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Review

Manipulating Cell Fate While Confronting Reproducibility Concerns

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**Title: Manipulating Cell Fate While Confronting Reproducibility Concerns****Jeannette M. Osterloh and Kevin Mullane<sup>1</sup>**

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[kevin.mullane@gladstone.ucsf.edu](mailto:kevin.mullane@gladstone.ucsf.edu)**Abstract**

Biomedical research is being transformed by the discovery and use of human pluripotent stem cells (hPSCs). Remarkable progress has been made, and assorted clinical trials are underway related to the application of stem cell therapy, including transplantation of hPSC-derived cells, *in situ* reprogramming or transdifferentiation, and utilization of targets and compounds identified from patient-derived stem cells. However, the pace of discovery is overwhelming efforts to replicate the work of others, prompting a concern over validity and reproducibility. Here, we address some sources of variability in reprogramming, maintaining, and differentiating hPSCs that impact interpretation of studies involving their use, and how it relates to efforts to move the field forward. The commitment in time and resources required to generate and maintain cell-lines, coupled with marked variations between hPSCs derived from patients with the same disease, has resulted in a fundamental change in how research is conducted. Dr. Michael

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