Executive Summary

Period 2 (January-December 2015)

Project rationale and overall objectives of the project

The European Bank for Induced Pluripotent Stem cells (EBiSC) Consortium will establish a facility for distributing qualified human, disease representative stem cell lines for research. The EBiSC cell line repository will make future drug development more effective and provide resources for future EU-funded iPSC projects.

Key objectives of EBiSC are to establish a single European iPSC repository with the unique identifying features of a catalogue created by user demand. It will: provide sustainable supply of quality assured, research grade lines on a not for profit basis; develop procedures for engaging a wide scientific and clinical community in a network of cell line derivation centres; apply scientific excellence for standardisation of optimised methodologies for deriving iPSC, their cryopreservation, recovery and differentiation; and demonstrate standards in quality control for the routine banking, characterisation and distribution of cell lines. The cell line distribution model will be supported by a harmonized ethics and legal governance framework and information management system developed to accommodate user-generated content. It will establish mechanisms to facilitate ongoing stakeholder enhancement of the biobanking process in support of a strategic business strategy based on a phased execution to ensure self-sustainability.

Overall deliverables of the project

Demonstrating effective project management, to include both strong financial and strategic leadership, developing the banking business rationale tuned to user's needs and linking this to an EBiSC brand are key deliverables from overall project development. A key consequence of developing a better understanding of user needs will lead to the recruitment of additional EPFIA companies as integrated partners.

Procuring cell lines that researchers will use to constitute the diversity collection and demonstrating effective infrastructure for centralized processing of these, storage and international distribution by harmonized protocols, are core deliverables from the bank operations. Phenotypic assay data from the use of selected cell lines and gene edited derivatives from the collection will ensure that the project delivers validation on all elements of the cell line supply chain.

The project will provide deliverables that reflect a movement beyond current art status in platforms for improved cell processing, cell line QC testing, information management and innovation in human cell line banking governance models. Deliverables related to the development of an EBiSC cell line collection that researchers are using and operations for engagement with paying customers will be key for future self-sustaining business.

Summary of progress versus plan since last period

The EBiSC iPSC Catalogue consists of the two components*:*

***Foundational Collection*:** This consists of a conservative estimate of **114** lines in process. The Hot Start activity for this has **47** processed iPSC lines by M24. This remains at 17% fewer than originally planned due to a combination of factors concerning nominated existing lines. These include a delay in central process QC due failure to comply with EBiSC SOPs for cell vial preparation (partner 13: KNAW) and failure to obtain ethical clearance to contribute lines into the collection (partner 18: BiP). Seeking completion of the Hot Start contribution was de-prioritized in Period 2 at the recommendation of the Interim Review panellists. The EBiSC project has nominated 200 lines from the Sanger hiPSCi project, for the preparation of vials for distribution by EBiSC and in Period 2, **31** lines had been contributed. There was a delay identifying which lines could be supplied with the appropriate consent from the Cambridge BioResource.

The StemBANCC and EBiSC co-ordinators and respective consortia had agreed to place a collaboration agreement to enable the cell line transfer with data (project foreground) into the EBiSC Foundational Collection in Period 2. This did not take place in Period 2 due to a delayed ability for StemBANCC to nominate who the cell line owners (thus depositors) are of these lines in the StemBANCC project. Cell line transfer with data is anticipated to begin in Period 3.

Pleasingly, an unexpected allocation of thirty six (**36**), third party lines (Partners 2 and 15) were deposited and processed by the Central Facility. The public launch of the catalogue was postponed into Period 3 to enable a substantial number of lines to be made available to DH-CC (partner 17a).

The Consortium Board (CB) has approved in Period 2 a further eight new commissioned cell line project proposals. In the New Cell Line Commissioning (NCLC) workstream, fifty five (55) new donor samples were processed for

reprogramming (23 at partner 3(RC) and 32 by other Derivation Centres), 6 new gene edited derivative lines were initiated. Approximately 270 future novel patient and gene edited cell lines are destined for the Foundational Collection. The total budget committed to these new derivation projects is €1,435,140, of which €1,076,355 is grant and €358,785 EFPIA contributions. These proposals were instigated in direct response to EFPIA partner interests in accessing novel lines.

Eighty two (82) qualified lines were distributed (21 to partner DH-ECACC, 45 to Fraunhofer IBMT, 16 to other users) and more than 3200 vials have been banked overall for all the lines in the catalogue.

