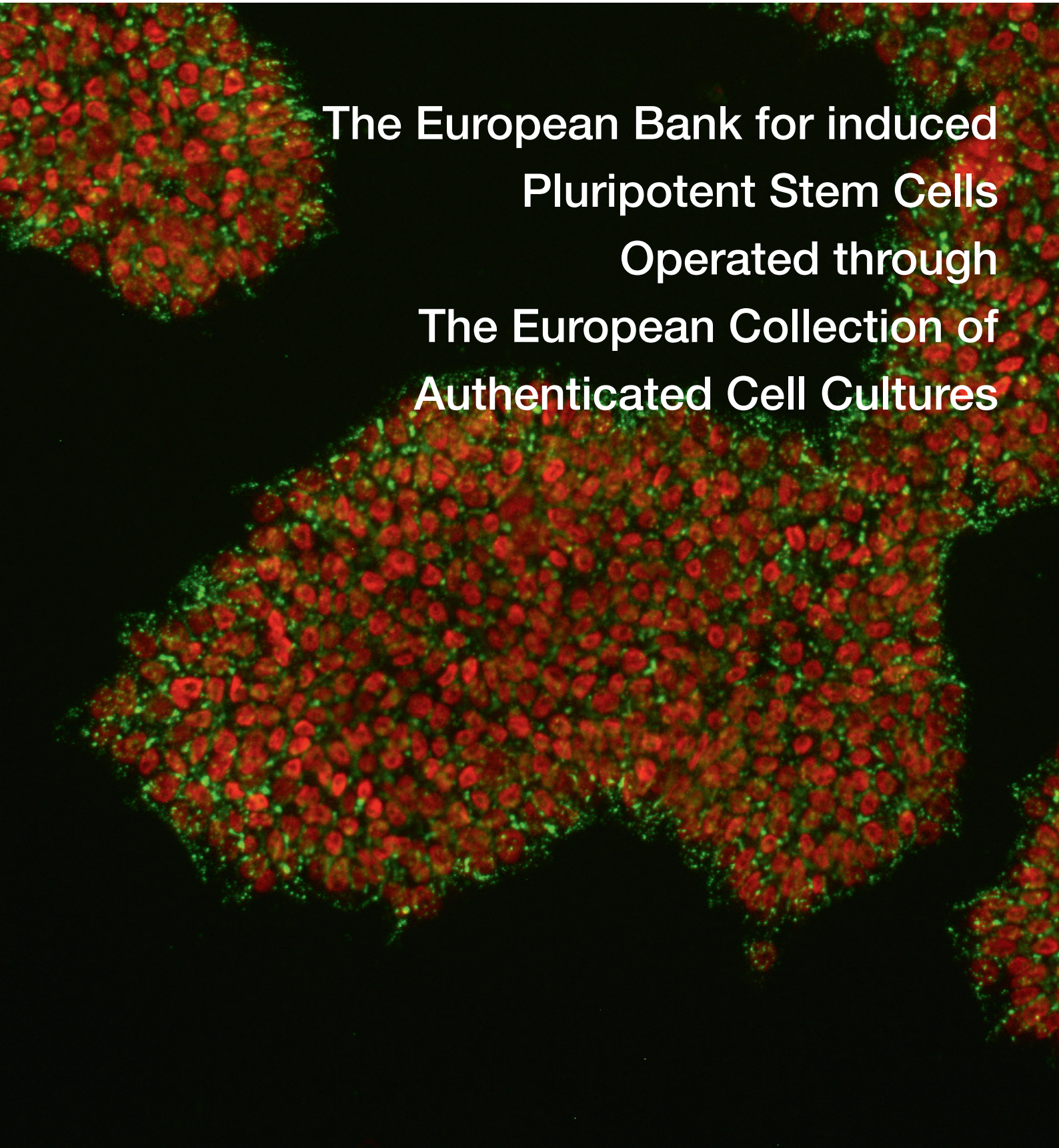
EBiSC
European Bank for induced pluripotent Stem Cells

ECACC
European Collection of Authenticated Cell Cultures
Operated by Public Health England



The European Bank for induced Pluripotent Stem Cells Operated through The European Collection of Authenticated Cell Cultures

Acknowledgements

The EBiSC Consortium represents relevant stakeholders including clinical, academic and industrial iPSC researchers and users. In this effort we would like to acknowledge the EBiSC partners:

DefiniGEN
CMR[B] Centre de Medicina Regenerativa de Barcelona Centro de Medicina Regenerativa de Barcelona Center of Regenerative Medicine in Barcelona
Inbiomed Regenerative Medicine Research Centre
Fraunhofer IBMT
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Image on front cover courtesy of Tomo Šarić, Medical Faculty, University of Cologne, Germany

efpia
imi innovative medicines initiative

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 over 400 iPSCs generated from a wide range of donors representing either specific disease backgrounds or healthy normal donors. The collection is steadily growing.

