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In This Issue

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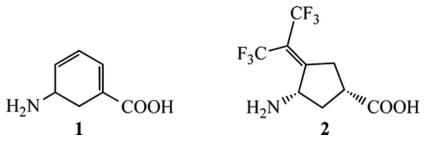
TARGETING OAT TO COMBAT LIVER CANCER

Cancer originating in the liver, also known as hepatocellular carcinoma (HCC), is the second leading cause of cancer death worldwide. Although there are a number of strategies aimed at treating HCC, including liver transplantation, radiofrequency ablation, and kinase inhibitor therapy, these efforts suffer from limited efficacy, and new targets for more effective HCC treatment are needed.

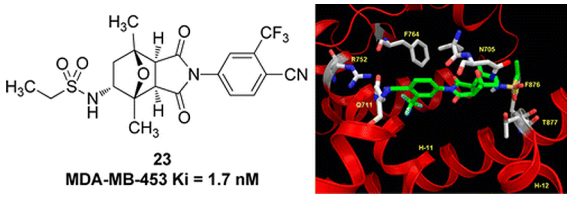
In this month's Featured Letter, Zigmond et al. (DOI: 10.1021/acsmedchemlett.5b00153) conduct DNA microarray analysis on samples from a spontaneous rodent model of HCC. The analysis suggests overexpression of the ornithine aminotransferase (OAT) gene as being an important marker for disease. The authors identify a selective inhibitor of OAT and demonstrate that selective inhibition of this gene not only reduces secretion of a known HCC biomarker both *in vitro* and *in vivo* but also suppresses tumor growth in HCC-harboring mice. Targeting OAT presents a promising new option for development of novel HCC therapy.



DEVELOPMENT OF A NEW ANDROGEN RECEPTOR ANTAGONIST

Prostate cancer is the most common form of cancer among men in the US. The current standard of care for advanced prostate cancer involves a combination of castration along with the administration of an antiandrogen therapeutic. Despite such aggressive attempts at androgen ablation, active signaling from the androgen receptor remains, and greater than 50% of patients develop castration resistant prostate cancer.

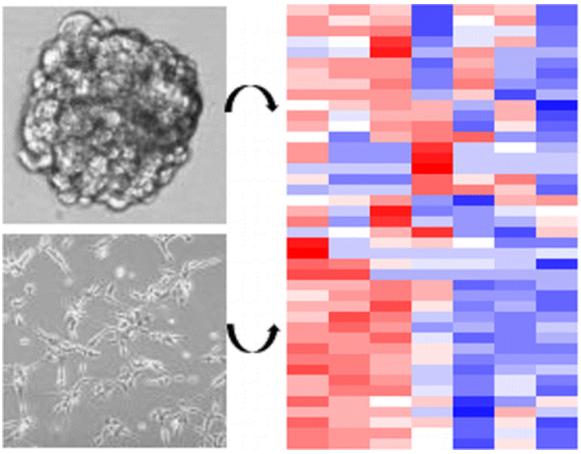
Here, Balog et al. (DOI: 10.1021/acsmedchemlett.5b00173) describe the discovery of a novel androgen receptor antagonist. The authors use molecular modeling and structure-based design to refine early lead molecules and ultimately identify a single compound as a clinical candidate that has progressed to Phase II clinical trials.



PERSONALIZING THE TREATMENT OF BRAIN CANCER

Precision medicine has recently emerged as a promising approach to disease treatment. Precision medicine caters therapy to the patient based on specific variables such as genetic differences. Given the potential for a large number of genetic variations, one challenge to the application of precision medicine is the requirement for screening a large number of compounds in order to identify a candidate drug that would be effective for a particular patient.

In this Technology Note, Quartararo et al. (DOI: 10.1021/acsmedchemlett.5b00128) investigate the potential of a patient-based approach for treatment of a deadly form of brain cancer, glioblastoma multiform. The authors develop a high-throughput screen using patient-derived cultures to test for potential glioblastoma therapeutics. The developed screen is highly adaptable and allows investigators to test both full dose–response curves and combinations of compounds for synergy, thus demonstrating promise for precision medicine in the treatment of glioblastoma.



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