Whole-genome mutational burden analysis of three pluripotency induction methods.

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Public Summary:
We used whole genome sequencing to ask whether reprogramming of human somatic cells introduced mutations that would be of concern for safety of the cells. We determined that three reprogramming methods in which the Yamanaka factors were delivered by retrovirus, Sendai virus, or mRNA did not introduce mutations that would make the cells inappropriate for cell transplantation therapy. Our conclusion is that reprogramming is generally benign.

Scientific Abstract:
There is concern that the stresses of inducing pluripotency may lead to deleterious DNA mutations in induced pluripotent stem cell (iPSC) lines, which would compromise their use for cell therapies. Here we report comparative genomic analysis of nine isogenic iPSC lines generated using three reprogramming methods: integrating retroviral vectors, non-integrating Sendai virus and synthetic mRNAs. We used whole-genome sequencing and de novo genome mapping to identify single-nucleotide variants, insertions and deletions, and structural variants. Our results show a moderate number of variants in the iPSCs that were not evident in the parental fibroblasts, which may result from reprogramming. There were only small differences in the total numbers and types of variants among different reprogramming methods. Most importantly, a thorough genomic analysis showed that the variants were generally benign. We conclude that the process of reprogramming is unlikely to introduce variants that would make the cells inappropriate for therapy.