



Indian Journal of Experimental Biology  
Vol. 62, July 2024, pp. 484-495  
DOI: 10.56042/ijeb.v62i07.12272

**NISPR**  
National Institute of Science Communication and Policy Research  
सीएसआइआर-निस्र

## Implication of HIF-1 $\alpha$ signalling in human growth hormone (hGH) induced mammary carcinoma

Poornachandar Gugulothu<sup>1\*</sup>, Dhatri Madduru<sup>2</sup>, Srinivas Baskari<sup>2</sup>, Suresh Velpula<sup>2</sup>, Venkata Ramana Devi<sup>1</sup>  
& Yerramsetty Suresh<sup>3</sup>

<sup>1</sup>Department of Biotechnology, Central University of Tamil Nadu, Thiruvarur - 610 005, Tamil Nadu, India

<sup>2</sup>Department of Biochemistry, Osmania University, Hyderabad - 500 007, Telangana, India

<sup>3</sup>Indian Institute of Chemical Technology, Hyderabad – 500 007, Telangana, India

*Received 31 January 2024; revised 05 April 2024*

Mammary carcinoma is the leading cause of cancer related mortality in women globally. Human growth hormone (hGH) plays a vital role in the development of mammary glands by promoting cell proliferation. Hence, alteration in human growth hormone can contribute to mammary carcinoma. In the present study, we investigated the role of hGH in mammary carcinogenesis and metastasis. We used MTT assay for cell proliferation, and wound healing assay for cell invasion and migration, the cell cycle analysis and analysis of apoptosis. Luciferase reporter assay and Western blot analysis were performed to find out the role of HIF-1 $\alpha$  signalling in association with hGH and also VEGF-A Western blot analysis was performed for angiogenesis regulating with hGH. Further, Western blot analysis was analysed for cadherin levels (E-cadherin and N-cadherin) and confocal microscopy and soft agar assay was performed to understand the role of hGH in metastasis through EMT. The results suggest that MCF-7 breast cancer cell lines transfected with hGH showed enhanced proliferation and cell cycle progression by decreasing apoptosis. This contributes to cancer cell progression via HIF-1 $\alpha$  signalling pathway which also enhances the expression of VEGF-A contributing to angiogenesis. The EMT markers MMP-2 and N-cadherin expression also increased with decreased E-cadherin expression suggesting the role of hGH in metastasis. In conclusion, the present study establishes the role of hGH in breast cancer progression and suggests the possible signalling pathway involved is mediated by HIF-1 $\alpha$ . These finding further helps in novel therapeutic interventions of mammary carcinoma. This present study reports that autocrine production of human growth hormone by human mammary cells alters cell morphology, proliferation and is responsible for enhanced migratory and invasive behaviour leading to breast cancer. Therefore, this study will further help in novel therapeutic interventions for the treatment of breast cancer, by utilizing knowledge of these signalling pathways as targets.

**Keywords:** Breast cancer, Hypoxia inducible factor-1 alpha (HIF-1 $\alpha$ ), Vascular endothelial growth factor-A (VEGF-A), Matrix metalloproteinases (MMPs)