



## **EGR 3 gene as a regulator of transition Epithelio-mesenchymal cancer: possible therapeutic implications**

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### **1 INTRODUCTION**

Breast cancer is one of the leading causes of death in women worldwide, and its incidence is increasing. Most cases occur in women between the ages of 40 and 59, although it can occur in younger women and even men. Breast cancer is caused by the disordered proliferation of cells in the organ.

Genetic, environmental, and behavioral factors may increase the risk of developing the disease. Reproductive risk factors include age at first menstruation, late menopause, not breastfeeding, and use of hormone therapy. Lifestyle habits, such as smoking, alcohol consumption, and poor diet, can also increase the risk of developing the disease. Mammography is the most widely used method for early breast cancer screening. The goal of screening is to detect the disease at early stages, when treatment is more effective and the chances of cure are greater. Primary prevention, through the adoption of healthy lifestyle habits, is fundamental for the prevention of breast cancer.

Estrogen is a hormone that plays an important role in mammary gland development and breast cancer. The EGR 3 gene is a transcription factor that may play an important role in the physiology of normal and malignant breast cells, since it is induced by estrogen and in turn induces the expression of other estrogen responsive genes. Treatment of breast cancer can involve different approaches, depending on the stage of the disease and other factors. Treatment options include local methods, such as surgery and radiation therapy, and systemic methods, such as chemotherapy, hormone therapy, and immunotherapy. Natural products are being studied as alternatives that are more selective for tumor cells and cause fewer adverse effects on the body. EGR proteins are transcription factors that respond to various stimuli and are expressed in tumor cells. They have a DNA-binding domain and act as transcription factors in response to extracellular signals.



## 2 OBJECTIVE

To conduct a literature review and investigate the role of the EGR 3 gene in the regulation of the epithelial-mesenchymal transition (EMT) in the tumor process, aiming to understand its potential as a therapeutic target for inhibition of tumor progression and metastasis.

## 3 METHODOLOGY

This is a literature review, developed with articles published in the last decade of international and national scientific articles accessed based on Scielo, Pubmed, and Web of Science.

## 4 DEVELOPMENT

The categories that emerged from this work were the relationship of the EGR3 gene and its negative regulation, and the epithelial-mesenchymal transition According to Shin, SH., Kim, I., Lee, J.E. et al, 2020, The EGR3 gene is an important transcription factor in the regulation of several biological processes, such as epithelial-mesenchymal transition (EMT) and cell invasion in breast and prostate cancer cells. Furthermore, EGR3 expression is associated with the promotion of EMT and cell invasion. Negative regulation of EGR3 is related to poor prognosis in gastric cancer patients, and regulates estrogen-mediated invasion in breast cancer. Overexpression of EGR3 strongly inhibits EMT and cell migration and invasion, while knockdown of EGR3 induces EMT and promotes cell migration and invasion. Recent studies have identified 11 genes that inhibit EMT or cell migration and found that ATF3, EMP1, GADD45B, SOCS3 and ZFP36 genes are commonly expressed in an EGR3-dependent manner. Furthermore, it was shown that EGR3 binds to the promoters of GADD45B, SOCS3 and ZFP36 genes and that the expression of these gene-encoded proteins is EGR3-dependent. Therefore, it is clear that EGR3 plays a crucial role in the regulation of cellular processes in normal and pathological conditions, especially in cancer, and is an important target for the development of effective cancer therapies.

## 5 CONCLUDING REMARKS

Although much has been discovered about the role of the EGR3 gene in regulating cellular processes in normal and pathological conditions, including cancer, there is still much to be investigated. Importantly, the epithelial-mesenchymal transition (EMT) is a complex process that involves the activation of several signaling pathways and transcription factors in addition to EGR3. Therefore, future research should focus on understanding how EGR3 relates to these pathways and factors, and how its regulation may be influenced by other factors.

Furthermore, identifying new therapeutic targets for cancer treatment is crucial, especially considering the increasing incidence of cases worldwide. As discussed earlier, EGR3 may be a



promising target for inhibiting tumor progression and metastasis, and it is important to continue studying and developing therapies that target EGR3. Caution is needed, however, when developing these therapies, as the regulation of EGR3 is also involved in important biological processes outside of cancer.

