Opiorphin Expression in Breast Cancer Cell Lines

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**ABSTRACT:** Cancer cell line studies are fundamental to the field and are strongly recommended for a number of reasons. They facilitate the search and creation of novel treatments, offer a host of useful benefits, and offer vital insights into the biology of cancer. Potential therapeutic targets may include proteins that are either overexpressed or expressed in cancer cells in a particular way. Opiorphin (QR FSR, peptide I), a naturally occurring inhibitor of enkephalin-inactivating enzymes in human neutral ecto-endopeptidase, was used in this work and incubated with cell lines from breast cancer. The aim of this study is to evaluate expression of Opiorphin in breast cancer cell lines. Cell seeding (MDA231 in 18 WELLS). After 24 hours of incubation, cell viability was assessed using the MTT assay, a colorimetric assay that evaluates mitochondrial metabolic activity as a proxy for cell proliferation. MTT powder was prepared in a 5 mg/mL PBS solution, and the resulting data were analyzed for statistical significance. The outcomes showed that opiorphin therapy significantly decreased the viability of cancer cells. The anti-proliferative activity of opiorphin in breast cancer cells was highlighted by the bar graph data, which showed a statistically significant suppression of tumor cell proliferation (\*\*p < 0.01; \*\*\*p < 0.001). These results point to a potential decrease in cellular metabolic activity and promotion of apoptosis. According to this study, opiorphin may have anti-tumor effects on breast cancer cell lines by inhibiting cell division and perhaps triggering apoptotic pathways. Opiorphin showed potential as a candidate for more preclinical research because it was able to produce detectable biological effects after just 24 hours of exposure. Extending the length of treatment and its extent may provide more insight into the underlying mechanisms and the wider therapeutic utility of opiorphin in oncology patients.

**Keywords:** Opiorphin, Cell line, Breast cancer cell line, MTT assay, anti proliferative activity. [(Chokkattu et al., 2023)](https://paperpile.com/c/WELooe/v2ItZ), [(Laghari et al., 2023; Ramakrishnan et al., 2023)](https://paperpile.com/c/WELooe/W7VoH+I8hhp), [(Muthuswamy Pandian et al., 2022)](https://paperpile.com/c/WELooe/ezWsz) [(Muthuswamy Pandian et al., 2022; Ramakrishnan et al., 2023)](https://paperpile.com/c/WELooe/ezWsz+W7VoH), [(Merchant et al., 2022)](https://paperpile.com/c/WELooe/LayVz), [(Sreevarun et al., 2023)](https://paperpile.com/c/WELooe/bLZI5)

