Clinical Cancer Research
Highlights
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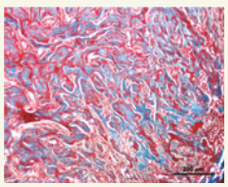
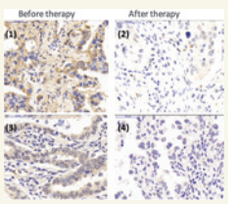
Therapeutic Efficacy of Trabectedin and Anti-PD1 Combination



Treatment options for osteosarcoma remain anchored to surgery and conventional chemotherapy, and are in need of additional and less toxic approaches. Ratti and colleagues developed osteosarcoma models in immunocompetent mice and showed the therapeutic efficacy of trabectedin, a clinically approved marine-derived drug, in halting osteosarcoma growth and metastases. The action of trabectedin was dual: direct on neoplastic cells, inducing their differentiation, and indirect on the immune microenvironment, increasing the infiltration of T cells. However, the latter highly expressed the inhibitory immune checkpoint PD-1. Consistently, combination of trabectedin and anti PD-1 antibody resulted in the best therapeutic effect. ■

See article by Ratti et al., p. 5149

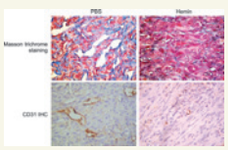
DNA Methylome Screen for Lung Adenocarcinoma with Erlotinib



The authors investigate whether epigenetic changes are involved in the response to tyrosine kinase inhibitor (TKI) treatment of epidermal growth factor receptor (*EGFR*) mutated lung cancer. To investigate methylation changes at the whole-genome level, Niu and colleagues applied methyl-sensitive cut counting sequencing (MSCC) in *EGFR* 19 deletion lung adenocarcinoma tissues before and after erlotinib treatment. A differential methylated region (DMR) of the *GABBR2* gene was identified and validated based on the results of whole methylome profiling, and upregulation of GABBR2 rescued erlotinib-induced apoptosis *in vitro*. This research shows promise in the epigenetic study of *EGFR*-mutated lung adenocarcinoma treated with TKI. ■

See article by Niu et al., p. 5003

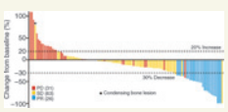
Hemin Conditioning Restrains Prostate Tumor Development



Conditioning strategies constitute a relatively unexplored and exciting opportunity to shape tumor fate by targeting the tumor microenvironment. In this study, Jaworski and colleagues adopted a strategy to remodel the stroma using hemin, a well-known inducer of the enzyme Heme Oxygenase-1, to counteract tumor development. Their results showcase a novel function of an already human-used drug as a means of boosting the endogenous response against prostate cancer, a major health care problem worldwide. In particular, hemin conditioning limits tumor development by simultaneously targeting both tumor vascularization and the cytotoxic T-cell responses. ■

See article by Jaworski et al., p. 5135

Phase II Study of Abemaciclib in HR$^+$/HER2$^-$ MBC



Hormone receptor positive (HR$^+$)/human epidermal growth factor receptor 2-negative (HER2$^-$) metastatic breast cancer (mBC) patients have limited treatment options. Targeting cyclin-dependent kinases (CDK), key components in the cell cycle that are dysregulated in many cancers, has emerged as a viable therapy strategy. In a phase II study of heavily pretreated refractory HR$^+$/HER2$^-$ mBC patients, abemaciclib, a selective oral inhibitor of CDK4 and CDK6, exhibited promising single-agent activity and a safety profile that allowed for dosing on a continuous schedule. Abemaciclib may represent a possible therapy advancement for HR$^+$/HER2$^-$ mBC patients. ■

See article by Dickler et al., p. 5218