COMBINATIONAL DRUG THERAPY FOR TREATMENT OF OVARIAN CANCER

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Technology description

Challenge

One of the many challenges in treating cancer lies in the fact that not all cancer cells are identical to each other within a single patient. In tumors, some cells are glutamine addictive and some are glutamine independent. Glutamine addictive cells require glutamine for the TCA cycle, balancing redox in cells, activating signaling, and serving as building blocks for cell proliferation and metastasis. Glutamine independent cells use the enzyme glutamine synthetase to generate necessary glutamine. Specifically, low-invasive ovarian cancer (OVCA) cells are glutamine independent while high-invasive ovarian cancer (OVCA) are glutamine dependent. Because of the different metabolic nature of the cells, simply using one drug to inhibit one of the pathways will not have a prominent effect on clinical outcomes.

Solution

This invention is a method of targeting ovarian cancer cells with a combinational drug therapy. The cancer prognosis is first determined using the ratio of glutamine catabolism over anabolism, a novel biomarker. Then, a glutaminase inhibitor, a glutamine synthetase inhibitor, and a STAT3 inhibitor are administered in combination. The administration of the glutaminase inhibitor and glutamine synthetase inhibitor may be an effective therapy for heterogenous tumors, those containing both high-invasive OVCA and low-invasive OVCA. STAT3 signaling, which can be activated by glutamine, is important for cell invasion and is a malignant state marker. Therefore, to further inhibit cancer cells' metastasis, a STAT3 inhibitor is combined along with the targets of glutamine pathways to block glutamine' s effect on metastasis, signaling, and tumor growth.

Technology Relevant Papers and Web Links

http://nagrathlab.rice.edu/
Yang L, Moss T, Mangala LS, Marini J, Zhao H, Wahlig S, Armaiz-Pena G, Jiang D, Achreja A, Win J, Roopaimoole R, Rodriguez-Aguayo C, Mercado-Uribe I, Lopez-Berestein G, Liu J, Tsukamoto T, Sood

AK, Ram PT, Nagrath D. Metabolic shifts toward glutamine regulate tumor growth, invasion and bioenergetics in ovarian cancer.Mol. Syst. Biol. **2014** , 12(5), 1-23.

Application area

This combinational drug therapy has been developed primarily for use in ovarian cancer therapy. The National Cancer Institute ranks ovarian cancer as the 17 th most common type of cancer in the United States. It is estimated that over 180,000 women were living with ovarian cancer in 2011 and that there will be over 21,000 new cases of ovarian cancer in 2014 in the United States. While improvements have been made in treating ovarian cancer, as of 2006, the 5-year relative survival rate was 45.2%.
Because glutamine plays an important role in other types of cancers, this combinational drug therapy may be applied toward other cancers.

Advantages

· The combinational drug therapy involves the administration of a glutaminase inhibitor, a glutamine synthetase inhibitor, and a STAT3 inhibitor.
· The combinational drug therapy targets tumors with different degrees of invasiveness.
· The ratio of glutamine catabolism over anabolism serves as a novel biomarker for cancer prognosis.

Institution

Rice University

Inventors

Deepak Nagrath

联系我们

叶先生

电 话：021-65679356

手 机：13414935137

邮 箱：yeyingsheng@zf-ym.com