Targeting CAR for CHOP-Based Lymphoma Treatment

Hedrich et al. __________ Page 392

CHOP regimen continues to be the frontline treatment for non-Hodgkin lymphoma (NHL), but associated relapse and toxicity illustrate a need for improved therapeutics. In this study, Hedrich and colleagues developed a novel multiorgan coculture model containing human hepatocytes, lymphoma cells, and cardiomyocytes to test the effects of human constitutive androstane receptor (CAR) activation on CHOP-based treatment of NHL. The authors showed that coadministration of CITCO, a selective human CAR activator, and CHOP resulted in significantly enhanced cytotoxicity in lymphoma cells, but not in cardiomyocytes, suggesting that this novel combination may offer improved antineoplastic activity without concomitant augmentation of off-target toxicity.

HSP90 Inhibition Kills Mutant KRAS Colon Cancer Cells

Wang et al. __________ Page 448

Oncogenic mutations of KRAS pose a great challenge in colorectal cancer treatment. In this study, Wang and colleagues showed that mutant KRAS colon cancer cells were more susceptible to apoptosis induced by the inhibitor of heat shock protein 90 (HSP90) AUY922 than those carrying wild-type KRAS. Moreover, activation of Bim though ER stress seemed to play an essential role in AUY922-induced apoptosis of mutant KRAS colon cancer cells. These results suggest that AUY922 alone or in combination with agents that enhance the apoptosis-inducing potential of Bim might be promising in the treatment of mutant KRAS colon cancers.

The Development of Immunogenic Picornaviruses as Cancer Therapy

Bell and Pavelko __________ Page 523

The generation of engineered viruses that specifically kill tumors has been the primary emphasis of virotherapy researchers for years. Although direct tumor lysis has been the focus, evidence suggests that the immune response to viruses may promote antitumor immunity. Bell and Pavelko have engineered an immunogenic picornavirus that promotes tumor regression through direct tumor killing and activation of T cells present within the tumor. This vector specifically targets melanoma in vitro and promotes tumor regression and tumor-specific T-cell activation after treatment in vivo. These findings highlight the clinical potential of small RNA viruses as both oncolytic therapy and cancer immunotherapy.