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 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:
https://cells.ebisc.org

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

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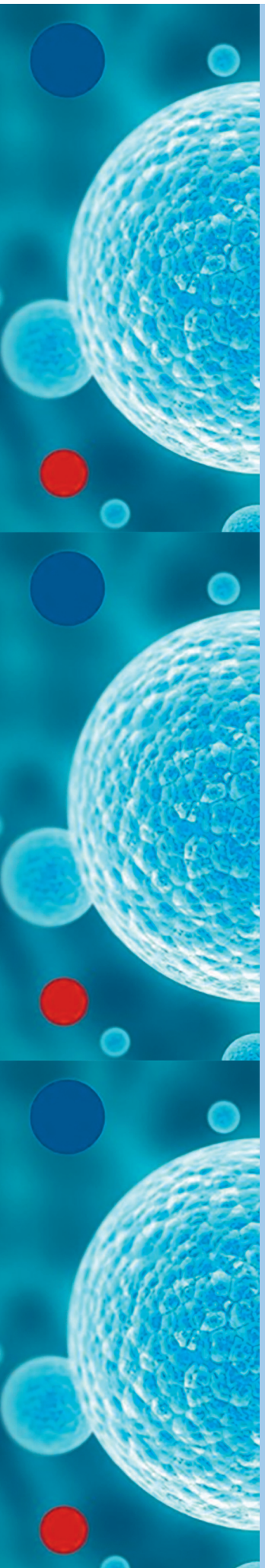

Range of diseases available

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 the 250 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 26 different diseases; a snapshot of the range of diseases represented is below:

Healthy Controls (250 lines)

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) (>22 lines)

Isogenic lines with high relevance to neurological disease traits have been created. All are based on a healthy control line and have been CRISPR gene-edited to carry Alzheimer's associated mutations in TREM2 (knockout, p.R47H and p.T66M), CD33 (exon2-deletion), and ApoE (2/2, 3/3, 4/3, 4/4 and knockout). Lines of interest for FTD research include C9orf72 lines from 3 different patients, MAPT (P301S and/or exon IVS10+16 splice mutants), TDP-43 mutant (A382T) line and a line carrying the R493X progranulin mutation.

Bardet-Biedl Syndrome (>22 lines)

Bardet-Biedl syndrome (BBS) is a ciliopathic human genetic disorder with pleiotropic effects. It is a rare autosomal recessive inherited genetic disorder, for which mutations in many different genes can be responsible. The HipSci project has deposited 22 BBS iPSC lines into EBiSC that come from individuals in which the disease-causing mutation is not in the same gene across the cohort of individuals.

Depression and Pain (15 lines)

A very recent addition to the EBiSC catalogue is a set of lines from patients diagnosed as having either unipolar or bipolar forms of major depressive disorder, including some familial controls. Lines for the study of pain include erythromelalgia I (with mutation in *SCN9A* gene) and congenital insensitivity to pain (with mutation in the *SCN11A* gene). An isogenic control line for one of the erythromelalgia patient lines will soon become available.

Diabetes Research (>13 lines)

The EBiSC catalogue contains 13 iPSC lines (HipSCi) derived from patients with monogenic diabetes. Exome and RNA sequencing data is available for all 13 iPSC lines, 11 have additional methylation and genotyping and expression array data is available for 2 lines. In addition, two lines developed by Bioneer are age/sex matched lines with normal and low birth weights, also linked to diabetes.

Eye Diseases (>20 lines)

The EBiSC catalogue contains a number of iPSC lines from patients with retinitis pigmentosa or age-related macular degeneration. All of the lines have been deposited by the University of Newcastle with an age range of 45-89 years.

Heart Disease (>23 lines)

The University of Cologne has deposited a number 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 (2 lines)

EBiSC stocks two lines from a patient with a 42 CAG repeat in the huntington *(HTT) gene*. 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 (28 lines)

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*). There is also an alpha-synuclein (SNCA) triplication line (4 alleles) which when differentiated into neural cells, shows a two-fold higher concentration of intracellular α-synuclein. In addition, the collection includes a set of isogenic controls in which the *SNCA* triplication has either been partially (3 alleles) or fully (2 alleles) corrected. The collection also includes iPSC lines derived from donors with sporadic PD.