# INTRODUCTION

The National Cancer Institute (NCI; Bethesda, MD) developed a "disease-oriented" drug screening method in the early 1990s. It used a panel of 60 human cancer cell lines that were taken from nine distinct cancer types (brain, colon, leukemia, lung, melanoma, ovarian, kidney, breast, and prostate).[(Wilding & Bodmer, 2014)](https://paperpile.com/c/WELooe/1s82)This strategy was created to enable high-throughput screening of numerous medications with adequate discrimination, ensuring that only a small percentage of medications would be chosen for additional preclinical testing in xenograft models[(Wilding & Bodmer, 2014)](https://paperpile.com/c/WELooe/1s82). Both genotypic and phenotypic drift can occur in cell lines when they are continuously cultured. This is especially prevalent among the most widely utilized cell lines, particularly those that have been kept in cell banks for a long time[(Burdall et al., 2003)](https://paperpile.com/c/WELooe/4hmL).Gene expression profiling and the immunohistochemical expression of ERα, PR, and HER2 demonstrated that breast cancer could be divided into at least five subtypes: luminal A, luminal B, HER2, basal, and normal. This heterogeneity was confirmed by the development of molecular profiling using DNA microarrays. The molecular properties of these subtypes[(Holliday & Speirs, 2011)](https://paperpile.com/c/WELooe/Gl5L). Apart from the above-mentioned cell line work hazards, the majority of these well-established breast cancer cell lines currently in use are derived from tumor metastases, particularly aspirates or pleural effusions, rather than primary breast tumors[(Mukherjee et al., 2021)](https://paperpile.com/c/WELooe/z5VZ). This indicates that most of these cell lines are not from the original lesion, but rather from more aggressive and frequently metastasized tumors [(Burdall et al., 2003)](https://paperpile.com/c/WELooe/4hmL).For more than 50 years, many methods for determining the prognosis and treatment of breast cancer have been established using breast cancer cells. Breast cancer cell line research has been used to evaluate and apply a number of well-known pathways [(Ezhilarasan et al., 2019)](https://paperpile.com/c/WELooe/Z5yT) [(Chokkattu et al., 2023)](https://paperpile.com/c/WELooe/v2ItZ), [(Laghari et al., 2023; Ramakrishnan et al., 2023)](https://paperpile.com/c/WELooe/W7VoH+I8hhp), [(Muthuswamy Pandian et al., 2022)](https://paperpile.com/c/WELooe/ezWsz) [(Muthuswamy Pandian et al., 2022; Ramakrishnan et al., 2023)](https://paperpile.com/c/WELooe/ezWsz+W7VoH), [(Merchant et al., 2022)](https://paperpile.com/c/WELooe/LayVz), [(Sreevarun et al., 2023)](https://paperpile.com/c/WELooe/bLZI5). BC cell lines are vital resources for BC research and have been extensively employed to clarify BC biology and develop novel treatments. Numerous studies have been conducted on cell lines' transcriptome, genome, and, to a lesser extent, epigenome due to their ease of genetic manipulation and propagation [(Grigoriadis et al., 2012; Holliday & Speirs, 2011)](https://paperpile.com/c/WELooe/Gl5L+xV25).The breast cancer cell lines are also listed according to their TP53 and protein status. This gene is frequently referred to as "the guardian of the genome" since it can activate genes involved in cell cycle arrest, apoptosis, and [(Grigoriadis et al., 2012)](https://paperpile.com/c/WELooe/xV25)DNA repair. Several articles address p53 mutations. This gene's mutations can result in a number of abnormalities that eventually translate into proteins that the body's cells shouldn't express[(Witt & Tollefsbol, 2023)](https://paperpile.com/c/WELooe/Y4jC)[(Aparna et al., 2021; Poornima et al., 2021; Verma & Muthuswamy Pandian, 2021)](https://paperpile.com/c/WELooe/E9lVj+DmZKj+jThG6), [(Merchant et al., 2022; Pandiyan et al., 2022)](https://paperpile.com/c/WELooe/RMPgX+LayVz), [(Chokkattu et al., 2022; Ramamurthy et al., 2022)](https://paperpile.com/c/WELooe/gR33K+TsEAq)[(Marya et al., 2022)](https://paperpile.com/c/WELooe/1BtE7), [(Jain & Verma, 2022; Marya et al., 2022)](https://paperpile.com/c/WELooe/1BtE7+ky52B), [(Wadhwani et al., 2022)](https://paperpile.com/c/WELooe/Ss71C)[(Adel et al., 2023)](https://paperpile.com/c/WELooe/Nc342), [(Subramanian & Harikrishnan, 2023)](https://paperpile.com/c/WELooe/IqdmH), [(Solanki et al., 2023)](https://paperpile.com/c/WELooe/JZRKW). Opiorphins stimulate pathways that may be able to get beyond the hypoxic barrier created during tumor growth and encourage the creation of androgen-insensitive PrCa[(Mukherjee et al., 2021)](https://paperpile.com/c/WELooe/z5VZ). Well-studied opiorphin biochemical activities and their role in benign disease point to potential pathways by which they could contribute to the onset and spread of cancer[(Mukherjee et al., 2021)](https://paperpile.com/c/WELooe/z5VZ). The current study sought to determine whether increased opiorphin gene expression was linked to the activity of cancer progression.

