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ON THE COVER

Tanaka and colleagues demonstrate that mTORC2 is activated in the majority of glioblastomas and mediates chemoresistance in an AKT-independent manner via NF-κB pathway activation. Surprisingly, they show increased activity of this mTORC2–NF-κB signaling pathway in GBM cells in response to rapamycin, which may provide an explanation for the failure of rapamycin to demonstrate efficacy in GBM clinical trials. Instead, dual mTOR kinase inhibitors that block the activity of both mTORC1 and mTORC2 may improve clinical outcome, particularly when combined with other chemotherapeutic agents. For details, please see the article by Tanaka and colleagues on page 524.