15th International Congress on American Pathology and Oncology Research
&
International Conference on Microbial Genetics and Molecular Microbiology
December 03-04, 2018 | Chicago, USA

Elucidating the role of Hexokinase-2 in hepatocellular carcinoma and implications for cancer therapy

Dannielle DeWaal
University of Illinois-Chicago, USA

Hepatocarcinogenesis (HCC) induces profound glucose metabolism reprogramming by repressing endogenous glucokinase (GCK) and expressing the high-a nity hexokinase-2 (HK2). is quality di erentiates HCC from normal hepatocytes that can be exploited to selectively target HCC. Hepatic deletion of HK2 inhibits DEN-induced hepatocarcinogenesis. Silencing of HK2 in human HCC cell lines increases cell death and inhibits tumorigenicity in vitro and in vivo, that could not be restored by GCK nor a mitochondrial binding de cient mutant. Metabolically, HK2 loss reduces glycolytic ux to pyruvate and lactate, but TCA ux is maintained. Cells were vulnerable to serine depletion, consistent with their increase in serine uptake/glycine secretion, suggesting an increase in one-carbon metabolism. Decreased glycolysis was, however, coupled to increased respiration, that could be diminished by treatment with metformin, which increased cell death and inhibited tumor growth. Interestingly, neither HK2 silencing nor metformin treatment alone inhibits mTORC1, whereas the combination inhibits mTORC1 signaling that is dependent on REDD1 and not AMPK. Lastly, HK2 silencing synergizes with the FDA-approved therapeutic, sorafenib, to inhibit tumor growth.

Biography

Dannielle DeWaal completed her graduate studies at the University of Illinois-Chicago in the Department of Biochemistry and Molecular Genetics in the laboratory RI 'U 1LVVLP +D\ $V D FDQFHU ELRORJLVW VKH H[DPLQHG DQG HOXFLGDWHG WKH UROH RI +H[RNLQDVH WDUJHW 6KH FRQWLQXHV KHU VWXGLHV DW 8,& DQG LV FXUUHQWO\ D 3RVWGRFWRUDO 5HVHDUFK $VVR using a GC-MS, which she has been learning and teaching the lab about. She currently serves on the Editorial Board of International Journal of analytical and bioanalytical methods.

ddewaa2@uic.edu

Notes: