Treatment of Metastatic Colon Cancer with B-subunit of Shiga Toxin

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Technology description

Technical Details:
Colorectal cancer is the second leading cause of death from cancer in the USA (Yokota, 2000). The high mortality associated with colorectal cancer is related to its ability to spread beyond the large intestine and invade distant organs. Therefore, increasing efforts are being directed to develop ways to identify markers that predicts the metastatic potential of colon cancer cells. Through a comparison of the tissue samples of human colonic adenoma and primary non-invasive colon cancer to metastatic colon cancer, we identified a molecule, which was expressed much more (at least 5 times) in metastatic colon cancer and almost not at all in non-metastatic colon cancer. A subpopulation of cells with these molecules significantly upregulated was present in several human epithelial colon cancer cell lines. Application of a chemoinvasive assay showed that only these cells could invade. Transient transfection of non-cancer epithelial cells with this molecule turned non-invasive cells into invasive cells. We concluded that this molecule might serve as a marker for metastasis in human colon cancer and potentially in other epithelial cancers and as a drug target to prevent colon cancer metastases.
The above molecule is a natural receptor for a low molecular weight protein. When this protein binds to its receptor, it is internalized and causes apoptosis of receptor bearing cells only, which as our data shows are potentially metastatic. Intratumoral injection of this protein into nude mouse xenograph of human colon cancer cells significantly inhibited tumor growth monitored over a 7 week period compared to control. We suggest that this protein itself or conjugated to conventional chemotherapeutic agent(s) can be used as a drug against metastatic colon cancer cells and possibly other metastatic cancers with similar characteristics.

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