Vitamin E Delta-Tocotrienol Targets Cancer Stem Cell Transcription Factors and Inhibits Human Pancreatic Cancer Metastasis

Kazim, Sayyada

a) Purpose of the experiment: The purpose of the experiment is to investigate the ability of vitamin E delta-tocotrienol (VEDT) to inhibit human pancreatic cancer stem cell growth and metastasis and induce apoptosis. b) Procedure: Human pancreatic cancer stem cells (PCSCs) and metastatic human pancreatic cancer cells (L3.6pl) were grown in stem cell and DMEM culture media, respectively. The cells were seeded in 96-well plate and treated with delta-tocotrienol (10-100 μM) and vehicle (<5% ethanol), incubated for 72 h and MTT assay was performed to calculate cell viability. Cells treated with VEDT (50 μM), harvested and counted live/dead cells and apoptosis (Annexin V/PI) by flow cytometry. VEDT treated cells were used for cell growth (soft agar), microsphere/spheroid formation, migration and invasion assays. Proteins extracted, estimated and separated by electrophoresis. Protein bands treated with antibodies (E-cadherin, vimentin, MMP9, Nanog, Oct4, Sox2 and ß-actin) followed by HRP conjugated antibody. Membrane exposed to film and developed. c) Data: The data show that VEDT significantly inhibited growth of PCSCs and metastatic L3.6pl cells in a concentration dependent manner. VEDT significantly inhibited malignant transformation, cancer stem cell self-renewal capacity (microsphere/spheroid formation) and pluripotency transcription factors (Nanog, Oct4 and Sox2), epithelial to mesenchymal transition (EMT), migration, invasion, and metastasis (MMP9) and induced apoptosis. d) Conclusions: Vitamin E delta-tocotrienol inhibits human pancreatic cancer stem cell growth and self-renewal capacity, inhibits metastasis and induces apoptosis targeting stem cell transcription factors hence warrants its clinical use for advanced pancreatic cancer.

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