Epithelial-Mesenchymal Plasticity (EMP) refers to reversible dynamic processes where cells can transition from epithelial to mesenchymal (EMT) or from mesenchymal to epithelial (MET) phenotypes. Both these processes are modulated by multiple transcription factors acting in concert. While EMT-inducing transcription factors (TFs)-TWIST1/2, ZEB1/2, SNAIL1/2/3, GSC, and FOXC2-are well-characterized, the MET-inducing TFs are relatively poorly understood (OVOL1/2 and GRHL1/2). Here, using mechanism-based mathematical modeling, we show that transcription factor KLF4 can delay the onset of EMT by suppressing multiple EMT-TFs. Our simulations suggest that KLF4 overexpression can promote a phenotypic shift toward a more epithelial state, an observation suggested by the negative correlation of KLF4 with EMT-TFs and with transcriptomic-based EMT scoring metrics in cancer cell lines. We also show that the influence of KLF4 in modulating the EMT dynamics can be strengthened by its ability to inhibit cell-state transitions at the epigenetic level. Thus, KLF4 can inhibit EMT through multiple parallel paths and can act as a putative MET-TF. KLF4 associates with the patient survival metrics across multiple cancers in a context-specific manner, highlighting the complex association of EMP with patient survival.