ARID1A-mutated bladder cancer cells are sensitized to BET protein inhibition with OTX-015
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Bladder cancer (BC) is a common and deadly disease. Inactivating ARID1A mutations (ARID1A\textsuperscript{mut}) occur in up to 30\% of metastatic BC tumors, making it the most commonly mutated epigenetic gene and the 4th most commonly mutated gene overall. ARID1A mutations are associated with decreased response to therapy and poor prognosis; thus, there is a need to develop therapies specifically targeting ARID1A mutant tumors. OTX-015 was 8-times more potent in ARID1A\textsuperscript{mut} HT1197 cells at 120 h than in ARID1A\textsuperscript{WT} 5637 cells (IC\textsubscript{50}: 0.12 μM vs. 1.0 μM). OTX-015 (1 μM) significantly reduced ARID1B and RAD51 mRNA expression versus 0.1\% DMSO control (83\% and 86\% reduction, respectively, both \(P\)ARID1B mRNA expression in (83\% vs. 62\% reduction, \(P\)=0.02) and RAD51 expression (86\% vs. 57\%, \(P\)=0.001) at 48 h. Interestingly, OTX-015 treatment (1 μM) did not result in significantly reduced MYC expression HT1197 cells (25\% reduction, \(P\)=0.31), but did significantly reduce MYC expression in 5637 cells (57\% reduction, \(P\))