SVCell software, powered by machine learning, enables the automated and standardized generation of patient-specific, clonal cell lines with reduced variability.

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Introduction
Induced pluripotent stem cells (iPSC) are increasingly being adopted for disease modeling, and as sources of tissue for regenerative medicine. However, the generation of patient-specific cell lines can be laborious, costly, and time-consuming. Current processes result in unwanted variations between iPSC lines. These differences can affect functional properties in disease modeling or after transplantation. Robotic patient cell generation systems are being developed to automate and standardize the generation of patient-specific cell lines in order to reduce the variability and costs.

SVCell is a machine learning enabled image recognition software for live cell time-lapse microscopy applications. It consists of a suite of application modules, called recipes, which provide critical functions for automated patient-specific cell generation systems. The SVCell recipes can assess the growth and doubling times of input patient cells, characterize and count the colonies that emerge during reprogramming, and assess the reprogramming status (i.e., full or partially reprogrammed). The recipes incorporate innovative machine learning technologies that provide for accuracy and robustness across systems. The SVCell ipSC Score provides the label-free identification of high quality iPSC clones without fluorescent markers. This uniquely enables the generation of true clonal, rather than polyclonal, cell lines having consistent reprogramming quality and differentiation potential.

Patient Colony Characterization

It has been shown that colony characteristics, such as number of colonies and colony morphology [8] vary between patients. These characteristics should be used to optimize the timing of colony picking in automated systems. We use the SVCell Colony Analyzer recipe to characterize patient cells undergoing reprogramming. Fibroblasts from three disease patients and one healthy adult control were subject to Sendai virus-mediated reprogramming with Klf4, Oct3/4, Sox2 and c-Myc. At approximately 25 days after infection, whole-well image composites were acquired on the Nikon BioStation CT under phase contrast optics at 4x magnification. We applied the SVCell Colony Analyzer recipe to quantitatively characterize the colonies that formed for each patient. We find significant differences in colony counts, colony area sizes and texture measurements (error bars show 95% confidence intervals) between patients. In a real time system, this type of information should be used to assess the quality of the reprogramming run, and guide the timing of colony picking in a patient-specific fashion.

Real-Time iPSC Quality Score

We have shown that the SVCell Colony Analyzer Recipe and Real Time iPSC Score can be used for patient-specific colony characterization including counts, area and texture data. This can be used to assess the quality of the reprogramming run and determine picking time. In addition, the Real Time iPSC score is successfully used to identify and rank fully reprogrammed colonies, resulting in reduced variation between clones. These results show that SVCell could enable automated and clonal patient-specific cell generation in next generation robotic systems to standardize patient-specific cell line generation with reduced variability.

Conclusions

We find significant differences in colony counts, colony area sizes and texture measurements (error bars show 95% confidence intervals) between patients. In a real time system, this type of information should be used to assess the quality of the reprogramming run, and guide the timing of colony picking in a patient-specific fashion.

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References