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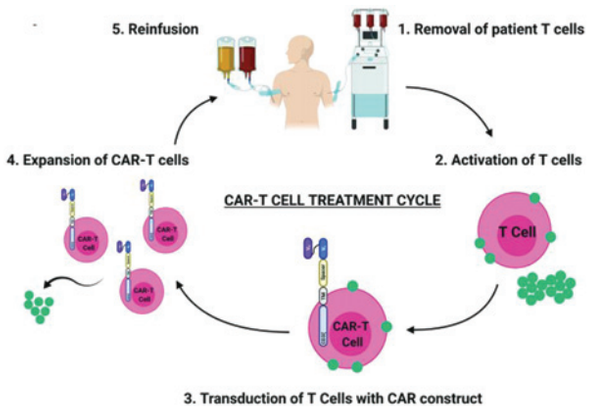
MOLECULAR CANCER THERAPEUTICS

HIGHLIGHTS

Selected Articles from This Issue

Emerging CAR T Cell Therapies in Triple Negative Breast Cancer



Dees *et al.* | Page 2409

There is an unmet medical need to develop novel treatment modalities for patients with triple negative breast cancer (TNBC), an aggressive breast cancer subtype characterized by poor survival rates. The immunogenic nature of TNBC has prompted researchers to exploit a type of adoptive cell therapy called chimeric antigen receptor (CAR)-T cell therapy for the treatment of TNBC. Strategies to address the inherent challenges associated with CAR-T cell therapy in solid tumors and emerging targets and ongoing clinical trials for CAR-T cell therapy in TNBC are discussed in this review.

Repurposing a TPr Inhibitor to Block Cancer Metastasis

Werfel *et al.* | Page 2454

One alternative to discovering novel drugs is to repurpose existing ones. In this study, Werfel and colleagues performed a phenome-wide association study (PheWAS) and identified clinical manifestations correlating with a thromboxane A2-prostanoid receptor (TPr) single nucleotide polymorphism associated with cancer metastasis in several cancer types. CPI211, a TPr inhibitor used in cardiovascular diseases, inhibited TPr in murine models and blocked spontaneous metastasis from primary tumors without affecting tumor proliferation. The study demonstrates the potential of drug repurposing and supports further study of CPI211.

Glutaminase Inhibitors Sensitize Resistant Cervical Cancers

Rashmi *et al.* | Page 2465

The standard of care for the treatment of locally advanced cervical cancer includes pelvic irradiation and cisplatin chemotherapy. Patients failing chemotherapy are salvaged with surgery or cisplatin/bevacizumab, but no cures are available for metastatic or recurrent disease. Therefore, Rashmi and colleagues sought a therapy effective in radiation-resistant cervical cancer. Radiation-resistant cervical cancer cells were found to be reliant on glutamine metabolism and glutaminase inhibition with telaglenastat sensitized xenografts through thiol-mediated oxidative stress. Moreover, PI3K pathway mutations were found to predict telaglenastat sensitivity.

Immunocytokine Synergizes with Oxaliplatin in Cancer Models

Bajic *et al.* | Page 2554

Immune checkpoint inhibitors in metastatic colorectal cancer remain only efficacious in microsatellite instable and deficient mismatch repair tumors. Alternatively, engineered cytokine products using tumor necrosis factor (TNF) can induce cell death. Bajic and colleagues outline a novel fusion of the monoclonal antibody Sm3E (targeting carcinoembryonic antigen, CEA) and TNF. The resulting fusion protein (Sm3E-TNF) was tested in immunocompetent mouse models transfected with human CEA and led to rapid necrosis of tumors that later regrew from the margin. Therefore, the authors combined Sm3E-TNF with oxaliplatin which generated complete tumor eradication in 40% of treated mice. Their results support the continued development of Sm3E-TNF for use with oxaliplatin in metastatic patients.