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LINKING METABOLISM TO STEM CELL MAINTENANCE

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LINKING METABOLISM TO STEM CELL MAINTENANCE

The role of cellular metabolism in stem cell maintenance and differentiation is poorly understood. In comparison to more differentiated cells, stem cell maintenance depends on the ability of glucose and/or glutamine catabolism to maintain a high level of intracellular α -ketoglutarate (α KG). Consequently, stem cells exhibit an elevated α KG/succinate ratio that promotes histone/DNA demethylation and maintains pluripotency. Direct manipulation of the intracellular α KG/succinate ratio is sufficient to regulate multiple chromatin modifications, including H3K27me3 and Ten eleven translocation (Tet)-dependent DNA demethylation that contribute to the regulation of pluripotency-associated gene expression. In vitro, supplementation with cell-permeable α KG directly supports self-renewal while cell-permeable succinate promotes differentiation. This work reveals that intracellular α KG/succinate levels can contribute to the maintenance of cellular identity and play a mechanistic role in the transcriptional and epigenetic state of stem cells.



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Craig B. Thompson, M.D. is the President and Chief Executive Officer of Memorial Sloan Kettering Cancer Center (MSKCC). Dr. Thompson received his BS from Dartmouth and MD from the University of Pennsylvania, followed by clinical training in internal medicine at Harvard Medical School and in medical oncology at the Fred Hutchinson Cancer Research Institute. Dr. Thompson has extensive research experience in cancer, immunology, and translational medicine. His current research focuses on the regulation of cellular metabolism during cell growth/differentiation and on the role that metabolic changes play in the origin and progression of cancer. Dr. Thompson is a member of the Institute of Medicine, the National Academy of Sciences, the American Academy of Arts and Sciences, and the Medical Advisory Board of the Howard Hughes Medical Institute.