# MATERIALS AND METHODOLOGY

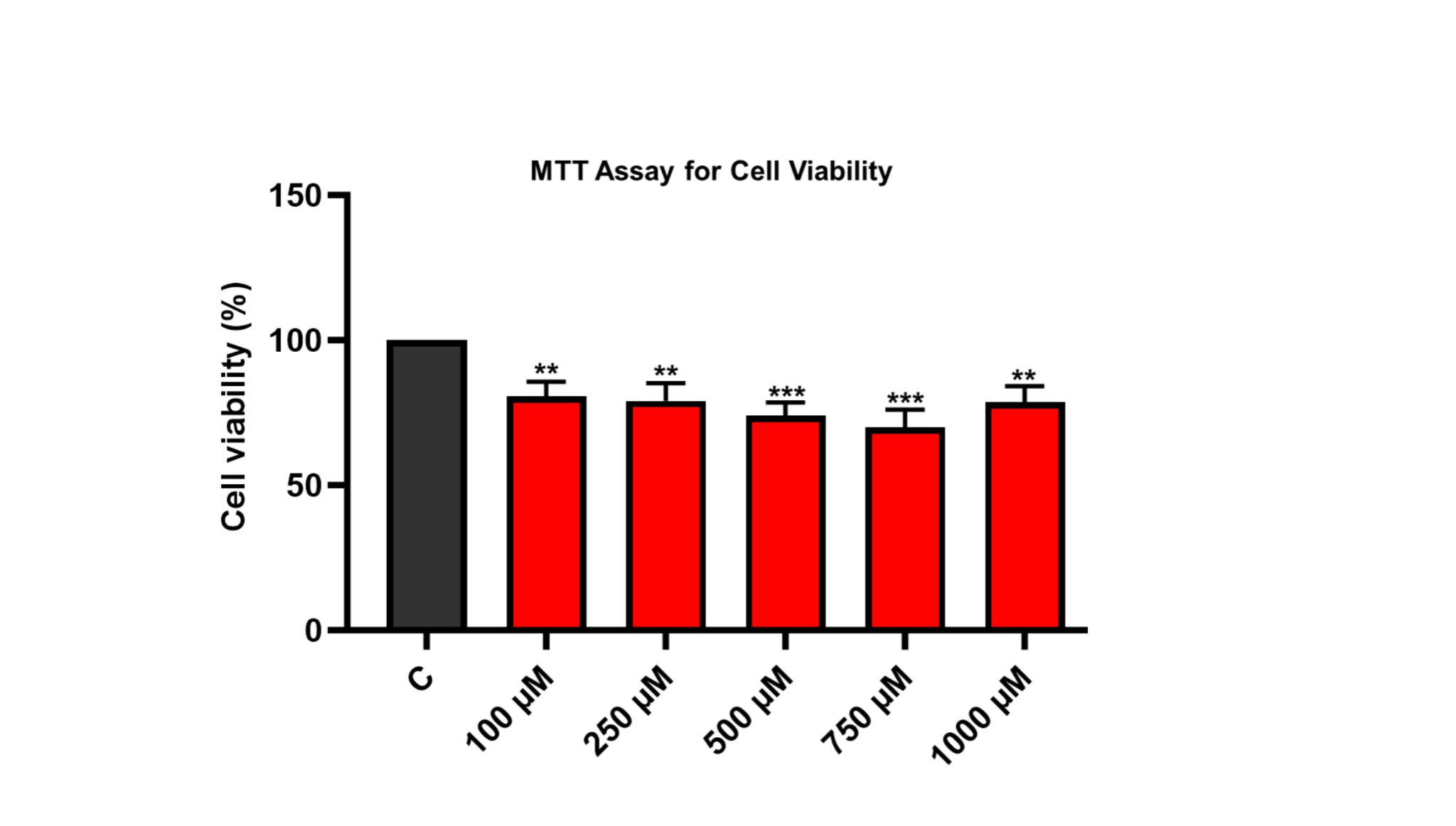
Opiorphin is purchased in a powdered form and diluted in nuclease free water. Procedure consisted of the following steps which includes cell seeding (MDA231 in 18 wells). Medium was performed in triplicate where 100ml of DMEM with serum is added and allows it to grow for 24hrs. After 24 hrs of incubation, replace it with serum free DMEM medium with drug(opiorphin). Followed by MTT assay, MTT(dimethyl thiazolyl diphenyl tetrazolium bromide) in powder form is diluted in 5 mg/ml PBS. After 3 hrs of incubation, MTT enzymes bind with live cells and form formason crystals. Adding DMSO solution 100ml/well. After a few minutes crystals dissolved by DMSO - which turns into purple color. The UV spectrometry is used at 570um, optical density values recorded by ELISA PLATE READER.

# STATISTICAL ANALYSIS

Graph pad prism 10.1.2; One way ANOVA used to differentiate control and case group.

# RESULTS

C represents the control group of MDA231 without any incubation of the drug. Results were obtained in a 24 hrs interval. Opiorphin of 10mg is diluted in nucleus free water as per the instructions in its manual. Different concentrations were made and astonishingly at different concentration cell lines showed cell death (apoptosis). At 100 micromoles, introducing Opiorphin in the cell line shows decrease in cell viability. Gradually, a very minimal decrease in expression of opiorphin at higher concentration. But at a very high concentration of 1000 micromoles, it exhibits drastic elevation. Which proves at concentration of 1000 micromoles it shows anticancer properties.



