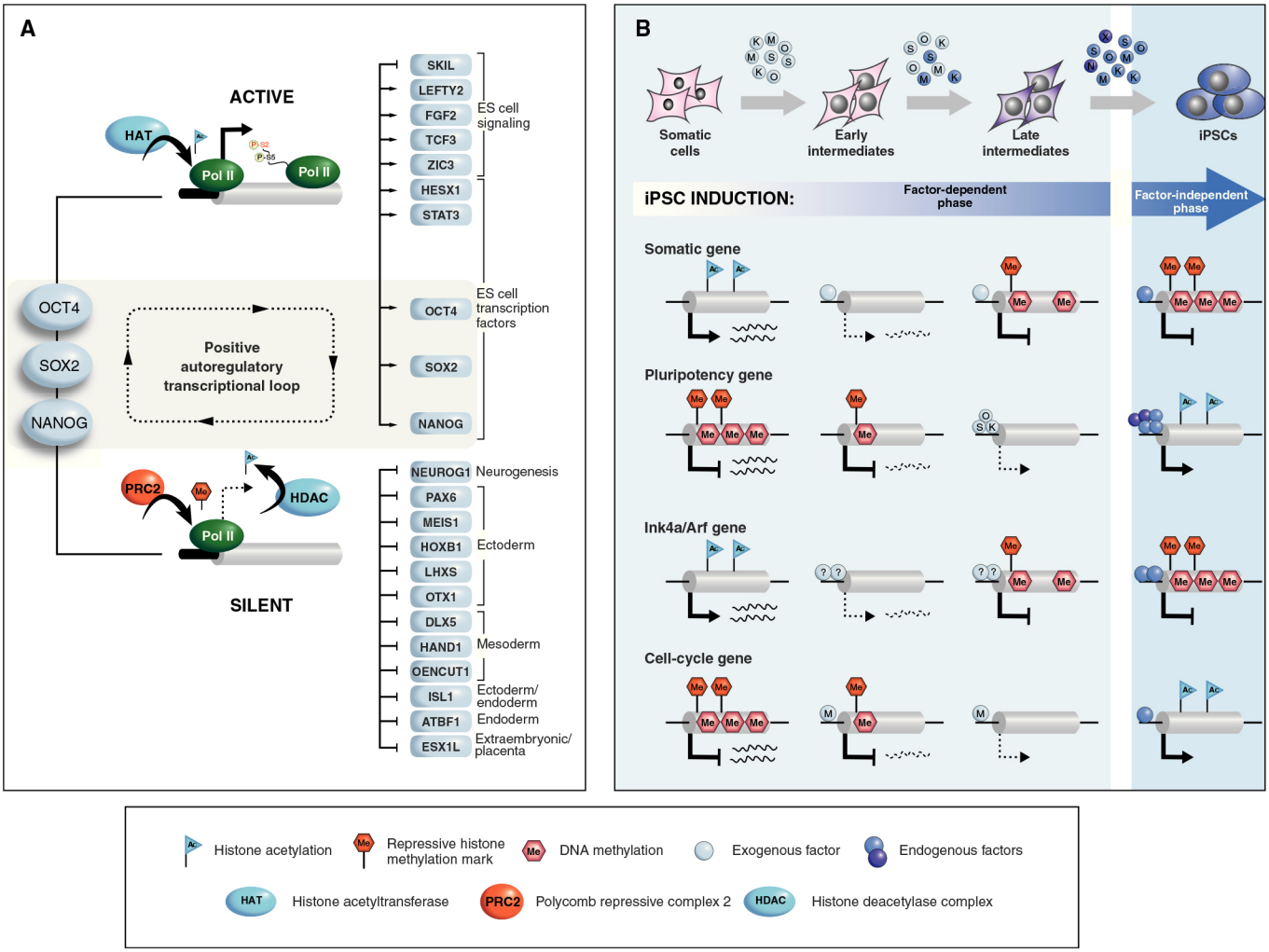

Figure 7. Roles of transcription factors in inducing and maintaining pluripotency. (*A*) The transcription factors Oct4, Sox2, and Nanog maintain the pluripotency of ES cells by activating genes important for self-renewal and suppressing genes that drive differentiation. These factors either collaborate with chromatin activators such as the histone acetyltransferase p300 (blue, HAT) and elongating RNA polymerase II (green, Pol II) to induce genes or with chromatin repressors such as PRC2 and histone deacetylase complexes (HDAC) to inhibit genes through repressive histone methylation and the removal of histone acetylation. Moreover, pluripotency factors positively regulate their own transcription, thus establishing a transcriptional circuitry typical of ES cells and iPSCs. (*B*) Model of how reprogramming factors act during iPSC induction. Somatic cells expressing exogenous reprogramming factors transition from "early intermediates" to "late intermediates" to iPSCs (blue circles: O, Oct4; S, Sox2, K, Klf4, M, c-Myc). To acquire pluripotency, cells must activate endogenous pluripotency genes (dark blue circles) as well as essential cofactors (blue circles labeled N, Nanog; X, other factors) to sustain self-renewal in the absence of exogenous factors. (*Bottom*) Model of how reprogramming factors establish pluripotency in somatic cells via their action at different types of genes. Single factors may suppress somatic genes early, whereas combinations of factors activate pluripotency genes late in reprogramming. Pluripotency is stabilized once suppressive chromatic marks are deposited at somatic genes and removed from silenced pluripotency loci. Successful reprogramming is tightly linked with the acquisition of indefinite self-renewal properties through activation of proliferation genes such as cyclins (mostly targeted by c-Myc) and suppression of cell-cycle inhibitor genes such as *Ink4a/Arf* by unknown factors. (*A*, Adapted, with permission, from Jaenisch and Young 2008; *B*, adapted, with permission, from Stadtfeld and Hochedlinger 2010.)