

# KEPU GRANT



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Mechanistic Studies to Understand Metastasis Breast Cancer: Towards the Effects of Microbial Derivatives of Testosterone Propionate on MDA-MB 231 Cell Migration

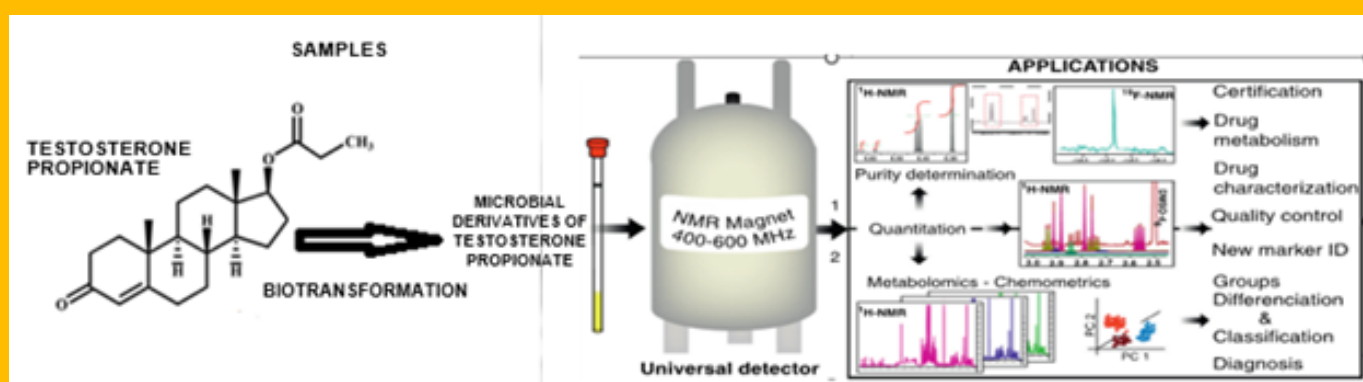
Cancer is a worldwide disease that can affect everyone. It is a genetic disease that arises by changing the function of genes such as proto-oncogenes, tumour suppressor gene and DNA repair gene. Cancer begins when cells grow uncontrollably and form a mass called tumour. Cancer can be classified into two, which are benign tumours or malignant tumours. A benign tumour is localised in the cells while a malignant tumour is a tumour that tends to invade and spread in the body.

One of the most common cancers that affect women worldwide is breast cancer. It is a heterogeneous disease that affects one in every eight women worldwide. Breast cancer is cancer that develops in breast cells. Cancer is derived from lobules and ducts of the mammary gland. In breast cancer, abnormal growth of cells will occur from epithelial cells that line both lobules and ducts. Breast cancer can be categorised into two types, which are invasive and non-invasive. Invasive breast cancer is cancer that spreads into surrounding tissues while non-invasive breast cancer does not spread from the original tissues. According to American Cancer Society (ACS), in 2018, there are 266,120 new cases of invasive cancer and 63,960 new cases of carcinoma in situ are estimated to be diagnosed. This led to breast cancer ranked as the second cause of cancer-related death in females.

Metastasis breast cancer is cancer that spreads from the breast to other parts of the body. Bone, brain, liver, and lung are the most common parts of metastasis breast cancer. Cancer cells can spread through the bloodstream and lymphatic system. It needs to undergo metastatic cascades such as intravasation, survival in circulation, extravasation into distant organs and angiogenesis to metastasize to a distant location.

Many treatments such as surgery, radiotherapy (RT), chemotherapy (CT) and hormone therapy have been used to treat breast cancer. The treatment for breast cancer depends on the stage and type of the disease. One of the most popular treatments for breast cancer is chemotherapy. Chemotherapy is a treatment that uses medications to kill cancer cells. Chemotherapy drugs have a specific class of medication known as cytotoxic agents that are designed to destroy the rapid growth of cancer cells. Doxorubicin, docetaxel, and cyclophosphamide are the most common drugs that are used in chemotherapy. Earlier diagnosis of breast cancer can improve the quality of life of patients. This proves the survival rate of breast cancer increased from 75% to 91% within 42 years (Chang et al., 2018).

Since there is no solid clinical treatment to prevent breast cancer metastasis, identification of new compounds that can be used to prevent the progression of breast cancer metastasis is urgently required. Yet, there are no drugs available to cure metastatic breast cancer, especially for triple-negative breast cancer. In view of that, by focusing on the treatment against metastasis breast cancer cells, a new anti-metastatic drug candidate was needed. Testosterone propionate (17 $\beta$ -hydroxy-androst-4-en-3-one-propionate) is the 17 $\beta$ -hydroxy ester derivative of testosterone, which is an important steroidal hormone responsible for secondary sexual characteristics. Testosterone propionate has been employed for the treatment of breast carcinoma. It is also used as an anabolic steroid by athletes. Previously, several biotransformation studies on testosterone propionate with various fungi such as *Trichoderma hamatum*, *Absidia coerulea*, *Acremonium roseum*, *Alphanocladium album*, and *Rhodotorula mucilaginosa* have been conducted.



## IDENTIFICATION OF METABOLIC ALTERATIONS INDUCED BY TESTOSTERONE PROPIONATE DERIVATIVES ON INHIBITION OF MDA-MB 231 BREAST CANCER CELL PROGRESSION

Therefore, to contribute to the advanced trends of research on Testosterone propionate, in this study, microbial derivatives of Testosterone propionate will be used to determine their anti-metastatic effect on metastasis of triple-negative breast cancer cells. NMR is a valuable tool that can be used for quantitative fingerprinting to identify different metabolites within tissue engineering scaffolds.

Moreover, NMR can also be exploited for targeted and untargeted human metabolic phenotype diversity. Proton (<sup>1</sup>H)-NMR has been employed to characterise molecules, drugs, and toxic substances in plasma samples. <sup>1</sup>H-NMR-based metabolomics profiling first became a popular technology in the early 2000s because it could be used to identify organic compounds within biological fluids. Metabolomics is now a well-established and mainstream tool for biomedical research.

Metabolites act as phenotype plasticity controls in cancer microcellular environmental regulation. Metabolites are biomarkers of phenotypic states, which are now receiving a great deal of attention. The metabolic pathway screening can be achieved using metabolomics but still requires some optimization to improve robustness. The <sup>1</sup>H-NMR-based activity of metabolome and/or small molecule integrity analysis and, thus, the fundamentals of NMR theory and chemometrics have also been discussed. The growth of NMR as technology has meant that highly complex molecules found in biofluids have been studied, resulting in the generation of structural and functional details at the molecular level.

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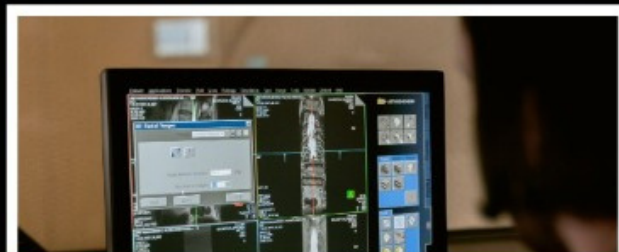
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