Case study: New panel of heart disease-specific iPSC lines for in vitro disease modelling and drug testing

Current therapeutic strategies for a variety of inherited cardiac conditions are mostly symptomatic and they neither take into account phenotypic and genetic disease heterogeneity nor inter-individual differences in the response to drugs. Cardiac myocytes derived from disease-specific iPSCs represent a novel *in vitro* system with an unprecedented potential for generating new mechanistic insight into diseases, pathophysiology and enabling assessment of drug efficacy and safety with better reliability and predictability for individual patients than currently used preclinical models.

A new set of high quality iPSC lines from patients with genetic heart diseases for *in vitro* use has been created by the team of scientists led by Tomo Šarić and Jürgen Hescheler at the Uniklinik Köln (UKK) in Germany with support from the Innovative Medicines Initiative (IMI) and Bayer AG as well as clinical collaborators at the Heart Centre Cologne (Daniel Steven) and the Institute for Genetics of Heart Diseases at the University Hospital Muenster (Eric Schulze-Bahr). The set includes cell lines derived from patients with long QT syndrome type 1 (UKKi029-A,B,C carrying mutation in *KCNQ1* gene - lines available soon), long QT syndrome type 2 (UKKi018-A,B,C; UKKi019-A,B,C and UKKi023-A,B,C lines carrying different mutations in *KCNH2* gene), Brugada syndrome (UKKi024-A,B,C line carrying mutation in *SCN5A* gene) and hypertrophic cardiomyopathy (UKKi025-A,B,C line carrying mutation in *MYH7* gene).

All lines were generated from donated blood cells using highly standardised non-insertional reprogramming procedure under feeder-free conditions. They underwent extensive characterization to ensure quality in terms of sterility, viability, identity, pluripotency, genetic stability, and absence of HIV, HBV, HCV and reprogramming vectors. This data and the associated clinical information are accessible on a searchable public registry for human pluripotent stem cell lines, hPSCreg https://hpscreg.eu/

These iPS cell lines represent a valuable resource of lines for the study of disease and the development of new treatments. Their value can be further increased by employing gene editing technologies to generate isogenic control lines or transgenic lines expressing lineage- or pathway-specific reporters to enhance developmental studies or establish specific drug screening assays.

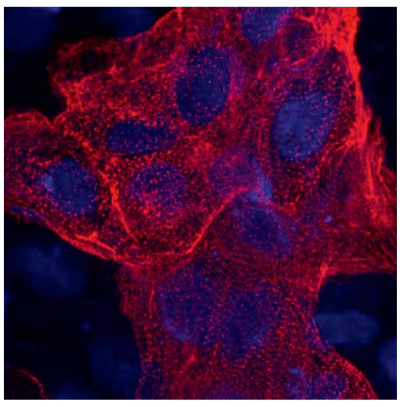

Image: Cardiomyocytes derived from iPSC line of a patient with hypertrophic cardiomyopathy carrying a mutation in *MYH7* gene encoding a myosin heavy chain beta (MHC-β) isoform. Red indicates the muscle protein alpha-actinin and blue the cell nuclei.

Image courtesy of Tomo Šarić and Karsten Burkert, Medical Faculty, University of Cologne, Germany

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.phe-culturecollections.org.uk/orderinginfo

What's to come?

A number of additional lines from the ADAPTED project for Alzheimer's disease research will be added to the collection shortly. Lines are edited sub-clones carrying ApoE4/E4, E3/E3, E2/E2, E3/E4 and KO from an age matched female control donor, and age matched male and sex affected donors carrying ApoE4/E4. Other new lines include 19 lines from individuals with Dravet syndrome, a form of epilepsy, and 20 lines from individuals with focal segmental glomerulosclerosis (FSGS), a form of kidney disease. In addition, over 400 lines from StemBANCC will also be added to the EBiSC collection.

ECACC has an established working partnership with Merck (formerly Sigma-Aldrich) for global distribution of ECACC cell lines. A similar agreement for the distribution of EBiSC lines has been agreed and will be implemented by the end of 2017.

About EBiSC

The EBiSC consortium is a public-private partnership project supported by the Innovative Medicines Initiative (IMI), consisting of, in addition to ECACC, a further 26 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 EBiSC on Twitter @EBiSC_cells

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

Information on EBiSC: https://ebisc.org
Access to the iPSC Catalogue: https://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 400 iPSC lines.

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