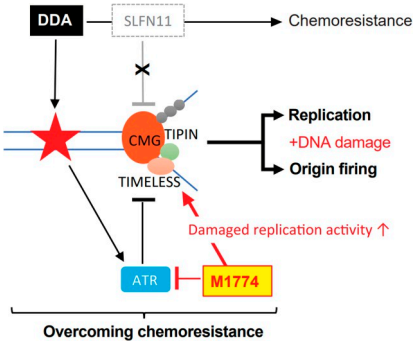
MOLECULAR CANCER THERAPEUTICS
HIGHLIGHTS

Selected Articles from This Issue

Therapeutic Strategies of Novel ATR Inhibitor M1774



Jo, *et al.* | Page 911

Ataxia Telangiectasia and Rad3-related (ATR) inhibitors are being intensively evaluated in phase I/II/III clinical trials. Here, Jo and colleagues report that Tuvusertib (M1774) is a high potent and orally available ATR inhibitor, suppressing cancer cell viability at nanomolar concentrations. They show that Tuvusertib efficiently abrogates the activation of the ATR-CHK1 checkpoint pathway and enhances cancer cell death by enabling unscheduled replication upon replicative damage. This study also demonstrates that Tuvusertib is highly synergistic with a broad spectrum of clinical DNA-damaging agents and provides a rationale for overcoming drug resistance in SLFN11-negative SCLC and patient selection for patients treated with ATR inhibitors.

The NCI PDXNet Consensus Recommendations

Meric-Bernstam, *et al.* | Page 924

Although patient-derived xenografts (PDXs) are commonly used for preclinical modeling in cancer research, a standard approach to *in vivo* tumor growth analysis and assessment of antitumor activity is lacking, complicating comparison of different studies and determination of whether a PDX experiment has produced evidence needed to consider a new therapy promising. Here, Meric-Bernstam and colleagues present the NCI PDXNet Consensus Recommendations for assessment of PDX growth and antitumor activity, providing public access to a suite of tools for *in vivo* growth analyses.

The Impact of TCB Design Targeting CEA in Colorectal Cancer

Elsayed, *et al.* | Page 1010

Colorectal cancer ranks as the second deadliest cancer worldwide, with nearly one million deaths each year. T cell engaging bispecific antibodies (TCBs) represent a promising class of biopharmaceuticals that redirect cytotoxic T cells towards tumor cells. Here, Elsayed, Plüss, and colleagues designed and screened multiple TCB formats that bind to CD3ε on T cells and CEA on tumor cells. The findings highlighted the importance of bivalent tumor targeting and a short spatial separation. The TCB candidate employing these features demonstrated superior *in vitro* activity and potent anti-tumor efficacy in immunocompetent mouse models of colorectal cancer.

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