**Figure 1:** In the above mentioned bar graph \* indicates significance valve, \*- p<0.05.\*\* - p<0.01. \*\*\*- p<0.001. Results came like \*\* and \*\*\* respectively, which means Opiorphin shows significant potential against cancer cells.

# DISCUSSION

Opiorphin has demonstrated potential in breast cancer research. It functions by stopping enkephalin degradation, which affects opioid receptor activation pathways that could impact the migration, proliferation, and survival of cancer cells[(Bocsik et al., 2015)](https://paperpile.com/c/WELooe/wjcA). Even though there isn't much study specifically on breast cancer cell lines like MCF-7 or MDA-MB-231, the effects might differ depending on the particular molecular traits of each cell[(Witt & Tollefsbol, 2023)](https://paperpile.com/c/WELooe/Y4jC). Further research is necessary to understand (Nikalje et al., 2024) (Chehelgerdi et al., 2023) the mechanisms and possible therapeutic benefits of opioids in breast cancer because of their capacity to alleviate pain associated with the disease while also possibly affecting tumor dynamics[(Ramani & Balkwill, 1988)](https://paperpile.com/c/WELooe/95Hf)[(Yamunadevi et al., 2020)](https://paperpile.com/c/WELooe/L91j)[(Saklecha et al., 2025)](https://paperpile.com/c/WELooe/vLnu). It prolongs the action of natural opioid peptides called enkephalins by blocking the enzymes that break them down[(Shete et al., 2023)](https://paperpile.com/c/WELooe/l3tR). By influencing cell growth factors, the extracellular matrix, and other physiologically active chemicals, NEP has been shown to be involved in the modification of the tumor microenvironment, including that of colon cancer [(Shete et al., 2023)](https://paperpile.com/c/WELooe/l3tR)[(Sivasakthivel et al., 2023)](https://paperpile.com/c/WELooe/7y7Z). The authors concur that the involvement of opioids and NEP in the development of cancer appears to vary depending on the origin, stage, and grade of the tumor as well as the inspection technique, despite some differences in the findings[(Mizerska-Dudka & Kandefer-Szerszeń, 2015)](https://paperpile.com/c/WELooe/8QTT).In another study, the expression and therapeutic importance of opiorphin prepropeptide (OPRPN), a different member of the opiorphin family, in radiation for head and neck squamous cell cancer (HNSCC) [(Mangueira et al., 2022)](https://paperpile.com/c/WELooe/09JW). The expression of SMR3A and OPRPN was examined both before and after fractionated irradiation (4x2 Gy) using immunohistochemistry (IHC) staining in ex vivo tumor tissues and double immunofluorescence staining in established HNSCC cell lines [(Rong et al., 2022)](https://paperpile.com/c/WELooe/xss2)[(Vouzas & Gilbert, 2023)](https://paperpile.com/c/WELooe/yH6h) . Although its significance in cancer biology is still developing, its actions are mostly researched in pain modulation[(Regad et al., 2015)](https://paperpile.com/c/WELooe/W2cm). Apoptosis or programmed cell death in cancer cells may be regulated by Opiorphin [(Mizerska-Dudka & Kandefer-Szerszeń, 2015)](https://paperpile.com/c/WELooe/8QTT)[(Efremov et al., 2018)](https://paperpile.com/c/WELooe/momY) In our study it is evident that Opiorphin has potency to decrease cell proliferation in tumor cells. In the above mentioned bar graph \* indicates significance valve, \*- p<0.05.\*\* - p<0.01. \*\*\*- p<0.001. Results came like \*\* and \*\*\* respectively, which means Opiorphin shows significant potential against cancer cells. Further studies have to be made to prove its toxicity and binding energy. Opiorphin's anti-nociceptive qualities may help cancer patients with their pain while also having an impact on tumor biology. To investigate its therapeutic potential, safety, and effectiveness in modifying the course of cancer, more research is required.

# CONCLUSION

Opiorphin has been shown to exhibit negative effects on cancer cell proliferation and apoptosis within a 24-hour period. This implies that it may have a function in preventing the formation of tumors and causing malignant cells to die. But prolonging the study past 24 hours might offer a more profound understanding of its long-term impacts on cell viability, survival strategies, and possible cytotoxicity. Long-term exposure may show if cells acquire adaptive resistance or whether opiorphin maintains its anti-cancer effects. It might also assist in determining the best dosage and window of therapy for possible therapeutic uses. To determine its full potential and mode of action in the treatment of cancer, more research is necessary.

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