

**Cancer Science 2019: PI3K/AKT-signalling pathway and immune-escape in triple-negative breast cancer - Dr. Jens Hahne - Department of Molecular Pathology, ICR London, UK**

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Breast cancer accounts for 23% of all new tumour cases and it is the most common cancer among women worldwide. A high percentage (15-25% of all breast cancer cases) is characterized as triple-negative breast cancer (TNBC). Although TNBCs are sensitive to chemotherapy, survival of patients with these tumours is poor.

Lack of effective therapies, younger age at onset and early metastatic spread have contributed to the poor prognosis and outcomes associated with TNBC. The phosphatidylinositol 3-kinase (PI3K)/AKT-pathway plays a critical role in malignant transformation of tumours and their subsequent growth, proliferation and metastasis as well as in activation of pathways that result in immune-escape mechanisms. Therefore, the PI3K/AKT pathway is considered an attractive candidate for therapeutic interventions.

A modified FATAL assay was used as an in-vitro system to investigate the interaction between TNBC cell lines and natural killer (NK)-cells. Furthermore the ability of PI3K/AKT inhibition with AEZS-126 to selectively target TNBC cell proliferation and survival was explored. In parallel we analysed mechanisms of cytotoxicity related to PI3K/AKT inhibition.

Breast cancer is the most prevalent cancer type in women as well as the leading cause of cancer mortality

in this population worldwide, with a peak incidence between 45 and 65 years of age. Although it is not common, breast cancer can also occur in men, with a frequency of 1 in 100 diagnosed cases, representing less than 1% of all cancers in men.

Among the most important risk factors associated with breast cancer are ageing, family history, nulliparity, hormonal factors, such as early menarche or late menopause, and other factors related to lifestyle, such as alcohol consumption, obesity, and physical inactivity. Breast cancer can be hereditary or sporadic. The most frequent mutations associated with hereditary cancer include those that affect DNA damage repair (DDR) genes, the most important of which are mutations in the BRCA1, BRCA2, and TP53 genes. Sporadic cancer represents approximately 85% of all cases of breast cancer and is associated with some of the risk factors mentioned above; however, it has also been associated with exposure to carcinogens, such as air pollutants, electromagnetic radiation, and DDR gene expression dysregulation.

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