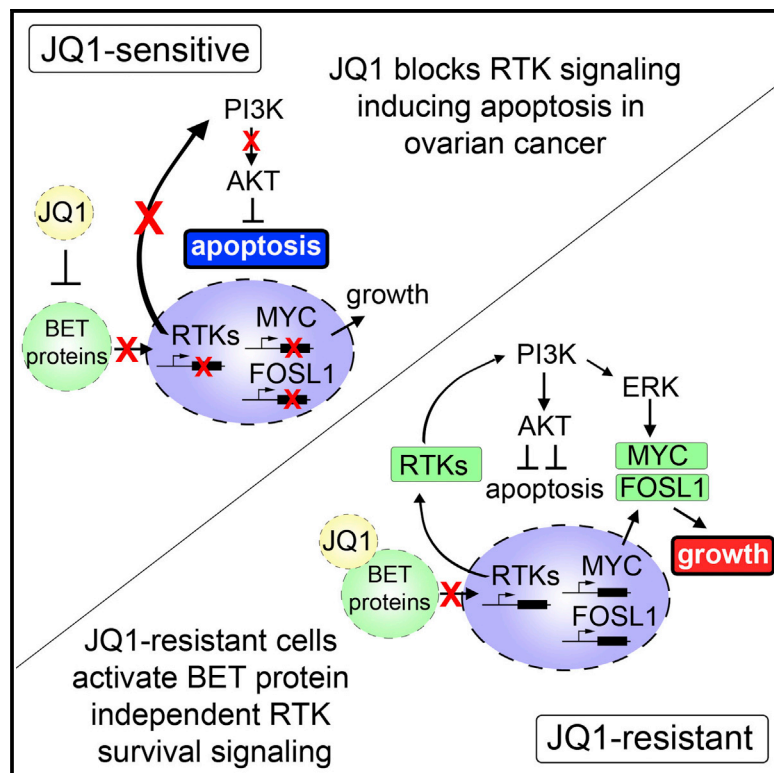


# Resistance to BET Bromodomain Inhibitors Is Mediated by Kinome Reprogramming in Ovarian Cancer

## Graphical Abstract



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## In Brief

BET inhibitors are currently being evaluated in clinical trials for a number of cancers, including ovarian cancer. Kurimchak et al. demonstrate that BET inhibitors may have limited success as single agents in ovarian cancer due to adaptive kinome reprogramming and will require combination therapies targeting kinases and BET bromodomain proteins

## Highlights

- Inhibition of BET proteins reprograms kinome activity in ovarian cancer cells
- Receptor tyrosine kinase activation overcomes BET inhibition, causing resistance
- Elevated PI3K/ERK activity stabilizes MYC/FOSL1 proteins in JQ1-resistant cells
- Co-targeting BET proteins and RTK or PI3K signaling enhances BET inhibitor therapy

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