Small molecules, big roles - the chemical manipulation of stem cell fate and somatic cell reprogramming.

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Public Summary:
Despite the great potential of stem cells for basic research and clinical applications, obstacles – such as their scarce availability and difficulty in controlling their fate – need to be addressed to fully realize their potential. Recent achievements of cellular reprogramming have enabled the generation of induced pluripotent stem cells (iPSCs) or other lineage-committed cells from more accessible and abundant somatic cell types by defined genetic factors. However, serious concerns remain about the efficiency and safety of current genetic approaches to cell reprogramming and traditional culture systems that are used for stem cell maintenance. As a complementary approach, small molecules that target specific signaling pathways, epigenetic processes and other cellular processes offer powerful tools for manipulating cell fate to a desired outcome. A growing number of small molecules have been identified to maintain the self-renewal potential of stem cells, to induce lineage differentiation and to facilitate reprogramming by increasing the efficiency of reprogramming or by replacing genetic reprogramming factors. Furthermore, mechanistic investigations of the effects of these chemicals also provide new biological insights. Here, we examine recent achievements in the maintenance of stem cells, including pluripotent and lineagespecific stem cells, and in the control of cell fate conversions, including iPSC reprogramming, conversion of primed to naı¨ve pluripotency, and transdifferentiation, with an emphasis on manipulation with small molecules.

Scientific Abstract:
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