Ashkan Emadi, Metabolomics 2016, 6:2(Suppl)
http://dx.doi.org/10.4172/2153-0769.C1.031

Interference with glutamine metabolism: A novel approach for treatment of acute myeloid leukemia

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In contrast to normal cells, rapidly dividing leukemia cells reprogram their nutritional requirements to match an increased metabolic demand. The two main nutrient sources for growth and survival of cancer cells are glucose and glutamine. Depletion of glutamine or interruption of its cellular processes can be detrimental to leukemia cells but not normal cells. Asparaginases deplete amino acids asparagine and glutamine and are FDA-approved drugs for the treatment of acute lymphoblastic leukemia (ALL). The anti-leukemia effect of asparaginases in acute myeloid leukemia (AML) is not established. Here we describe the preclinical effect of different asparaginase products on the survival of AML cells with or without isocitrate dehydrogenase (IDH) mutations, which culminates in glutamine depletion resulting in disruption of protein synthesis downstream of mammalian target of rapamycin (mTOR) causing strong apoptotic and autophagic responses. The clinical experience with asparaginase in AML patients will also be discussed. Moreover, the cytotoxic effect of pharmacologic inhition of glutaminase, the enzyme that converts glutamine to ammonia and glutamate, will be reported in AML cells with different mutational status.

Biography

Ashkan Emadi received his MD at Tehran University of Medical Sciences and his PhD in Organic Chemistry at the Illinois Institute of Technology. He developed novel methodologies for the regiospecific synthesis of multiple naphthoquinone derivatives related to the natural product conocurvone, and was granted "Highest Standards of Academic Achievement Award". Following completion of his PhD, he completed his internship and residency in Internal Medicine at the University of Kentucky and the University of Cincinnati, respectively. Subsequently, he was trained in Hematology and Medical Oncology Fellowship Program at Johns Hopkins University Sidney Kimmel Comprehensive Cancer Center. He joined the University of Maryland Marlene and Stewart Greenebaum Cancer Center as an Associate Professor of Medicine, Pharmacology and Experimental Therapeutics at the University of Maryland School Of Medicine and serves as Director of the ACGME-accredited Hematology and Oncology Fellowship Program. He previously served as medical officer at the Division of Hematology Products (DHP), United States Food and Drug Administration (FDA), and as visiting scientist at Division of Adult Hematology, Department of Internal Medicine, School of Medicine, Johns Hopkins University. He has experience and in-depth understanding of the multiple aspects of cancer drug development including basic organic chemistry and molecular synthesis, *in vitro* and *in vivo* studies, and all phases of clinical trials as well as regulatory science.

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