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Guide RNA Molecule and Method for Treating Cancer

Health & Wellness

Others

Biomedical and Genetic Engineering

Others

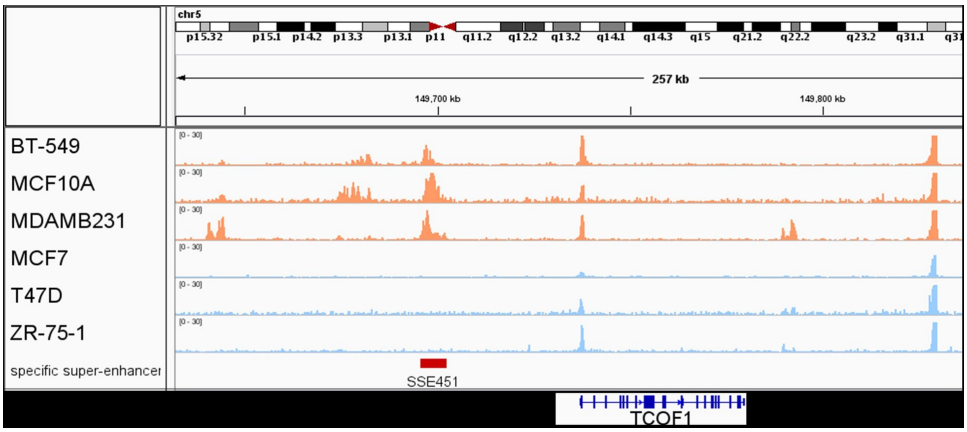
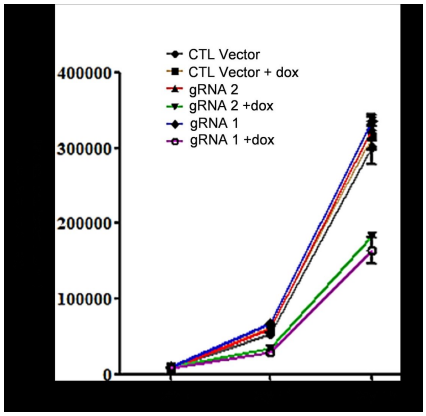


Figure 1. Preferential overexpression of TCOF1 in TNBC. Comparison of H3K27Ac patterns in TNBC and luminal breast tumor lines reveals a TNBC-specific super-enhancer at TCOF1 proximal enhancer region.



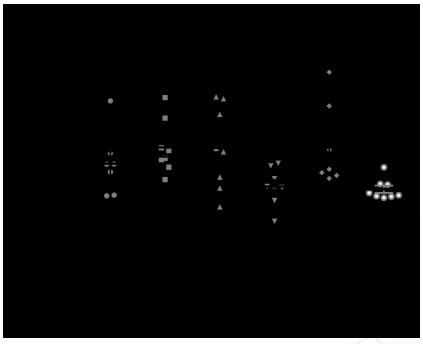


Figure 2. TCOF1 gRNA 1- or gRNA 2- infected treatments with doxycycline treatment could inhibit the growth of TNBC spheroids and xenografts, tested through 3D cell proliferation and xenograft nude mice model.

Opportunity

Breast cancer is the most common type of cancer affecting women worldwide; it is also the second-most common cause of death of women. Breast cancer has three major subtypes: luminal, HER2+/ER−, and basal-like. In triple-negative breast cancer (TNBC), ~70% of basal-like tumors are triple-negative tumors—named so because they lack the three common types of receptors, i.e., those for estrogen, progesterone, and HER-2/neu. TNBC is also highly associated with abnormal expression of the TCOF1 gene. TNBC cannot be treated with therapies or drugs that work by targeting those three

IP Status
Patent granted

Technology Readiness Level (TRL) 5

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receptors; thus, few treatment options exist outside of chemotherapy, usually with high toxicity. Therefore, new options for treating TNBC and/or alleviating TNBC-associated symptoms are urgently needed, ideally with reduced risk of side effects.

Technology

The inventors developed a method using CRISP/Cas9 gene-editing technology that facilitates the inhibition of TCOF1 gene expression to reduce the proliferation of cancer cells. The invention relates to a guide RNA (gRNA) molecule comprising a first domain complementary to at least a portion of the TCOF1 gene, and a second domain for binding with the Cas9 protein. In the developed method, cancer cells are contacted with a first recombinant vector containing the gRNA and a second recombinant vector encoding the Cas9 protein. The administration of an inducible promoter induces the transcription of the gRNA and production of the Cas9 protein, which is guided by the gRNA to cut the target gene (i.e., the TCOF1 gene) at a specific location, ultimately inhibiting TCOF1 gene overexpression. Thus, this invention can treat diseases associated with abnormal TCOF1 gene expression, in particular TNBC.

Advantages

- The gRNA molecule allows gene editing in a cell such as a cancer cell to alter the expression of the target gene.
- Using CRISPR/Cas9 technology with gRNA probes against TCOF1 may show greater therapeutic efficacy with less toxicity as compared with chemotherapy.
- This invention provides a novel, alternative approach to treat TNBC via a targeted therapy.

Applications

- This invention has medical applications including therapies, diagnosis, research, and the like.
- The gRNA molecule and related kit may be used to treat and/or prevent diseases associated with abnormal TCOF1 gene expression.
- This invention may be used to treat a subject suffering from breast cancer, particularly TNBC.

Hu JY, Lai Y, Huang H, Ramakrishnan S, Pan Y, Ma VW, Cheuk W, So GY, He Q, Lau CG, Zhang L, Cho WC, Chan KM, Wang X, **Chin YR**. TCOF1 upregulation in triple-negative breast cancer promotes stemness and tumor growth, and correlates with poor prognosis. *Br J Cancer 126:57-71* (2022) PMID: 34718356