CultureTrax

Controlled study measuring the impact of a new software application on reproducing a stem cell protocol

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Summary

This NIH-funded controlled lab study tested the impact of CultureTrax software on scientists' ability to replicate a protocol they had not run before, demonstrating dramatically improved success rates and reduced time for more complete documentation versus a skill-matched control group using conventional methods .

Many stem cell scientists experience challenges reproducing protocols they have not previously run. Much of this difficulty arises from incomplete documentation of highly complex protocols and associated material recipes in typical scientific publications and other source documents. In addition, troubleshooting new protocols is difficult using paper lab notebooks, in which it is time-consuming to capture and later find critical details.

Here we report on a controlled laboratory study of the impact of the CultureTrax® software on how successfully stem cell scientists could reproduce and document a protocol they had not seen previously.

CultureTrax® software

CultureTrax is cloud-based software designed for stem cell research. A key feature is the protocol template that can readily be created and updated by users, which is built from actions with associated materials and methods (Figure 1). Current protocols, recipes, experimental work and results are easily shared within a lab group.

Scientists select protocol templates and start culture tracks with specific cells contained in culture vessels or wells. Each day as the experiment proceeds, the actions called for in the protocol provide both information needed for execution and rapid, efficient recording of experimental details and results.

CultureTrax automatically creates linkages between data objects that are maintained across experiments or even in different labs (Figure 2). For example, patient fibroblasts reprogrammed in a cell banking lab may be expanded, differentiated into two type of cells and combined into a disease model to test drugs in a different lab. A researcher could use these data linkages to find patient genomic data collected by the banking lab years before.

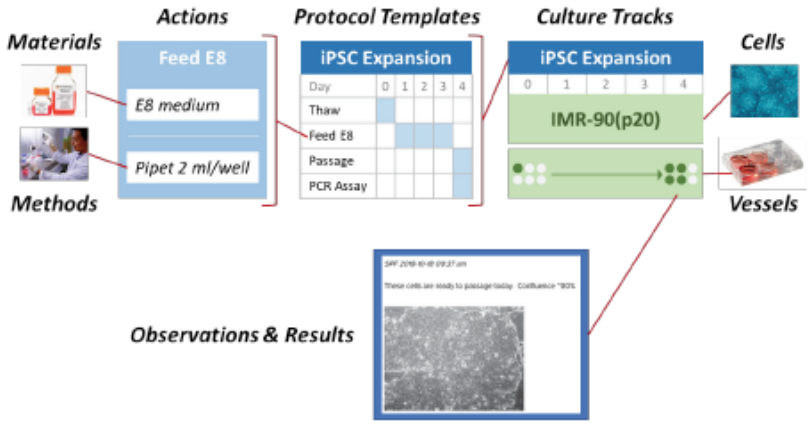


Figure 1 — CultureTrax combines user-defined actions, arranged on a timeline to form protocol templates, which can be used as the foundation for an experiment, updated as processes evolve and shared within a lab group.

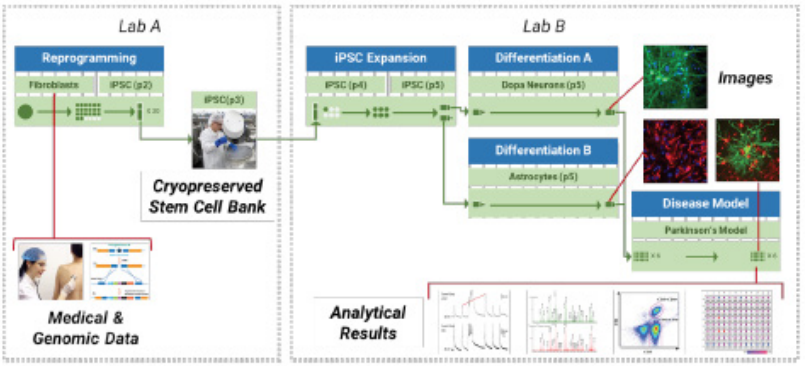
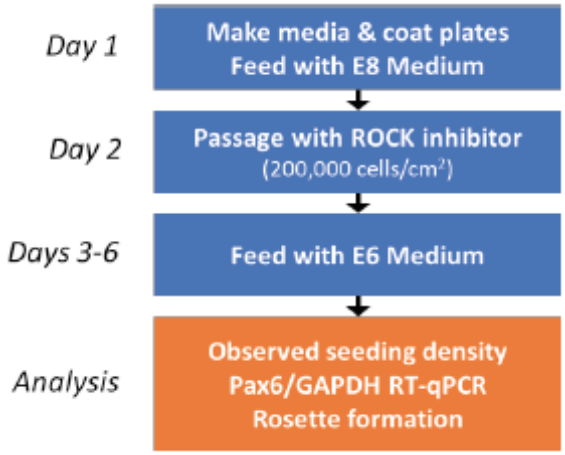


