Biomarkers to Identify Abnormal DNA Repair in Therapy-Resistant Breast Cancers

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Technology description

A a method for identifying solid tumors suitable for treatment using inhibitors of alternative (ALT) non-homologous end joining (NHEJ) factors.
This research shows that an ALT NHEJ pathway is upregulated in breast cancer cell lines that are either intrinsically resistant or have acquired resistance to antiestrogen therapies and that these cell lines are hypersensitive to DNA repair inhibitors that target the ALT NHEJ pathway. The results show that ALT NHEJ is a novel therapeutic target in breast cancers that are resistant to frontline therapies and changes in NHEJ protein levels serve as biomarkers to identify candidates for this therapeutic approach.

Background

According to the National cancer institute’ s SEER Cancer Statistics review, it is estimated that 226,870 women will be diagnosed with cancer in 2012. The review also states that the survival rate is only 82.5%. Although the majority of breast cancers are estrogen-dependent and effective antiestrogen therapies have been developed, there is an urgent need to develop new and improved therapeutic strategies for patients whose disease is refractory to antiestrogen therapies. Alterations in the network of pathways that respond to DNA damage and maintain genome stability are presumed to underlie the genomic instability and increased sensitivity of cancer cells to cytotoxic DNA damaging agents used in cancer treatment. These abnormalities are potential targets for the development of therapeutics that either alone or in combination with cytotoxic DNA damaging agents will specifically enhance killing of cancer cells.

Technology Description

Researchers have developed a method for identifying solid tumors suitable for treatment using inhibitors of alternative (ALT) non-homologous end joining (NHEJ) factors. This research shows that an ALT NHEJ pathway is upregulated in breast cancer cell lines and tumors that are either intrinsically resistant or have acquired resistance to antiestrogen therapies. These cell lines are hypersensitive to DNA repair inhibitors that target the ALT NHEJ pathway demonstrating that ALT NHEJ is a novel

therapeutic target in breast cancers that are resistant to frontline therapies and that changes in NHEJ protein levels serve as biomarkers to identify candidates for this therapeutic approach.

Publications

Targeting abnormal DNA repair in therapy-resistant breast cancers.
Targeting abnormal DNA double-strand break repair in tyrosine kinase inhibitor-resistant chronic myeloid leukemias.

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Application area

Potentially a more effective therapy for breast cancer patients with acquired antiestrogen resistance, intrinsic resistance to antiestrogen and anti-HER2 therapies
Serves as biomarkers to identify breast cancer patients whose disease is likely to respond to DNA repair inhibitors that target ALT NHEJ
Determines the expression levels in specific cells of the ALT NHEJ factor PARP1 and the NHEJ factor Ku.
The same approach may be applicable to other cancers, including ovarian cancer and leukemias, with similar DNA repair abnormalities.

Institution

The University of New Mexico

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