論 文 要 旨

The transcription factor LEF-1 induces an epithelial–mesenchymal transition in MDCK cells independent of β-catenin

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The epithelial–mesenchymal transition (EMT), a key process in the tumor metastatic cascade, is characterized by the loss of cell–cell junctions and cell polarity, as well as the acquisition of migratory and invasive properties. LEF-1 is a member of the lymphoid enhancer-binding factor/T-cell factor (LEF/TCF) family of DNA-binding transcription factors, which interact with nuclear β-catenin and act as central transcriptional mediators of Wnt signaling. To investigate the role of LEF-1 in EMT, we generated stable LEF-1 transfectants using MDCK cells. The transfectants had a spindle-shaped mesenchymal morphology, and enhanced migration and invasiveness relative to control cells. These EMT changes were accompanied by the downregulation of an epithelial marker protein, E-cadherin, and the upregulation of mesenchymal marker proteins, vimentin and N-cadherin. Consistent with these observations, the mRNA levels of Slug, ZEB1, and ZEB2—EMT-related transcription factors—increased significantly. Although the N-terminally deleted mutant LEF-1 cannot interact with β-catenin, it retained the ability to induce EMT. Consistent with these observations, neither the expression of a dominant negative β-catenin/engrailed chimera, nor the expression of a cytoplasmic domain of E-cadherin that sequesters β-catenin from binding to LEF/TCF, reversed LEF-1-induced EMT. Together, these data indicated that the nuclear function of β-catenin was not necessary for the induction of Slug, ZEB1, and ZEB2 expression leading to EMT.