



Prospective clinical sequencing of adult glioma

Zheng *et al.* _____ Page 991

Treatment of adult glioma has not changed for over a decade, and it remains unclear how to best translate insights from genomic studies to bedside. Zheng and colleagues tested the utility of panel sequencing for assisting in glioma diagnosis, prognosis prediction, and informing targeted therapy using a prospective cohort of 237 gliomas. The study showed that the platform can identify IDH mutations that align with disease histopathology and outcome, and had high specificity and modest sensitivity in predicting 1p/19q codeletion. It also enabled stratification of hypermutators. Three out of ten patients whose treatments were tailored based on this panel achieved exceptional responses.

Targeting copper transport in breast cancer

Karginova *et al.* _____ Page 873

Treatment of aggressive breast cancer remains challenging. Finding novel anti-cancer targets is critical for progress. In this study, Karginova and colleagues evaluate the efficacy and biological activity of the small molecule DCAC50, designed to inhibit intracellular copper transport through chaperones ATOX1 and CCS. DCAC50 triggers apoptosis in breast cancer cells and suppresses tumor angiogenesis in xenograft models. Co-treatment with paclitaxel enhances cytotoxicity in breast cancer cells. Mechanistically, DCAC50 disrupts copper homeostasis and generates oxidative stress. The ability of DCAC50 to induce apoptosis in cancer cells and suppress angiogenesis supports intracellular copper transport as a promising target for breast cancer therapy.

Next generation sequencing of tissue and circulating tumor DNA

Shatsky *et al.* _____ Page 1001

This study by Shatsky and colleagues compares and contrasts solid tumor tissue NGS and ctDNA NGS technology to assess for potentially actionable genomic alterations in advanced breast malignancies. Both technologies were found to be useful and potentially complementary in the discovery of actionable alterations. In addition, ctDNA was found to have prognostic significance, as patients with greater than or equal to 5% ctDNA had a poorer overall survival. Both types of NGS have potential value that may add to targeted treatment options and further our understanding of advanced breast cancer.

Preclinical investigation of ²¹²Pb-DOTAMTATE in neuroendocrine tumors

Stallons *et al.* _____ Page 1012

Peptide receptor radiotherapies with β -emitters are currently used to treat neuroendocrine tumors in patients. However, not all patients respond to treatment and most patients experience hematological toxicity. α -emitters, however, have a shorter pathlength and higher linear energy transfer allowing them to be more potent agents. This study by Stallons and colleagues examined ²¹²Pb-DOTAMTATE in a preclinical neuroendocrine model and was more effective at controlling tumor growth in a single dose efficacy than previously published data with a beta-emitting somatostatin analog with little hematological toxicity. These studies support the therapeutic potential and possible advantage of ²¹²Pb-DOTAMTATE and have led to the initiation of a phase I clinical trial.

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