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Proteome analysis in breast cancer cells reveals differential expression of signatures involved in pre-mRNA alternative splicing events in response to 17 β -estradiol and CRH**Siti Sarah Hamzah**

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Studies show that 70% of breast cancers are estrogen receptor-positive (ER+) and activation of cellular processes involved in several tumorigenesis-associated events are detected predominantly in ER+ breast cancer. To characterize the global proteomic alterations affected by sex hormone estrogen, a label-free quantitative proteomic method was used to identify and quantify the differentially expressed proteins in the hormone-responsive MCF7 cells exposed to 17 β -estradiol (E2) for 24 h. Using a selection filter cut-off of >2-fold change and p value < 0.01, 3,000 proteins were identified: 93 of them were upregulated whereas 64 were downregulated by E2. The list of upregulated proteins included the 91 kDa serine-arginine protein kinase 1 (SRPK1), a key kinase involved in the phosphorylation of serine-arginine proteins (SRPs) during pre-mRNA alternative splicing that also found to be overexpressed in malignant cancer cells. Follow up studies employing qRT-PCR and Western blots revealed increased phosphorylation signal of SRp40 and SRp30 as well as increased production of aberrant CD44 mRNA isoforms. In cellular models of ER+ breast cancer, SRPK1 expression was also positively regulated by corticotropin-releasing hormone (CRH) a hypothalamic hormone involved in adaption to stress. In contrast, proteome analysis using Nano-flow Ultra HPLC coupled to Orbitrap fusion demonstrated that CRH did not affect SRPK1 expression in ER-breast cancer and phosphosites analysis in cells depleted with SRPK1 kinase resulted in reduced detection of signal specific for phosphorylation site of SRp40 and SRp30. Altogether, these results identify potential targets of hormone-altered proteome profiles in different types of cancer cells hence triggering signaling networks that could enrich proteome diversity by producing distinct oncogenic protein isoforms.

Biography

Siti Sarah Hamzah is a final year PhD student at University of Warwick, United Kingdom. She received a Bachelor degree in Biochemistry and Molecular Biology from The University of Melbourne, Australia and an Honours degree in Pharmaceutical Sciences from Monash Institute of Pharmaceutical Sciences, Australia. After 2 years as Medical Scientist in the Biochemistry Dept. of Institute for Medical Research, Ministry of Health Malaysia, she is now serving in the Endocrinology Dept. of the same institute. Her current research involves study of the role of alternative splicing (AS) in epithelial-to-mesenchymal transition (EMT) in breast cancer models.

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