ToxBank

Deliverable D4.4

Evaluation Process for Suppliers of hPSCs

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1. Executive Summary

1.1. The ToxBank data warehouse

The ToxBank data warehouse will provide a web accessible shared repository of know-how and experimental results to support the SEURAT-1 cluster in developing a replacement for *in vivo* repeated dose toxicity testing. The information within the ToxBank data warehouse is uploaded from the research activities of the cluster partners as well as relevant data and protocols from other sources, such as public databases. The data will be collected to enable a cross-cluster integrated data analysis leading to the prediction of repeated dose toxicity. The warehouse should continue to provide access to this knowledge after SEURAT-1 for academic and industrial uses, as a potentially self-sustainable operation.

1.2. Requirements gathering

Prior to designing the ToxBank data warehouse, the ToxBank consortium implemented a detailed requirements gathering exercise. As part of this process, ToxBank partners visited around 20 partner's sites and conducted interviews with individual scientists. These discussions covered a variety of activities including, cell differentiation, cell engineering, biomarker identification, dose response analysis, toxicity testing, 'omics experiments, chemical analysis, and cell banking. The interviews focused on understanding in detail what specific steps were performed across a variety of tasks performed, and this can only be accurately recorded by observing the work. Notes were taken along with examples of documents used. This information was collected to ensure any system design both meets the needs of scientists across the entire cluster at the same time as fitting within current workflows. The interviews along with other requirements gathering exercises resulted in over 1,000 separate notes and 40 tasks outlined. The ToxBank team organized and analyzed the notes, descriptions of tasks, and associated documents as a group and developed a design for the ToxBank data warehouse directly from this analysis. The design was subsequently tested using a paper prototype where the major components of the user interface were sketched out on paper. This allowed for further testing of the usability of the system, resulting in a refinement of the user interface where problems were encountered using this mock-up to perform different scenarios.

1.3. ToxBank overview

ToxBank is being developed to manage and provide access to all protocols and experimental data across SEURAT-1 to support an integrated data analysis.

Once a new protocol has been developed, documented, and reviewed within the partner's organization, it can be uploaded to the ToxBank data warehouse by the laboratories' principal investigator. ToxBank will provide guidelines concerning the content and organization of this document. The protocol will be loaded through the ToxBank user interface where additional information will be entered and associated with the protocol. This includes summaries of the protocol, identification of the protocol's owner, authors of the protocol, and a specification of who should have access to the protocol. In addition, keywords based on a cross-cluster keyword hierarchy, will be assigned to support searching. Study data is loaded in a similar manner;

however, a protocol must have been already loaded that defines how individual steps of the study were performed and what data is generated. The data should be in a defined and standardized format agreed across the cluster. Once any new protocols or study data are loaded into the system, a regularly scheduled email alerting scientists across SEURAT-1 who have registered an interest in a specific type of information is sent out.

The protocols and data loaded can be accessed via a simple free text search. This will return summaries of any information matching the query. The protocols or study data can then be viewed or downloaded directly along with links to related information, such as the Gold Compound wiki.

Where the investigator does not have permission to view the specific protocol or study data, only the summary information will be displayed. The investigator is then free to contact the principal investigator who loaded the content to request access rights. ToxBank will provide documents to support any bilateral agreements between the two parties. Once an agreement is in place, the principal investigator who loaded the information would modify permission levels accordingly.

ToxBank Vision

The focus of the first phase of the ToxBank data warehouse project is the development of the unified data access. As this is being implemented over the next year, the ToxBank consortium will continue to collect requirements for the integrated data analysis to be implemented as phase 2 of the project.

The benefits of this approach include:

- The approach provides access to existing and new protocols and data, as well as facilities for uploading information through a simple web interface
- The use of standardized data templates and controlled terms supports cross-cluster experimental consistency and will enable an integrated analysis
- The approach supports protocol development and collaboration which is close to current work activities, especially the SEURAT-1 focus on experimental development
- This approach will link public databases and in-house data

2. Introduction

This has been developed from the joint SCR&Tox-ToxBank Publication at SEURAT-1 annual meeting April 2012 and completion of deliverable 4.2 . The prototype process for evaluation of suppliers comprises three phases of assessment which are intended to assist toxicologists without expertise in selection of appropriate cell line suppliers to make their own selection of source of cells.

3. Requirements Analysis

Phase 1: This comprises an investigation by ToxBank to ensure that core quality controls are under taken by the supplier. This is based on the checklist in 4.2 of Del 4.2.

Phase 2: This involves NIBSC in distributing a questionnaire to each supplier requesting completion the table to indicate how the supplier meets the requirements of best practice in the banking testing storage and distribution of hPSCs according to the International System of Cell Banking Initiative (ISCBI, 2009). This has been addressed for specific application in SEURAT-1 and the necessary questions derived from section 4.2 of Del 4.2 and the draft questionnaire is shown in Figure 5.

Phase 3: ToxBank will review the responses from Phase 1&2 and classify the information received into one of 4 levels as follows:

Level 1: Basic and essential QC claimed to be performed – cell line identity, mycoplasma testing, cell phenotype characterization

Level 2: Level1 met and response provided on compliance with quality criteria

Level 3: Levels 1& 2 met and response to level 2 indicates up to ¾ requirements of level 2 are addressed

Level; 4: Levels 1 met and response to level 2 indicates compliance with more than ¾ points to consider (ISCBI, 2009)

Each level met is asterisked if additional data is available which is not specifically required in ISCBI 2009. Such additional data will be highlighted where it is of direct relevance to toxicological studies.

Evaluation Form for Suppliers of Cell Lines

Complete the following sections to show how the supplier meets the criteria for supply of human cells and cell lines

Ethical Issues

How does the supplier address the requirement that:

1) for each cell line there is traceability to fully informed consent on the original tissue without exposing the identity of the donor.

Give explanation here:

2) any constraints implemented on the use of the cells are documented and made available to recipients of lines?

Give explanation here:

During the consenting process how was the donor was aware that :

1) derived lines may be exploited commercially but that donors would not receive personal financial benefit.

Give explanation here:

2) derived hPSCs could be used for a wide range of purposes in different laboratories and may be tested for genetic characteristics, microbiological contamination and other features of the cells.

Give explanation here:

Commercial Issues

How does the supplier identify the owner/s of the cell line and whether ermission has been granted by the owner/s or their agents for the intended use or is the line released for general research without constraint (see also ethics criteria re: donor constraints).

How does the supplier assure that the intellectual property rights relating to each cell line or any components used to derive the cell line (e.g. DNA constructs) are clear and would not influence their use for commercial application?

Give explanation here:

What constraints does the supplier place on commercialisation of the cell line?

Give explanation here:

How does the supplier record and/or publish information on the derivation procedure for each cell line?

Give explanation here:

Banking (culture, preservation and storage)

Does the supplier operate a tiered banking system for supplied cells and how does this meet the recommendations in ISCBI (2009) for

1) Procurement of Cell Lines

Give explanation here:

2) Cell Banking Procedures and Documentation

Give explanation here:

3) Cell Bank Quality Control

Give explanation here:

4) The Process of Releasing Cell Banks

Give explanation here:

Testing and Characterization

Please complete the following table to exlain how the supplier completes quality control and characterisation:

Test	Specific Methods and controls used	Release criteria
Identity of cell line		
Karyotype		
Sterility (bacteria/fungi)		
Mycoplasma		
Viral contamination		
Post-thaw recovery		

Pluripotency		
Growth characteristics		
Antigen expression		
Gene expression		
Genetic stability		

The supplier is encouraged to respond to the recommendations in ISCBI (2009).

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