

Vitamin C promotes widespread yet specific DNA demethylation of the epigenome in human embryonic stem cells.

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Public Summary:

Scientific Abstract:

Vitamin C (ascorbate) is a widely used medium supplement in embryonic stem cell culture. Here, we show that ascorbate causes widespread, consistent, and remarkably specific DNA demethylation of 1,847 genes in human embryonic stem cells (hESCs), including important stem cell genes, with a clear bias toward demethylation at CpG island boundaries. We show that a subset of these DNA demethylated genes displays concomitant gene expression changes and that the position of the demethylated CpGs relative to the transcription start site is correlated to such changes. We further show that the ascorbate-demethylated gene set not only overlaps with gene sets that have bivalent marks, but also with the gene sets that are demethylated during differentiation of hESCs and during reprogramming of fibroblasts to induced pluritotent stem cells (iPSCs). Our data thus identify a novel link between ascorbate-mediated signaling and specific epigenetic changes in hESCs that might impact on pluripotency and reprogramming pathways.

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