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Puissant and colleagues screened a compendium of cancer cell lines to identify those most sensitive to the bromodomain and extraterminal domain (BET) protein inhibitor JQ1. Neuroblastoma cell lines were among the most JQ1-sensitive cell lines, and MYCN amplification, which is commonly observed in high-risk neuroblastoma, was the feature most predictive of JQ1 sensitivity. JQ1 displaced the BET family member BRD4 from the MYCN promoter, leading to decreased expression of MYCN and MYCN target genes, and significantly prolonged survival in several MYCN-amplified neuroblastoma models. These findings thus implicate MYCN amplification as a genetic predictor of BET inhibitor sensitivity and provide support for the development of BET inhibitors in MYCN-amplified neuroblastoma.

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