# The mechanism research on polyamine targeting ZNF133-L1CAM axis to suppress malignant progression of breast cancer

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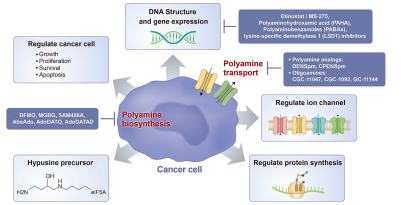
## Abstract

We have previously reported that ZNF133 is associated with a favorable prognosis for breast cancer; ZNF133 can inhibit the transcriptional activity of L1CAM gene promoter, inhibit the proliferation and invasion of breast cancer cells in *vitro*, and inhibit the growth and metastasis of breast cancer in *vivo*. Polyamines can reduce the level of ZNF133 protein and weaken the inhibitory effect of ZNF133 on the proliferation and invasion of breast cancer cells. Polyamine synthesis inhibitors can increase the level of ZNF133 protein and promote its transcriptional inhibition of L1CAM, thus inhibiting the proliferation and invasion of breast cancer cells.

## Introduction

- Polyamines accumulate in large quantities in tumor tissues, blood, and urine of breast cancer patients. They are involved in regulating gene expression, protein modification, synthesis and degradation, affecting membrane permeability, and promoting proliferation, thereby facilitating the malignant progression of tumors.
- ZNF133 is a member of the KRAB C2H2-type zinc-finger protein family. In our previous research, we confirmed the important roles of several tumor suppressor members within the C2H2 ZNFs family in inhibiting the occurrence and development of breast cancer.
- L1 cell adhesion molecule (L1CAM) is a key metastatic factor for breast cancer cells; depletion of L1CAM renders breast cancer cells unable to metastasize and colonize in multiple organs such as the lung, bone, brain, and liver.

## Introduction




Polyamine functions and inhibitors ( from Ita Novita Saril, et al. Metabolism and function of polyamines in cancer progression. Cancer Letters, 2021, 519, 91-104)

## Results

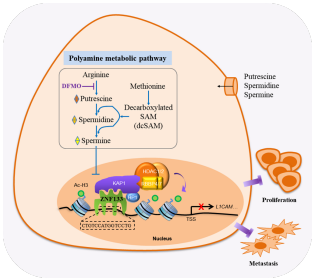



**Figure 1.** Polyamine Metabolism Reduces ZNF133 Levels to Regulate L1CAM Expression and Promote Malignant Progression of Breast Cancer

## Results

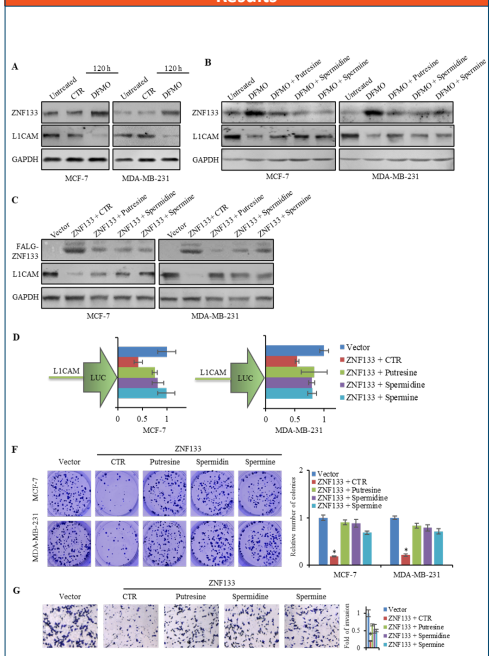



**Figure 2.** Polyamine Reduces ZNF133 Levels, Thereby Weakening Its Inhibitory Effect on L1CAM Expression and further affecting the proliferation and invasion of Breast Cancer Cells

## Results

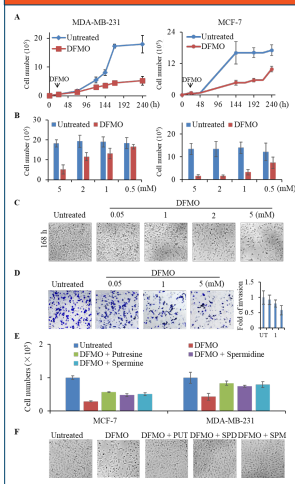



**Figure 3.** DFMO, a Polyamine Synthesis Inhibitor, Inhibits the Proliferation and Invasion of Breast Cancer Cells

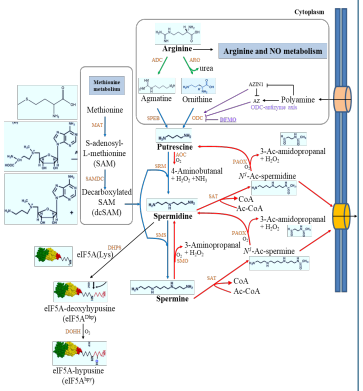



**Figure 4.** Polyamine Biosynthesis and Catabolism

## Conclusions

Polyamines promoted the transcription of L1CAM by inhibiting ZNF133, thus promoting the malignant progression of breast cancer. We elaborated the molecular mechanism of polyamine regulation of ZNF133 protein level in breast tumor cells and ZNF133 inhibition of L1CAM transcription. We verified the effect of polyamine metabolism on regulation of ZNF133-L1CAM axis in the malignant progression of breast cancer, providing a new target for the diagnosis and treatment of breast cancer.

## Contact

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