DNA replicative stress regulates responses to ICT in non-hypermutated tumors

Brief Synopsis:

Recent studies have shown significant responses to immune checkpoint therapies (ICT) in patients with non-hypermutated cancers, including breast cancer. However, biomarkers established in hypermutated 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-hypermutated patient cohorts. Furthermore, manipulation of RSR status was sufficient to modulate response to ICT. Our research, therefore, may help to stratify non-hypermutated cancer patients for ICT and to provide effective combination therapies to expand the treatable population.