Klf4 interacts directly with Oct4 and Sox2 to promote reprogramming.

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**Authors:** Zong Wei, Yang Yang, Peilin Zhang, Rosemary Andrianakos, Kouichi Hasegawa, Jungmook Lyu, Xi Chen, Gang Bai, Chunming Liu, Martin Pera, Wange Lu  
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**Public Summary:**  
This paper describes the mechanisms of somatic cell reprogramming. It reports that the binding of Klf4 with Oct4 and Sox2 is important for somatic cell reprogramming.

**Scientific Abstract:**  
Somatic cells can be reprogrammed to induced pluripotent stem (iPS) cells by ectopic expression of specific sets of transcription factors. Oct4, Sox2, and Klf4, factors that share many target genes in embryonic stem (ES) cells, are critical components in various reprogramming protocols. Nevertheless, it remains unclear whether these factors function together or separately in reprogramming. Here we show that Klf4 interacts directly with Oct4 and Sox2 when expressed at levels sufficient to induce iPS cells. Endogenous Klf4 also interacts with Oct4 and Sox2 in iPS cells and in mouse ES cells. The Klf4 C terminus, which contains three tandem zinc fingers, is critical for this interaction and is required for activation of the target gene Nanog. In addition, Klf4 and Oct4 co-occupy the Nanog promoter. A dominant negative mutant of Klf4 can compete with wild-type Klf4 to form defective Oct4/Sox2/Klf4 complexes and strongly inhibit reprogramming. In the absence of Klf4 overexpression, interaction of endogenous Klf4 with Oct4/Sox2 is also required for reprogramming. This study supports the idea that direct interactions between Klf4, Oct4, and Sox2 are critical for somatic cell reprogramming.

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