Figure 2 — The data structure within CultureTrax creates links between all of the experimental details of a project over time, connecting culture histories to analytical results.

Study cell culture protocol

The culture protocol (Lippmann et al, Stem Cells 2014) used in this study induces neuroepithelial differentiation from iPSCs. On Day 1 IMR90-4 iPSCs are fed with E8 medium. On Day 2 the cells are passaged and then fed for 4 days with E6 medium, which has the same composition as E8 but missing the growth factors FGF2 and TGF-β1 (Fig 3).



The published reference emphasized the importance of the correct seeding density (2.0 X 10^5 cells/cm2) for the Day 2 passage. The actual seeding density was estimated microscopically. The presence of cell 'rosettes' (an indicator of neuroepithelial differentiation) was assessed microscopically on Day 6 of the culture.

RT-qPCR was performed for both the Pax6 neuroepithelial differentiation marker and GAPDH as an internal reference. The fold-difference in the Pax6/GAPDH ratio between cells passaged into E6 and control cells maintained in E8 was calculated.

Figure 3 — Overview of the study's experimental plan for a neuroepithelial differentiation protocol.

Study methodology

The control group (n=12) was supplied with the original and supplemental references, manufacturer instructions, and a list of materials. They were asked to translate these resources into a personal culture plan that could be followed by other scientists without further clarification. The software group (n=15, experience-matched to the control group) was trained on the software using the protocol translated into a protocol template.

The control group then executed their plans in the lab over 3 evenings, using a lab notebook to document their results. The CultureTrax group executed the protocol in the lab using a prototype version of the software run on iPads in the lab to guide and document their work.

The study was conducted in the teaching laboratory at Madison College.

Translating references into culture plans

The control group translated the published references and other resources into personal culture plans, which were evaluated against a standard over 12 categories using a 5-point scale. The average translation score was only 65%(range 18-97%). The scores showed a loose correlation with years of experience in stem cell culture. These results underscore the challenges involved in translating a published protocol into a plan with enough detail and accuracy to be successfully executed.

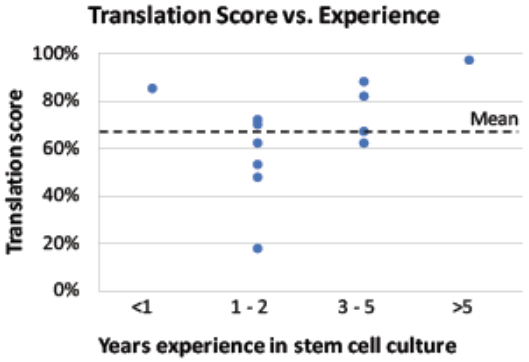


Figure 4 — The ability of the Control Group scientists to successfully translate the original references into a detailed culture plan varied widely.

Completeness of documentation

Both groups were instructed to record enough detail in their notebook or the software to 'permit troubleshooting of the experiment'. Their documentation was evaluated for accuracy and completeness in three categories (material batch records, lot numbers of materials and observations of cell morphology) using a 5-point scale. The CultureTrax group subjects had significantly better scores in these categories.

