Does the PARP inhibitor Olaparib increase anti-tumor activity of the BET inhibitor JQ1 in invasive lobular carcinoma cells?

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Invasive lobular carcinoma (ILC) is the second most common sub-type of breast cancer, compromising 10% of all cases. BET inhibitors represent a novel class of anticancer agents that are clinically relevant in the treatment of ILC, however, their efficacy as single agents are limited. Recent studies demonstrate increased anti-tumour activity of BET inhibitors with the addition of a PARP inhibitor. The aim of this project was to investigate the effects of combining the BET inhibitor, JQ1, with the PARP inhibitor Olaparib, in an *in vitro* model of ILC. Molecular characterization via western blotting identified the CAMA-1 and OCUB-M cell lines as appropriate models of ILC. Initial IC50 characterization experiments completed using the MTT assay demonstrated CAMA-1 cells were more resistant to JQ1 inhibition. Subsequent analysis of the expression of BCL2, an anti-apoptotic gene, was carried out in both cell line models, with the CAMA1 cells demonstrating higher expression of this gene, suggesting an intrinsic resistance to cell death. Synergy assays performed revealed synergistic effects of combination treatment JQ1 and Olaparib. This was further shown through enhanced PARP cleavage seen in the CAMA1 cells, suggesting sensitization of CAMA1 cells to JQ1 induced death with the addition of Olaparib. In OCUB-M cells, PARP cleavage was not affected by the addition of Olaparib to JQ1. The results observed in the CAMA1 cells demonstrate the potential of sensitizing BRCA proficient cells to treatment with PARP inhibition, and the use of a combination therapy for anti-cancer treatment.

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