***Collaboration Collection*:** (cell lines generated in other EU funded projects). EBiSC has identified a large number of existing EU funded iPSC generation projects, with conservative estimates that the catalogue can be augmented by an additional 2,500 distinct patient derived lines. Working with the H2020 unit on Innovative tools, technologies and concepts in health research (Health Directorate), we have identified at least 32 projects to contact and work was initiated in Period 2.

Work-package highlights underpinning EBiSC workflow

Standard Operating Procedures (SOPs) for the central workflow continue to be deployed widely in the consortium. Iterative adaptation of the ethical and legal governance frameworks that constitute the Bank has taken place. Adaptation of the EBiSC documents for consent, cell line deposition and access has enhanced banking operations.

The central workflow operates now by an established quality management system (QMS). From successful multi-site experiments with different cell lines, recommendations were made on protocols for an accelerated and improved expansion of cell lines, using bioreactor systems, at the central facility and fully operational mirror site (Sulzbach/Germany).

An international standard cell line Quality Control (QC) platform is operating with determination of cell line identity, plus also both gene and protein marker expression confirmation of pluripotency.

Unique data sets from collaborative disease modelling using project lines have been generated based on the distribution to EFPIA partners of cell lines. Progress has taken place in the refinement of protocols for generating both endoderm and ectoderm derived cell types for phenotyping and the development of specific assays of disease modelling based on these.

Work-package highlights underpinning EBiSC business strategy

An additional survey was made of the research community, plus feedback captured on what users want to see in the Foundational Collection with EBiSC consortium participation at the ISSCR annual conference (June, 2015, Stockholm). Version 2.0 of the business plan is being formulated. Inter-operability with data flow for a number of IMS services (IMS, hPSCreg, Biosamples and ECACC) has been automated and tested. EMBL-EBI setup the data validation service to check for consistent of cell line meta data across these four services. The internal test version of the cell line catalogue was launched and user testing conducted. Synchronization across IMS services is now live.

Progress towards meeting planned Deliverables & Milestones

Of the 23 deliverable reports due in the second reporting period (P2), 20 are now submitted or pending submission. The remaining 3 will be submitted in Period 3 as they relate to the need to update the EBiSC Policies and Contracts Manual, design the next version (V2.0) of the Business Plan and decide on the precise timing of the public launch of the cell line catalogue.

Of the 27 project Milestones due in the second reporting Period (P2), 24 are now submitted or pending submission. The remaining 3 will be submitted in Period 3 as they relate to the need to be kept updated as the project develops. These include a re-review of the iPSC regulatory and ethical landscape, completion of the collection of data/information from depositors and users and the ongoing promotion of EBiSC, receiving and processing orders.

New project partners

The following partners have joined the consortium:

- Bayer Pharma AG (joint the consortium on 1 July 2015)
- Eli Lilly & Co. (joint the consortium on 1 November 2015)

- Roslin Cells Sciences (replacing Roslin Cells, partner 3, since 1 December 2015)

The investigator base of partner 15 UCL has been extended:

- 15-b: UCL-b Division of Biosciences – Department of Cell and Developmental Biology (Lab of Saverio Tedesco)
- 15-c: UCL-c Great Ormond Street Hospital Children's Charity (GOSHCC) – Institute of Child Health Developmental Neuroscience (Lab of Francesco Muntoni)

Significant achievements since last report

Executive Office has prepared V2.0 of the Strategic plan. Amendment 1 to the GA has been approved by the IMI-JU and the EBiSC project has successfully had an Interim (progress) Review. The Foundational Collection has increased 1.5 fold. Reference iPSC continue to be used throughout the workflow. Foundational Collection cell lines have been delivered to DH-CC. Donor consent forms, harmonized deposition and user/access agreements have been deployed and are being optimised based on in the field validation. Ongoing gap analysis of what EFPIA partners need defined the commissioning of new lines. All aspects of central processing are in place. In readiness for the EBiSC Catalogue launch the ECACC website has been modified to accommodate EBiSC including faceted searching and reciprocal feeds from the EBiSC main Information Management System (IMS). Successful processing of a test order has occurred through to delivery to end user. The business strategy to recruit EFPIA partners into the consortium has paid dividends with Bayer and Lilly joining. Expansion of the investigator base in the project to take in response of the Interim Review has occurred, to make stronger links to the clinical healthcare sector for potential procurement of patients with unaddressed childhood disease.



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Access to the EBiSC iPSC Catalogue
https://cells.ebisc.org
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