Molecular Cancer Therapeutics

Highlights

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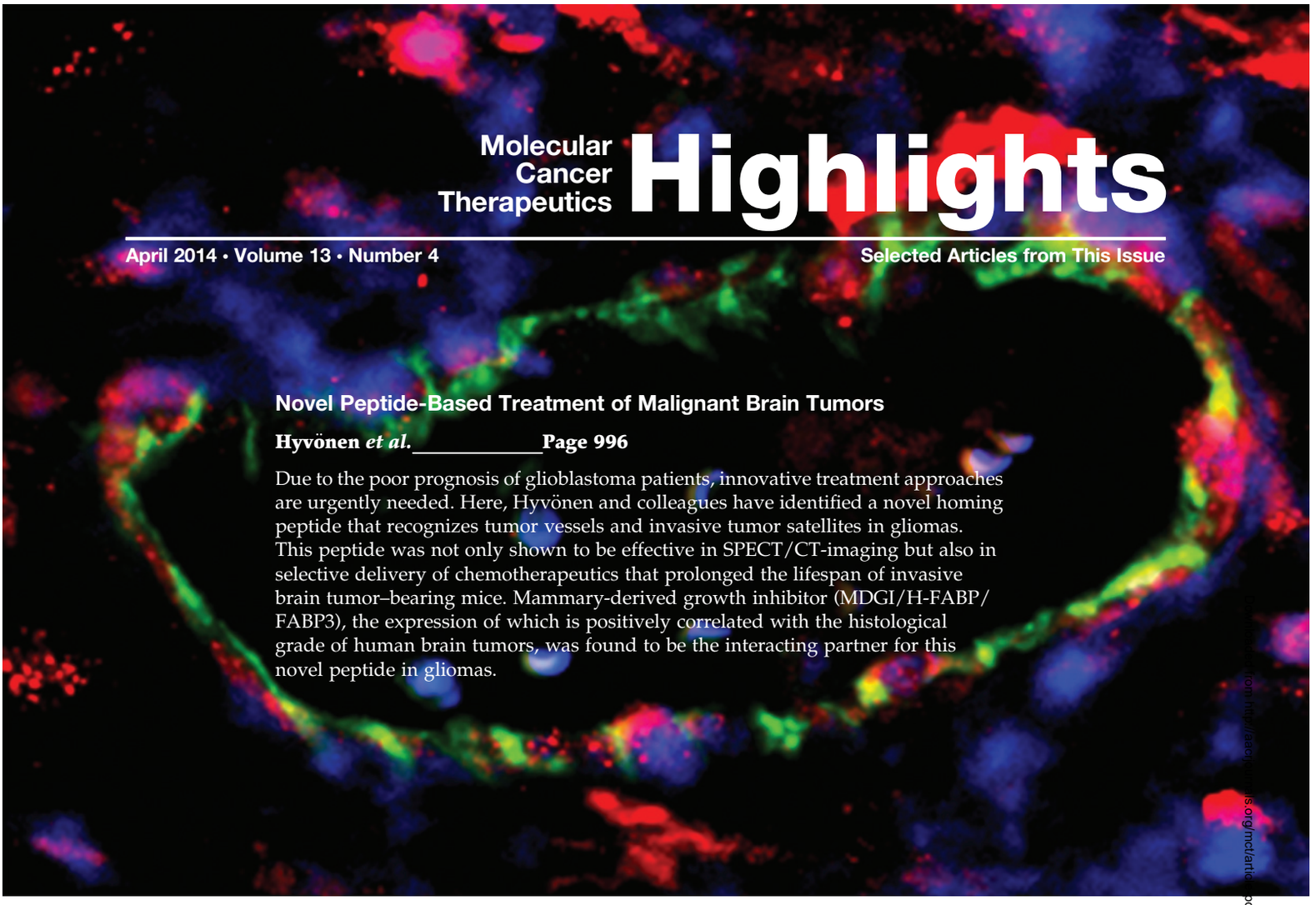
Selected Articles from This Issue



Novel Peptide-Based Treatment of Malignant Brain Tumors

Hyvönen *et al.*_____Page 996

Due to the poor prognosis of glioblastoma patients, innovative treatment approaches are urgently needed. Here, Hyvönen and colleagues have identified a novel homing peptide that recognizes tumor vessels and invasive tumor satellites in gliomas. This peptide was not only shown to be effective in SPECT/CT-imaging but also in selective delivery of chemotherapeutics that prolonged the lifespan of invasive brain tumor–bearing mice. Mammary-derived growth inhibitor (MDGI/H-FABP/FABP3), the expression of which is positively correlated with the histological grade of human brain tumors, was found to be the interacting partner for this novel peptide in gliomas.

Niclosamide Is Cytotoxic to BLBC Stem Cells

Londoño-Joshi and Arend *et al.*_____Page 800

The presence of cancer stem cells (CSC) contributes to the chemoresistance and relapse of basal-like breast cancers (BLBC). Niclosamide inhibits the Wnt/β-catenin pathway involved in CSC regulation. TRA-8 antibody, specific to TRAIL death receptor 5, is cytotoxic to BLBC cell lines and CSC. In this study, Londoño-Joshi, Arend and colleagues demonstrate that niclosamide in combination with TRA-8 reduced Wnt/β-catenin activity and produced increased cytotoxicity against BLBC cell lines, tumor xenografts, and patient-derived BLBC tumor cells. These results suggest that niclosamide or its analogs may be useful for the treatment of BLBC patients.

A Potent EZH2 Inhibitor Shows Efficacy in EZH2-Mutated Lymphoma

Knutson and Kawano *et al.*_____Page 842

Genetic alterations affecting the histone methyltransferase activity of EZH2 have been implicated as oncogenic drivers of a spectrum of human cancers; this includes heterozygous expression of point mutations, within EZH2, in a subset of non-Hodgkin lymphoma (NHL) patients. Knutson, Kawano and colleagues report detailed, preclinical characterization of a potent, selective, orally bioavailable EZH2 inhibitor, EPZ-6438 (also known as E7438), which is currently in phase I clinical testing. Twice daily oral administration of this compound to mice bearing human NHL xenografts, with different EZH2 mutations, resulted in profound and durable tumor regression, thus illustrating the potential clinical utility of this drug.

Single-Cell Pharmacokinetics of Poly ADP Ribose Polymerase (PARP) Inhibitors

Thurber *et al.*_____Page 986

The heterogeneous delivery of drugs in tumors has been a challenge for achieving effective treatment outcome. In the present study, Thurber and colleagues developed fluorescent PARP inhibitor olaparib drug conjugates that retain their target binding but are designed with different physiochemical and, thus, pharmacokinetic properties. The drug distribution in cell culture and tumor xenografts was followed with temporal resolution of seconds and subcellular spatial resolution. These measurements, including *in vivo* permeability of small molecule drugs, can be used directly in predictive pharmacokinetic models for the design of therapeutics and companion imaging agents.