Limiting Esophageal Cancer Metastasis With KRT16 siRNA

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Despite being the sixth most fatal cancer worldwide, esophageal cancer is largely overlooked. The high mortality rate of esophageal cancer stems largely from its high metastatic capability. Metastasis occurs when rigidly polarized epithelial cells transform into migratory and invasive mesenchymal cells in a process called the epithelial-mesenchymal transition (EMT). By decreasing the rate at which EMT occurs, the metastatic capability of a cancer may be significantly diminished. The expression of keratin-16, a cytoskeletal intermediate filament responsible for cell structure, is directly proportional to the rate of EMT; thus downregulating KRT16 expression may decrease the rate of EMT in esophageal cancer cells. This hypothesis was tested by treating OE19 esophageal tumor cells with three concentrations of KRT16-targeted siRNA (20nM, 40nM, 80nM), then measuring the expression of the mesenchymal biomarker protein vimentin, as well as the cells' migration. OE19 cells are naturally epithelial; a high concentration of vimentin denotes mesenchymal cells, meaning EMT has occurred. OE19 cells were treated with hypoxic conditions for 48 hours to mimic EMT. An in-cell western blot was then performed to evaluate the extent of EMT through the expression of vimentin; a significant ($p < 0.01$) decrease in vimentin was found with an increase in siRNA concentration. In a scratch assay, higher siRNA concentrations corresponded with significantly ($p < 0.01$) decreased cell migration. These results show that knocking down keratin-16 expression shows promise towards improving patient prognosis and ease of esophageal surgeries, opening up KRT16-targeted siRNA as a way to raise the 20% survival statistic.

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