

The Genomic Landscape of Deubiquitinating Enzymes Across Breast Cancer Subtypes

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Breast cancer, the most frequently diagnosed malignancy in women worldwide, is a highly heterogeneous disease on the molecular level and is classified into multiple subtypes [1]. There are 4 major subtypes of breast cancer that are grouped based on the presence/absence of hormone receptors (HR) (estrogen and progesterone receptor) and HER2 receptor which is a growth factor receptor: HR+/HER2-, HR+/HER2+, HR-/HER2-, and HR-/HER2+ [2].

Hemodynamic regulation of protein synthesis and degradation is one of the critical components of cellular physiology. Ubiquitination of proteins as a posttranslational modification is emerging as a key regulatory mechanism for regulating protein degradation and signaling activity. Ubiquitination is mediated by ubiquitin ligases and can be reverted by deubiquitinases (DUBs) [3]. DUBs are proteases that remove ubiquitin tags from substrates, therefore, involved in various cellular functions by regulating the activity and stability of their substrates. The DUB family consists of 103 members in the human genome, and these are frequently misregulated in various cancers including breast cancer [4]. DUBs have emerged as attractive therapeutic targets for the development of novel molecules in recent years as they are amongst the most druggable enzymes in the ubiquitination systems due to their enzymatic protease activities and open ubiquitin pockets [5].

Despite the large in vitro and in vivo studies, DUB profiles of each breast cancer subtype are lacking. Because of the association of the HR and HER2 receptors to tumorigenesis, each subtype requires a unique treatment strategy. Knowing the expression level and mutation types of DUBs in each subtype can give us the potential to develop the best treatment strategy against cancer. Therefore, we are conducting an *in silico* screen to explore genomic and transcriptomic signatures of DUBs using patients' cohort data from Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) and The Cancer Genome Atlas (TCGA) [6]. We are aiming to reveal the profile of DUBs in breast cancer subtypes to lay a foundation for developing relevant therapeutic strategies.

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