TITLE

Blind SELEX Approach Identifies RNA Aptamers that Regulate EMT and Inhibit Metastasis

RUNNING TITLE

Anti-vimentin RNA Aptamer in Pancreatic Cancer

ABSTRACT

Identifying targets that are exposed on the cell surface of tumor cells, but expressed internally in normal cells, is a fundamental issue for improving the specificity and efficacy of anticancer therapeutics. Using blind cell SELEX (Systemic Evolution of Ligands by EXponetial enrichment) which is untargeted SELEX, we have identified an aptamer, P15, which specifically bound to human pancreatic adenocarcinoma cells. To identify the aptamer binding plasma membrane protein, liquid chromatography tandem mass spectrometry (LC-MS/MS) was used. The results of this unbiased proteomic mass spectrometry approach identified the target of P15 as the intermediate filament vimentin, biomarker of epithelial-mesenchymal transition (EMT), which is an intracellular protein but is specifically expressed on the plasma membrane of cancer cells. As EMT plays a pivotal role to transit cancer cells to invasive cells, tumor cell metastasis assays were performed in vitro. P15 treated pancreatic cancer cells showed the significant inhibition of tumor metastasis. To investigate the downstream effects of P15, EMT related gene expression analysis was performed to identify differently expressed genes (DEGs). Among five DEGs, P15 treated cells showed the down-regulated expression of matrix metallopeptidase 3 (MMP3), which is involved in cancer invasion. These results, for the first time, demonstrate that P15

binding to cell surface vimentin inhibits the tumor cell invasion and is associated with reduced MMP3

expression. Thus, suggesting that P15 has potential as an anti-metastatic therapy in pancreatic cancer.

IMPLICATIONS

Implications: This study reveals that anti-vimentin RNA aptamers selected via blind-SELEX inhibits tumor cell metastasis.