Clinical Cancer Research

Highlights

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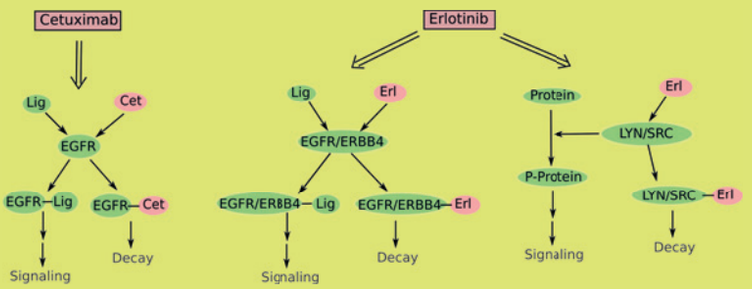
Selected Articles from This Issue



An Alternative for Patient-Derived Xenograft

Li *et al.* Page 2167

Preclinical evaluation of targeted therapies does not follow simple criteria and often heavily relies on the use of patient-derived xenograft (PDX), which present major disadvantages: potential failure of tumor transplantation, long waiting-time to response evaluation, and extensive laboratory cost. Alternative clinical decision-making tools, therefore, are needed. This study compares PDX-based treatment response of targeted therapies in lung cancer patients with the result of a specific *in silico* response prediction (ISRP) tool and provides evidence for a substantial agreement between an ISPR and PDX response prediction. The ISPR allows fast and cheap individual-targeted response prediction in parallel for several substances.

Heterogeneity of PD-L1

Mansfield *et al.* Page 2177

The heterogeneity of programmed cell death ligand 1 (PD-L1) expression may not be accurately represented by analysis of a single tumor. Mansfield and colleagues assessed the distribution of PD-L1 expression in paired, resected multifocal lung cancers and used mate pair next-generation sequencing to define the lineage relationship of these lesions. The expression of PD-L1 was heterogeneous among independent primary lung cancers, but there were high levels of agreement among related, intrapulmonary metastases. These data highlight that a single biopsy may not accurately capture PD-L1 expression status and emphasize the need for novel methods of patient selection for immunotherapy.

Tumor Microenvironment Immune Type in Pan-Cancer

Ock *et al.* Page 2261

PD-L1 status and tumor-infiltrating lymphocyte (TIL) recruitment have been suggested to be the most theoretical biomarker to predict the good responder of anti-PD-1/PD-L1 inhibitors. To prove this concept, Ock and colleagues analyzed the immunogenomic properties in The Cancer Genome Atlas (N = 9,677) according to the classification of tumor into four groups based on PD-L1 expression and TIL status, assessed by CD8A expression. Tumor microenvironment immune types (TMIT) I, high PD-L1, and CD8A expressions were significantly associated with a high number of somatic mutations as well as neoantigen, *PD-L1* amplification, and infection with Epstein-Barr virus or human papillomavirus.

PDE5 Enhances Breast Cancer Cell-Invasive Potential

Catalano *et al.* Page 2271

The increased expression of phosphodiesterase (PDE) 5 in various human malignancies, coupled with the success of PDE5 inhibitors in different diseases, has led to interest in investigating the role of this enzyme in cancer. Catalano and colleagues showed that PDE5 overexpression increased motile and invasive properties of breast cancer cells. In patients, PDE5 is differentially expressed according to molecular subtypes, with a positive correlation with tumor grading, and high levels predict a worse prognosis. This study holds promise for PDE5 as a valuable candidate with prognostic significance and an attractive target for future therapy in breast cancers.

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