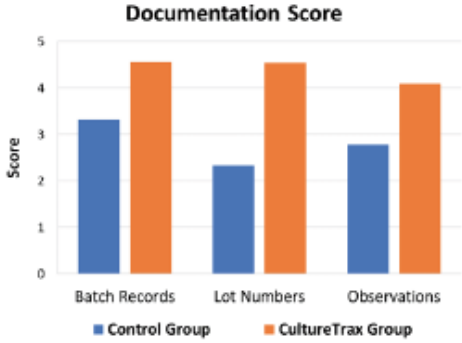


Figure 5 — Both groups were evaluated for completeness of their documentation of critical troubleshooting parameters.

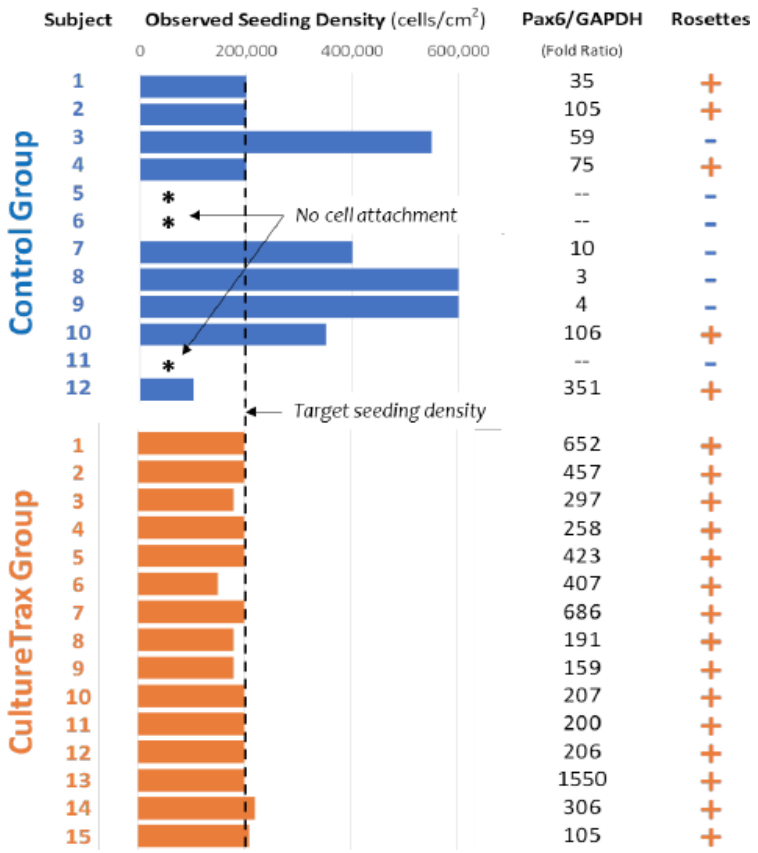
Time for lab work & documentation

All participants were timed in each session for both hands-on execution and documentation. The CultureTrax group spent an average of 32% less total time compared to the control group (113 +/- 27 minutes S.D. versus 167 minutes +/- 38 minutes S.D.).

Cell culture results

As shown in the figure below, only 9 out of 12 Control Group subjects successfully passaged their cells, with 3 subjects having no cell attachment. Of these 9, only 3 achieved the target seeding density. All showed some increase in Pax6 expression, but rosette morphology was observed for only 5 subjects (which also showed higher Pax6 expression).

In contrast, all 15 CultureTrax Group subjects passaged their cells to the target seeding density, showed high Pax6 expression and readily-observed rosette morphology.



Conclusions

— Only 25% (3/12) of the Control Group was fully successful replicating a previously unseen protocol.

— 100% (15/15) of the CultureTrax software group achieved completely correct results on the first run.

— The CultureTrax group took 32% less total time on average for lab work and documentation.

— The CultureTrax group produced more complete records of the experiment.

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