In addition, personalized therapy may be a more effective approach to cancer treatment. Genomic and proteomic analysis of patients can help identify the signaling pathways involved in tumor progression and provide valuable information for the development of patient-specific therapies.

In summary, the study of the EGR3 gene and its relationship to cancer progression is a constantly evolving field, and there is much to be discovered. It is important to continue researching and developing effective therapies for the treatment of cancer, especially considering the significant impact this disease has on society. A deeper understanding of cancer biology and EGR3 regulation is critical to improving the quality of life for patients and to the advancement of medicine in general.



## REFERENCES

- Barnard M, Boeke C, Tamimi R (2015) Established breast cancer risk factors and risk of intrinsic tumor subtypes. *Biochim Biophys Acta Rev Cancer* 1856:73-85
- BRAZIL, Ministry of Health. Breast cancer. Available at <<https://www.gov.br/inca/pt-br/>>. Accessed on: 7 feb 2023
- BRITO, N. M. B.; SAMPAIO, P.C.M.; CASTRO, A. A. H.; OLIVEIRA, M. R. Characteristics clinics of women with invasive ductal carcinoma undergoing neoadjuvant chemotherapy. *Rev Para Med.* 21(4):1-10, 2007.
- DEVITA, Vincent T.; LAWRENCE, Theodore S.; ROSENBERG, Steven A. *Cancer Principles & Practice of Oncology*. 11th. ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins, 2018.
- Elston CW & Ellis IO 1991 Pathological prognostic factors in breast cancer. I. The value of histological grade in breast cancer. Experience from a large study with long-term follow-up. *Histopathology* 19 403-410.
- GOMES DO NASCIMENTO, Renan; OTONI, Kaléu Mormino. Histological and molecular classification of breast cancer: what do we know? *Mastology*, [S. l.], v. 30, p. 20200024, 2020. DOI: 10.29289/25945394202020200024.
- Goldhirsch A, Glick JH, Gelber RD, Coates AS, Thurlimann B & Senn HJ 2005 Panel members. Meeting highlights: international expert consensus on the primary therapy of early breast cancer. *Annals of Oncology* 16 1569-1583.
- Collaborative Group on Hormonal Factors in Breast Cancer (2001) Breast Cancer family: collaborative reanalysis of individual data from 52 epidemiological studies, including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet* 358:1389-1399
- HADDAD, C. F. Trastuzumab in breast cancer. *Femina*. 38(2):73-77, 2010.
- Shin, SH., Kim, I., Lee, JE et al. Loss of EGR3 is an independent risk factor for metastatic progression in prostate cancer. *Oncogene* 39 , 5839-5854 (2020). <https://doi.org/10.1038/s41388-020-01418-5>
- MCPHERSON, K.; STEEL, C.M.; DIXON, J.M. Breast Cancer - epidemiology, risk factors, and genetics. *British Medical Journal*, London, v. 321, p. 624-628, 2000.
- Tower L, Bray F, Siegel R, Ferlay J, Lortet-tieulent J, Jemal A (2015) Global cancer statistics, 2012. *CA Cancer J Clin* 65:87-108
- Hemminki K, Granstrom C, Czene K (2002) Attributable risks for familial breast cancer by status and morphology of the proband: a national epidemiological study from Sweden. *Int J Cancer* 100:214-219
- Hayashi SI, Eguchi H, Tanimoto K, Yoshida T, Omoto Y, Inoue A, Yoshida N & Yamaguchi Y 2003 The expression and function of estrogen receptor alpha and beta in human breast cancer and its clinical application. *EndocrineRelated Cancer* 10 193-202
- Inoue A, Yoshida N, Omoto Y, Oguchi S, Yamori T, Kiyama R & Hayashi S 2002 Development of cDNA microarray for expression profiling of estrogen-responsive genes. *Journal of Molecular Endocrinology* 29 175-192.
- Inoue, A., Omoto, Y., Yamaguchi, Y., Kiyama, R., & Hayashi, S. I. (2004). Transcription Factor EGR3 is involved in the estrogen-signaling pathway in breast cancer cells. *Journal of molecular endocrinology*, 32(3), 649-661.



World Cancer Research Fund/American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington DC: American Institute for Cancer Research; 2007

Zago EA, Montes RM: Chemotherapeutic process in women with breast cancer: understanding the meaning and subjective experiences. Rev Bras Oncologia Clínica 2005 vol. 2 (6) 15-24.