Methods of Sensitizing Estrogen Receptor-Positive Breast Cancer to Endocrine Therapy

Technology

Dr. Schneider's lab has identified a cellular pathway in Estrogen receptor-positive (ER+) breast cancer cells that can be targeted by known therapeutics that act on the mRNA translation machinery to re-sensitize tamoxifen resistant breast tumor cells to tamoxifen and improve treatment outcomes. Tamoxifen-resistant, ER+ breast cancer cells rely on activation of alternative pathways, including mTOR, MNK kinase, and MAPK pathways, to maintain increased translation of oncogenic genes that permit tamoxifen resistance, promote metastasis, and cancer cell survival. The researchers found that disrupting these pathways with specific small molecule inhibitors of mTOR and MNK kinases reduces translation of genes that promote tamoxifen resistance, thereby restoring sensitivity. Additionally, targeting this specific mRNA translation mechanism while treating with tamoxifen reduced cell proliferation and survival over tamoxifen alone. Overall, these data indicate a novel combination treatment of MAPK/MNK inhibitors with mTOR inhibitors to overcome tamoxifen-resistant ER+ breast cancer.

Background

Estrogen receptor-positive (ER+) breast cancers comprise the majority (70%–80%) of breast cancers and the majority of breast cancer deaths resulting from metastatic disease. Approximately 1 in 8 women will be diagnosed with breast cancer in their lifetime. In 2022, there were approximately 300,000 new cases and approximately 50,000 deaths from breast cancer in the US. In 2019, patients paid a collective $3.14 billion in out-of-pocket expenses. Anti-estrogen therapy with tamoxifen remains a cornerstone of therapy for ER+ premenopausal breast cancer, but resistance occurs in a third of patients and often progresses to metastasis and death. More needs to be learned about ER+ breast cancer progression and development, as well as more effective therapies or approved combinations of known therapies that best combat cancer.

Application

Targeting either MAPK/ERK/MNK or mTORC1 in combination with treatment with tamoxifen could be an effective therapy for ER+ Breast Cancer patients who have developed tamoxifen resistance.

Advantages

- Sensitizing ER+ tumors to the anti-estrogen drug, tamoxifen, allows for specific, targeted treatment.
- This invention can be quickly translated to clinical applications using the various FDA-approved mTORC inhibitors or the known MAPK/ERK inhibitor.

Intellectual Property

Technology ID

SCH03-09

Category

Life Sciences/Therapeutics/Oncology
Life Sciences/Therapeutics/Women's Health

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A US patent has been issued

- Publication # US20200197400A1

About the PI

Dr. Robert J Schneider is a world-renowned researcher with over 190 peer-reviewed publications in breast cancer and cancer biology, immunology, inflammation, and autoimmunity. His research is directed to the development, progression and metastasis of breast cancer, the interplay of the inflammatory response, and the development of new therapeutics for metastatic breast cancer. Dr. Schneider is a co-founding scientist of seven biotechnology/small pharmaceutical companies including ImClone Systems, PTC Therapeutics, Canji, GenCell, Charterhouse Pharmaceuticals, ENB Therapeutics and most recently Regerna Therapeutics.

References

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