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MOLECULAR CANCER THERAPEUTICS
HIGHLIGHTS

Selected Articles from This Issue

Discovery of OATD-02 – A Dual ARG1/2 Inhibitor

Borek *et al.* | Page 807

Arginase 1 (ARG1) and in recent years Arginase 2 (ARG2), have been described as attractive therapeutic targets in immuno-oncology giving rise to interest in drugs designed to address both novel targets. In this paper, Molecure discloses the structure, medicinal chemistry, broad characterization, and human PK predictions of OATD-02 – the first-in-class, orally bioavailable inhibitor which uniquely targets both intracellular ARG1 and ARG2. Additionally, the long drug-target residence time, moderate volume of distribution, and low clearance of OATD-02 may provide a novel drug against arginase-associated tumor immunosuppression and ARG2-dependent tumor cell growth which is currently being investigated in clinical trials.

Inhibiting Mesenchymal Tumors is Therapeutic for LAM and TS

Unachukwu *et al.* | Page 844

Tuberous Sclerosis (TSC) leads to neoplasms in multiple organ systems including the lung (Lymphangioleiomyomatosis) and kidney (Angiomyolipomas). Current therapies are tumoristatic with mortality remaining at 4–14%. Our group utilized the tyrosine kinase inhibitor, Imatinib, which inhibits the PDGF pathway, as a novel agent in the treatment of TSC. Imatinib reduced tumor cell survival by 30–70% in vitro and decreased volume of renal carcinomas by 45% in animal models through tumoricidal induction of apoptosis. By targeting the PDGF pathway we have identified a novel therapy in the treatment of patients with TSC and highlight the importance of neural crest signaling.

ATM Inhibition Boosts Antitumor Efficacy of ATR Inhibitors

Turchick *et al.* | Page 859

The DNA damage response offers multiple intervention points for cancer therapy and has become an attractive area for development of novel treatments. Here, Turchick and colleagues show that suppression of both the cell cycle checkpoint control and the DNA repair function of ATM kinase account for the synergistic enhancement of ATR kinase inhibition in cells. The ATR/ATM combination demonstrated superior efficacy in xenograft models and in a patient-derived triple negative breast cancer xenograft panel, suggesting a novel treatment strategy for cancer patients.

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