J C Hahne et al., Breast Can Curr Res 2017, 2:4 (Suppl)
DOI: 10.4172/2572-4118-C1-009

Role of PI3K/AKT-signaling pathway in triple-negative breast cancer

J C Hahne, A Lampis, S R Meyer, A Honig, J B Engel and **N Valeri**
The institute of Cancer Research, Russia

Breast cancer accounts for 23% of all new tumor 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 triple-negative cancers are sensitive to chemotherapy, survival of patients with these tumors 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 tumors 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. We used a modified FATAL assay as an *in-vitro* system to investigate the interaction between TNBC cell lines and natural killer (NK)-cells. Furthermore we explored the ability of PI3K/AKT inhibition with AEZS-126 to selectively target TNBC cell proliferation and survival. In parallel we analyzed mechanisms of cytotoxicity related to PI3K/AKT inhibition. Our results show that TNBC cells (MDA-MB468, HCC1806, HCC1937) can stimulate the NK-cell immune response significantly stronger than estrogen-receptor (ER)-positive breast cancer cells (MCF-7). These findings could explain the increased presence of immunosuppressive Tregs infiltrate in human specimens of TNBC compared to ER-positive breast cancer tissue. AEZS-126 showed good anti-tumor activity in *in-vitro* models of TNBC as well as in MCF-7 cells. Main mechanism of cytotoxicity seems to be programmed cell death, which could be abrogated by co-incubation with z-VAD-fmk in MCF-7 and MDA-MB468 cells. In HCC1806 cells, addition of necrostatin-1 has only slightly protective effects, but in HCC1937 cells, the addition of necrostatin-1 has the same protective effect as co-incubation with z-VAD-fmk, and this observation argues for cell death caused by apoptosis and necroptosis in this cell line.

Biography

J C Hahne is currently working for The institute of Cancer Research, Russia. He has several publications in the reputed journals.

hahnejen@yahoo.de

Notes: