



β III-Tubulin Mediates Brain Metastasis

Kanojia *et al.* _____ Page 1152

Breast cancer cells that metastasize to the brain overexpress genes predominantly expressed within neuronal tissues. In this study, Kanojia and colleagues demonstrate that a neuronal predominant marker, β III-tubulin, is overexpressed in both brain metastatic breast cancer cell models and human brain metastatic tissue. Knockdown of β III-tubulin decreased invasion, brain micrometastatic lesions, and improved survival in a mouse model of breast cancer brain metastases. These results establish β III-tubulin as a molecular marker of brain metastatic breast cancer as well as a bona fide target for therapeutic intervention of breast cancer brain metastases.

Efficient Intracellular Delivery of Tissue Factor Antibody-Drug Conjugates

de Goeij *et al.* _____ Page 1130

A better understanding of the target requirements is needed for optimal intracellular delivery of cytotoxic agents by antibody-drug conjugates (ADCs). de Goeij and colleagues compared the efficacy of ADCs targeting tissue factor (TF), HER2 and EGFR, with the target characteristics required for an ADC approach. Unlike HER2 and EGFR, TF was constitutively being internalized and degraded in tumor cells. When conjugated with the tubulin inhibitor duostatin-3, TF-ADC was relatively potent in reducing tumor growth compared with EGFR- and HER2-ADCs. It was found that the high turnover of TF on tumor cells might be the reason why this protein is specifically suitable for an ADC approach.

TSC2 Loss in Liver Cancer Predicts Everolimus Response

Huynh and Hao *et al.* _____ Page 1224

Everolimus (mTORC1 inhibitor) failed to show survival benefits in unselected hepatocellular carcinoma (HCC) patients (EVOLVE-1 clinical trial) and thus biomarkers predicting everolimus response in HCC are urgently needed. From a proteomic biomarker study, Huynh, Hao, and colleagues discovered the loss of TSC2 in HCC cell lines and xenograft models and demonstrated its predictive value for everolimus sensitivity. In addition, the authors found that a subset of EVOLVE-1 patients with TSC2-null/low tumors benefited from everolimus treatment. TSC2 loss was also enriched in Asian HBV⁺ HCC. These data indicate that TSC2 loss is a promising patient selection biomarker for the treatment of HCC patients with everolimus.

An Enhanced Newcastle Disease Virus for Melanoma Treatment

Cuadrado-Castano *et al.* _____ Page 1247

Newcastle disease virus (NDV) is a promising viral candidate for cancer therapy. Exploring new ways to improve its therapeutic potential, Cuadrado-Castano and colleagues developed the recombinant rNDV-B1/Fas virus, armed with the human tumor necrosis receptor Fas. Overexpression of Fas receptor upon rNDV-B1/Fas virus infection resulted in coactivation of both extrinsic and intrinsic apoptotic pathways leading to earlier and higher tumor cell cytotoxicity as compared to wild-type NDV virus infection. *In vivo*, rNDV-B1/Fas virotherapy promoted complete tumor remission in melanoma-bearing mice. Expression of proapoptotic factors during cancer virotherapy might be a general strategy to improve antitumor clinical responses.

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