



## Chemosensitivity study of colon cancer using PDSX model

Maekawa and Miyoshi *et al.* \_\_\_\_\_ Page 2187

Patient-derived xenograft (PDX) received much attention as a mouse model for chemosensitivity studies. However, its practical problems have also been highlighted recently (e.g., *Nature* 560:156-157, 2018). By transplanting cultured tumor-initiating cells (cancer stem cells) into nude mice, Maekawa, Miyoshi and colleagues show that some of such key problems can be overcome, and that the chemosensitivity in this PDSX (patient-derived spheroid xenograft) model precisely reflects the findings in a retrospective study with the colorectal cancer patients. These results suggest that PDSX could be an alternative model to PDX with improved efficiency that can help the development of personalized clinical service.

## Leelamine inhibits AR and CRPC

Singh *et al.* \_\_\_\_\_ Page 2079

Clinical management of castration-resistant prostate cancer (CRPC) resulting from androgen deprivation therapy remains challenging. CRPC is driven by aberrant activation of androgen receptor (AR) through different mechanisms, including expression of splice variants (e.g., AR-V7). Herein, Singh and colleagues present *in vitro* and *in vivo* evidence for therapeutic vulnerability of prostate cancer cells, including those that are resistant to enzalutamide, to a novel plant-based small molecule (leelamine).

## Antibody driven T cell immunotherapy of CRC

Wu *et al.* \_\_\_\_\_ Page 2164

Long term control of metastatic colorectal cancer (CRC) remains a major unmet medical need worldwide. In this article, Wu and colleagues report a novel tetravalent T cell engaging bispecific antibody (T-BsAb) called huA33-BsAb which targets CRC associated antigen GPA33. The *in vivo* subcutaneous and intraperitoneal xenograft models demonstrate that HuA33-BsAb drives circulating polyclonal T cells to infiltrate and to kill GPA33 positive colon and gastric cancer cells, including cancers with high risk genotypes. Using a novel affinity maturation system for BsAb, the authors found that picomolar anti-GPA33 affinity did not appreciably improve the antitumor properties of huA33-BsAb.

## CD44 facilitates EMT upon TKI resistance

Suda *et al.* \_\_\_\_\_ Page 2257

Epithelial to mesenchymal transition (EMT) is one of the mechanisms of acquired resistance to EGFR-TKIs in lung cancers with *EGFR* mutations. In this study, Suda and colleagues identified that high CD44 expression is correlated with mesenchymal phenotype in TKI-resistant cell lines and tumors. In addition, the authors found cell lines that often acquire resistance via EMT (HCC4006 and NCI-H1975 cells) have high CD44 expression prior to EGFR-TKI exposure. These findings suggest that CD44 is a useful biomarker to predict the emergence of EMT-mediated resistance to EGFR-TKIs and can be a therapeutic target to prevent EMT-mediated resistance.

# Molecular Cancer Therapeutics

## Highlights of This Issue

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