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Role of sphingosine-1-phosphate in estrogen receptor signaling in breast cancer

Breast cancer remains the most common malignant disease in women. The estrogen receptor-α (ERα) and its ligand 17β-estradiol (E2) play important roles in breast cancer. E2 elicits cellular effects by binding to ERα in the cytosol followed by receptor dimerization and translocation to the nucleus where it regulates gene expression by binding to ERE response elements. However, it has become apparent that E2 also exerts rapid non-genomic effects through membrane-associated receptors. There is emerging evidence that this induces formation of the bioactive sphingolipid metabolite sphingosine-1-phosphate (S1P). S1P in turn regulates many processes important in breast cancer progression and metastasis. One of the enzymes that produce S1P, sphingosine kinase 1 (SphK1), is upregulated in breast cancer and its expression has been correlated with poor prognosis. This lecture will focus on the role of the SphK/S1P axis in estrogen signaling and breast cancer progression. I will also discuss new data showing that ERα36 is the E2 membrane receptor required for E2-mediated SphK1 activation and rapid secretion of S1P, which regulates some of the non-genomic effects of E2. Our data also suggests that targeting SphK1/S1P signaling may potentially be a new therapeutic option for treatment of triple negative breast cancer.

Biography

Sarah Spiegel is the Chair Person of the Department of Biochemistry and Molecular Biology at Virginial Commonwealth University School of Medicine and directs the cancer cell signaling program at the MCC. Her research is focused on sphingosine-1-phosphate (S1P), whose functions as a pleiotropic signaling lipid were discovered in her lab that opened a new areas of research focused on this bioactive sphingolipid metabolite. As a result of her work, it is now recognized that S1P regulates numerous biological processes and is critical for health and diseases. She has published more than 300 papers and received many awards for her work.

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