

## **DNA replicative stress regulates responses to ICT in non-hypermuted tumors**

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#### Brief Synopsis:

Recent studies have shown significant responses to immune checkpoint therapies (ICT) in patients with non-hypermuted cancers, including breast cancer. However, biomarkers established in hypermuted cancers have shown no predictive accuracy. Notable, we discovered that a replication stress response (RSR) defect gene signature accurately predicted ICT response in many non-hypermuted patient cohorts. Furthermore, manipulation of RSR status was sufficient to modulate response to ICT. Our research, therefore, may help to stratify non-hypermuted cancer patients for ICT and to provide effective combination therapies to expand the treatable population.