22.Induction of mesenchymal-epithelial transition in fibroblast-like spindle cancer cells by reprograming factors

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It was reported that induced pluripotent stem (iPS) cells went through mesenchymal-epithelial transition (MET) when they were generated from embryonic fibroblasts by introduction of reprogramming genes. The results prompted us to study whether cancer cells under epithelial-mesenchymal transition (EMT) could be reversed by the reprogramming genes. To this end, we used fibroblast-like squamous cell cancer (SCC) lines derived from mouse skin, and the piggyBac transposon system to deliver the reprogramming factors (Oct3/4, Sox2, Klf4, c-Myc and Lin28), which were linked by self-cleaving peptides. The piggyBac transposon and piggyBac transposase expression vector were co-transfected into spindle-shaped SCC cells. The stable transformants were obtained after the puromycin selection, and they showed polygonal morphology with well-established cell-cell adhesion. Quantitative RT-PCR and immunoblotting revealed increased epithelial markers and reduced mesenchymal markers in the transformed cells compared with the parental SCC cells. Also, the transformed cells showed N-cadherin at the cell-cell border and actin bundles, similar to those found in epithelial cells. Cell proliferation and cell invasion activity were reduced in the transfected cells. The EMT in human SCC cells also showed a reversal with the reprogramming genes. Taken collectively, these results suggested that a malignant process associated with EMT was reversed by introduction of the reprogramming genes for iPS cells. This finding provides an idea for the potential therapeutic use of the reprogramming genes to attenuate malignant nature of metastatic cancer.