論 文 要 旨

Novel technologies to directly eliminating tumorigenic cells in pluripotent stem cells

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Human pluripotent stem cells (hPSCs) are a promising source of regenerative material for clinical applications. However, hPSC transplant therapies pose the risk of teratoma formation and malignant transformation of undifferentiated remnants. Most current strategies for handling this issue are classified as “indirect” approaches that aim at partial reduction, but not complete elimination, of tumorigenicity. Given the intrinsic genome instability of hPSCs and selective growth advantage of cancer cells, the conventional strategies are unlikely to completely overcome issues related to hPSC tumorigenesis. Consequently, even a few contaminating tumorigenic cells in the original sample may form cancers or teratomas. In addition, undifferentiated and/or malignantly transformed cells have a growth advantage over differentiated cells. Therefore, to facilitate safe clinical applications, it is necessary to develop new approaches to directly, completely, and specifically eliminate undifferentiated hPSCs. We here develop two novel technologies to “directly” and “specifically” kill tumorigenic hPSCs. One is an oncolytic virus–based strategy that specifically and efficiently kills undifferentiated hPSCs. The other is a novel method for efficiently generating diverse candidates for tumorigenic cell-targeting lentiviral vectors (TC-LVs), enabling systematic identification of the best suicide gene in combination with the most suitable promoter for this purpose. These technologies will help to overcome the problems of hPSC tumorigenesis in the context of regenerative medicine.