Haibo Zhu, Endocrinol Metab Synd 2014, 3:2
http://dx.doi.org/10.4172/2161-1017.S1.005

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Endocrinology
October 20-22, 2014 DoubleTree by Hilton Hotel Chicago-North Shore, USA

A novel AMPK activator, IMM-H007, improves lipid metabolism disorders *in vitro* and *in vivo*

Haibo Zhu
Chinese Academy of Medical Sciences & Peking, China

Aims: Our overall objective was to investigate the effect of the adenosine derivative 2',3',5'-tri-O-acetyl-N6-(3-hydroxylaniline) adenosine (IMM-H007) on AMP-activated protein kinase (AMPK) activation and lipid metabolism and to also assess the underlying mechanisms involved in these processes.

Methods: HepG2 cells and hamsters fed a high-fat diet were used to test the effects of IMM-H007 on lipid metabolism. Western blots, chemical intervention, HPLC, SAMS peptide assay, 14C-labelled acetate and palmitate assays, molecular docking assay and siRNA targeting the AMPK γ1 subunit were used to investigate the effect of IMM-H007 on AMPK activation as well as the underlying mechanism involved in this activation.

Key findings: IMM-H007 treatment resulted in the dose-dependent activation of AMPK in HepG2 cells, increasing lipid oxidation and decreasing lipid biosynthesis. In hamsters that were fed a high-fat diet, IMM-H007 (2 mg/kg per day and above) reduced serum triglyceride (TAG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and hepatic cholesterol and triglyceride contents. Oil Red O staining of liver tissue also showed that IMM-H007 improved lipid accumulation. IMM-H007-induced AMPK activation was essentially abolished by treatment with compound C, and the addition of IMM-H007 did not alter the intracellular AMP:ATP ratio. In HeLa cells endogenously lacking LKB1, IMM-H007-mediated AMPK activation was not impaired, even following co-treatment with STO-609, a selective inhibitor of Ca2+/calmodulin-dependent protein kinase kinase (CaMKK). The results from the molecular docking assays and experiments targeting the AMPKγ1 subunit with siRNA indicated that IMM-H007 may activate AMPK by binding to and regulating the γ subunit of AMPK.

Significance: Our data indicate that IMM-H007 can regulate lipid metabolism through the activation of AMPK. IMM-H007 may activate AMPK by binding to and regulating the AMPK γ subunit.

Biography

Haibo Zhu is a professor of Cardio-Cerebral Vascular Pharmacology Lab, Dept. of Pharmacology, Institute of Materia Medica, Peking Union Medical College & Chinese Academy of Medical Science, Beijing, P. R. China. He is also a concorde Scholar, Outstanding Professor of Peking Union Medical College, a Standing Member of Cardiovascular Committee of Pharmacology of Chinese Pharmacological Society, and a member of British Pharmacological Society. His research interests are in identification of novel activators of AMPK for the treatment of dyslipidemia and atherosclerosis. For now he has published over 30 articles in his research field.

zhuhaibo@imm.ac.cn