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Co-crystallisation of BRCA1 BRCT with small molecule inhibitors

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Germ-line mutations in BRCA 1 (Breast Cancer Susceptibility gene 1) gene have been reported to confer risk of 60-80% for breast cancer and 15-60% for ovarian cancer. Majority of these mutations are found in BRCT and RING domain and BRCA1 association with cancer progression has led to numerous studies investigating the functions of BRCA1 gene and its interacting partners(1). It has been observed that different mutations localized within the BRCT domain are responsible for the pathogenic phenotypes. The BRCT domains are found in proteins involved in DNA damage repair and cell cycle regulations. Protein-Protein Interactions (PPIs) with BRCA1 BRCT and phosphopeptide containing consensus sequences of pS-X-X-F motif promotes trans-activation functions. Small-molecule BRCA1 inhibitors capable of disrupting these BRCT dependent interactions are promising anticancer agents. Therefore, in order to understand PPIs at atomic level, BRCA1 BRCT domain was purified and co-crystallised with small molecule inhibitors(2). The small molecule inhibitors agreeably stained the BRCA1 BRCT crystals. The crystal pictures with the diffractions pattern will be highlighted along with the X-ray diffraction data of co-crystals.

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