AAV-mediated Persistent Bevacizumab Therapy Suppresses Tumor Growth of Ovarian Cancer

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Technology description

This invention provides compositions and methods to treat ovarian cancer with a single administration of adeno-associated virus (AAV)-mediated intraperitoneal expression of bevacizumab.
Ovarian cancer is the most lethal gynecologic cancer and fifth leading cause of cancer in the United States. Ovarian cancer patient with high expression of the key angiogenesis factor, vascular endothelial growth factor (VEGF), is associated with poor progression-free survival and overall survival. One strategy to treat ovarian cancer is inhibition of angiogenesis.
Bevacizumab is a humanized monoclonal IgG1 antibody that targets VEGF-A, a member of VEGF family involved in tumor angiogenesis. It has been approved by FDA to treat multiple cancers. Anti-angiogenesis therapies, such as bevacizumab, have been tested against ovarian cancer, but transient and low peritoneal drug levels are likely a factor in treatment failure.
This invention provides AAVrh.10BevMab, a rhesus sertotype 10 adeno-associated viral vector coding bevacizumab, for a single peritoneal administration of bevacizumab to treat ovarian cancer. The inventors demonstrated that: AAVrh.10BevMab mediates persistent and high levels of bevacizumab in the peritoneal cavity following a single intraperitoneal administration in mice; in AAVrh10.BevMab treated A2780 human ovarian cancer-bearing mice, tumor growth was significantly suppressed and the area of blood vessels in the tumor was decreased; survival of mice with A2780 xenografts or SKOV3 xenografts was greatly prolonged in the presence of AAVrh10.BevMab; administration of AAVrh10.BevMab 4 days after A2780-luciferase cell implantation reduced tumor growth and increased mouse survival; combination of AAVrh10.BevMab with cytotoxic reagents paclitaxel or topotecan proved to be more effective in increasing survival than treatment with cytotoxic reagent alone.

Additional Information

AAV-mediated persistent bevacizumab therapy suppresses tumor growth of ovarian cancer. Gynecol. Oncol., 2-14, 135, 325-32 .

Application area

AAV-mediated bevacizumab therapy for the suppression of ovarian cancer growth

Advantages

Provides persistent and high levels of bevacizumab without repeated antibody administration

Institution

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