MicroRNA-145 regulates OCT4, SOX2, and KLF4 and represses pluripotency in human embryonic stem cells.

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Public Summary:
MicroRNAs (miRNAs) are posttranscriptional modulators of gene expression and play an important role in many developmental processes. We report here that expression of a microRNA is low in self-renewing human embryonic stem cells (hESCs) but highly upregulated during differentiation. We identify the pluripotency factors as direct targets of this micro. This work reveals a direct link between the core reprogramming factors and miR-145 and uncovers a double-negative feedback loop involving pluripotency factors.

Scientific Abstract:
MicroRNAs (miRNAs) are posttranscriptional modulators of gene expression and play an important role in many developmental processes. We report here that expression of microRNA-145 (miR-145) is low in self-renewing human embryonic stem cells (hESCs) but highly upregulated during differentiation. We identify the pluripotency factors OCT4, SOX2, and KLF4 as direct targets of miR-145 and show that endogenous miR-145 represses the 3' untranslated regions of OCT4, SOX2, and KLF4. Increased miR-145 expression inhibits hESC self-renewal, represses expression of pluripotency genes, and induces lineage-restricted differentiation. Loss of miR-145 impairs differentiation and elevates OCT4, SOX2, and KLF4. Furthermore, we find that the miR-145 promoter is bound and repressed by OCT4 in hESCs. This work reveals a direct link between the core reprogramming factors and miR-145 and uncovers a double-negative feedback loop involving OCT4, SOX2, KLF4, and miR-145.