Molecular Cancer Therapeutics **Highlights**

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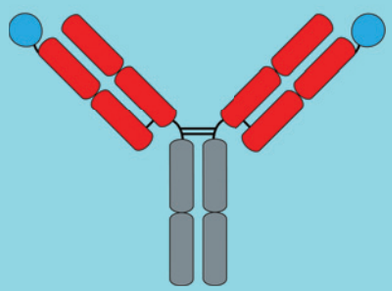
Selected Articles from This Issue



Bispecific HER2-Targeting FynomAb with Superior Antitumor Activity

Brack *et al.*_____Page 2030

In this study, Brack and colleagues created a series of bispecific HER2-targeting antibodies (FynomAbs) capable of simultaneously targeting two distinct epitopes on HER2, among which COVA208 proves to be the most potent in inhibiting HER2-mediated signaling. Compared with two FDA-approved anti-HER2 antibodies, trastuzumab and pertuzumab, COVA208 showed a different mechanism of action and superior antitumor activity in four different xenograft models. The bispecific FynomAb COVA208 has the potential to enhance the clinical efficacy of HER2-directed therapies, and delineates a paradigm for designing a new class of antibody-based therapeutics for other receptor targets.

FAK-β5 Integrin Control of Ovarian Carcinoma Spheroid Growth

Tancioni *et al.*_____Page 2050

Interactions between integrins and their ligands trigger focal adhesion kinase (FAK) activation that enables ovarian tumor growth and dissemination. Here, Tancioni and colleagues identify a bidirectional signaling linkage between osteopontin, β5 integrin, and FAK in serous ovarian cancer showing elevated β5 integrin and FAK levels associated with decreased serous ovarian cancer patient survival. Pharmacological or genetic inhibition of FAK activity reduces β5 integrin and osteopontin levels that prevent anchorage-independent tumor spheroid growth. FAK activity maintains a tumor spheroid microenvironment of elevated osteopontin and β5 integrin signaling. Reduction in β5 integrin levels may serve as a biomarker for FAK inhibitor effectiveness in ovarian cancer.

microRNAs in Mesothelial Cells Suppress Ovarian Cancer Dissemination

Sugiyama *et al.*_____Page 2081

Mesothelial cells are primary components of the tumor microenvironment for ovarian cancer cells. Sugiyama and colleagues found that TGFβ-stimulated mesothelial cells are able to promote the attachment and proliferation of ovarian cancer cells. Moreover, the expression of miR-200 family was downregulated in mesothelial cells after TGFβ stimulation, which subsequently promoted the expression of fibronectin that is essential for the attachment of ovarian cancer cells to the monolayer mesothelial cells. In contrast to that, miR-200–transfeced mesothelial cells inhibited the implantation and dissemination of ovarian cancer cells *in vivo*. This study indicates the potential therapeutic role of miR-200 in ovarian cancer.

Defining the Therapeutic Utility of the Mitotic Kinesin CENP-E

Kung and Martinez *et al.*___Page 2104

Due to the poor prognosis in triple-negative (primarily basal-like) breast cancer patients, there is an urgent need of new therapeutics for this disease. In this study, Kung, Martinez, and colleagues identified a therapeutically relevant role of the mitotic kinesin centromere protein E (CENP-E) in basal-like breast cancer through a complementary assembly of genomic and pharmacologic approaches. A new CENP-E motor inhibitor, PF-2771, was found to have dramatic antitumor outcomes *in vitro* and *in vivo*. These data suggest that CENP-E may be an effective therapeutic target for triple-negative/basal-a breast cancer patients.